



Consensus



Expert Consensus on Clinical Applications of Fecal Microbiota Transplantation for Chronic Liver Disease (2025 edition)

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Abstract

The gut microbiota is crucial in maintaining host health and liver function. Fecal microbiota transplantation (FMT) has shown promising potential in treating chronic liver diseases. To help clinicians quickly master and standardize the clinical application of FMT for chronic liver disease, the Liver Related Digestive Diseases Group of the Chinese Society of Hepatology of the Chinese Medical Association has developed the "Expert Consensus on the Clinical Application of FMT for Chronic Liver Disease." This consensus addresses the key aspects of FMT, including the indications, contraindications, efficacy, safety, donor selection, transplantation routes, precautions, and the prevention and management of adverse reactions for chronic liver conditions, such as chronic hepatitis, cirrhosis, and liver cancer, thereby offering reference and guidance to clinicians implementing FMT in the treatment of chronic liver disease.

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Introduction

The gut-liver axis has become a key focus of life sciences study in recent years, especially regarding the management

of chronic liver disease. Fecal microbiota transplantation (FMT), also known as intestinal microbiota transplantation, has attracted widespread attention as an emerging therapeutic modality. Chronic liver diseases encompass a wide range of pathological conditions, including chronic viral hepatitis, alcoholic liver disease (ALD), metabolic dysfunction-associated steatotic liver disease (MASLD), autoimmune liver disease (AILD), liver cirrhosis (LC), hepatic encephalopathy (HE), and liver cancer. A growing body of evidence supports the presence of gut microbiota dysbiosis in these chronic liver diseases. Studies have revealed that the diversity and composition of the gut microbiota play critical roles in the onset and progression of liver diseases. It has been proposed that restoring the balance of the gut microbiota, such as through FMT, could improve liver function, alleviate inflammatory responses, and enhance patients' quality of life. Indeed, multiple clinical studies have confirmed the therapeutic efficacy of FMT in treating various types of chronic liver diseases, including improving liver function, preventing HE, and increasing patient survival rates. However, the indications, contraindications, and standardized procedural protocols for FMT in chronic liver disease have not yet been fully elucidated. To help clinicians rapidly and comprehensively understand the key aspects of FMT in chronic liver disease management, the Chinese Society of Hepatology of the Chinese Medical Association convened a panel of experts from the fields of hepatology, gastroenterology, infectious diseases, and microbiology to jointly develop the "Expert Consensus on the Clinical Application of FMT in the Treatment of Chronic Liver Diseases." This consensus provides comprehensive guidance on the application of FMT in chronic liver disease management.

It should be emphasized that this expert consensus and its recommendations do not constitute mandatory standards. The recommendations are primarily based on the clinical studies available at the time of writing and accumulated practical experience. Therefore, the recommendations do not fully encompass or address all issues related to the diagnosis and treatment of chronic liver disease. Disease management should primarily be grounded in the treatment of the underlying etiology, guided by the fundamen-

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Table 1. Quality of evidence and strength of the recommendations

Level	Description
Quality of evidence	
High (A)	The credibility of the efficacy evaluation results is very high, and further research is unlikely to change the results
Moderate (B)	The credibility of the efficacy evaluation results may be affected by further research, and the results may be subject to change
Low or very low (C)	The credibility of the efficacy evaluation results is likely to be affected by further research, and there is a strong likelihood that the results will change
Strength of recommendation	
Strong (1)	Robustly demonstrates that the desirable effects of the intervention outweigh its undesirable effects or that the undesirable effects of the intervention outweigh its desirable effects
Weak (2)	The balance between desirable and undesirable effects is uncertain, or the availability of both high- and low-quality evidence indicates that the desirable and undesirable effects are comparable

tal principles outlined in this consensus, and tailored to the patient's specific condition while considering local medical resources and clinical practice experience. To improve the effectiveness and safety of FMT, interdisciplinary cooperation is important, and a multidisciplinary team should be established to participate jointly in patient diagnosis, treatment plan formulation, treatment process management, and postoperative follow-up. Patients should be given full information about what FMT entails and fully informed of the potential risks and benefits, as well as the source and legality of the donor feces, so that they can make informed decisions. Their written informed consent should be obtained before proceeding with FMT.

Following a rigorous expert selection process, an expert panel was convened to develop this consensus, which is endorsed by the Chinese Society of Hepatology. This consensus defines the target population (patients with chronic liver disease), intended users (clinicians), and primary objective (standardizing the application of FMT in chronic liver disease management). Eleven key clinical issues are outlined and addressed in the consensus document, and recommendations are provided for addressing each issue.

Relevant literature on FMT for chronic liver disease was collected through searches of PubMed, Web of Science, Cochrane Library, Embase, China National Knowledge Infrastructure, Wanfang Data, and VIP journal databases. Core English and Chinese search terms included "fecal microbiota transplantation," "chronic liver disease," "chronic hepatitis," "alcoholic liver disease," "metabolic dysfunction-associated steatotic liver disease," "autoimmune liver disease," "liver cirrhosis," "hepatic encephalopathy," and "hepatocellular carcinoma". The search covered the period from each database's inception to May 2025. Meta-analyses, randomized controlled trials, non-controlled studies, observational studies, cohort studies, case series, and case reports, as well as relevant consensus statements and guidelines, were included as references for the development of this document.

The development process followed the standard procedures and methodology recommended by authoritative academic organizations for the formulation of clinical guidelines and consensus statements. It was based on the Grading of Recommendations Assessment, Development, and Evaluation system and utilized both the Delphi method and the nominal group technique to assess the recommendations in terms of the quality of evidence supporting each recommendation and the strength of each recommendation (Table 1).¹ The quality of evidence was categorized as high (A), moder-

ate (B), or low/very low (C), while the strength of each recommendation was classified as strong (1) or weak (2). These gradings are provided in the recommendations for each of the 11 issues below.

Issue 1: Indications for FMT in the treatment of chronic liver disease

Recommendation: FMT is applicable to chronic liver diseases of various etiologies, excluding drug-induced liver injury, including chronic hepatitis B (CHB), ALD, MASLD, AILD, LC, HE, and liver cancer (to enhance sensitivity to antitumor therapy). (B1)

Explanation: Dysbiosis of the gut microbiota is closely associated with the onset and progression of chronic liver disease. Reduced microbial diversity, the depletion of specific beneficial bacterial taxa, and the overgrowth of pathogenic bacteria can exacerbate hepatic inflammation and accelerate fibrosis progression²; FMT not only has the potential to correct imbalances of the gut microbiota, but it can also modulate intestinal immune responses and metabolic pathways, thereby alleviating hepatic inflammation and fibrosis and ultimately improving liver function.^{3,4}

Viral hepatitis is a major cause of liver disease, particularly infection with the hepatitis B virus (HBV). The global burden of HBV infection remains high, especially in the Asia-Pacific region. According to data released by the Polaris Observatory Collaborators, in 2024, there were approximately 249.9 million individuals infected with HBV worldwide, of whom more than 165.5 million (66%) resided in the Asia-Pacific region. HBV infection can lead to the development of chronic liver disease, LC, and liver cancer.⁵ Studies have demonstrated that gut microbiota dysbiosis in patients with HBV infection is closely associated with their hepatic pathological status.⁶ Metabolites produced by intestinal microorganisms, such as short-chain fatty acids, influence hepatic immune responses and inflammatory processes and may exacerbate liver injury by modulating the function of hepatic immune cells.⁷ In several clinical trials, FMT has been applied in the treatment of patients with CHB, with significant improvements in liver function parameters observed following such treatment (including liver enzymes and bilirubin) and a reduction in the degree of liver fibrosis.⁸

ALD results from liver injury caused by prolonged and

excessive alcohol consumption. It encompasses a spectrum of conditions, including fatty liver, hepatitis, fibrosis, and LC.⁹ Severe alcoholic hepatitis (SAH) has an extremely poor survival rate, with a 28-day mortality rate of 13%–30%. The therapeutic options for alcoholic hepatitis (AH) are very limited. Prednisone is one option and may improve short-term survival in SAH; however, its efficacy remains unsatisfactory.¹⁰ Gut microbiota dysbiosis and increased intestinal mucosal permeability are among the most common triggers of AH. These abnormalities activate the immune system, thereby aggravating liver injury.¹¹ SAH patients often present with marked gut microbiota disturbances. Studies have shown that FMT can effectively alleviate ascites, reduce the incidence of HE, and prolong survival in SAH patients.¹²

MASLD, previously referred to as nonalcoholic fatty liver disease (NAFLD), is one of the most prevalent chronic liver diseases worldwide. Gut microbiota dysbiosis is considered one of its pathogenic mechanisms, with evidence showing that intestinal microbes and their metabolites influence hepatic lipid metabolism and inflammatory responses via the gut–liver axis.¹³ Both clinical and experimental studies have demonstrated that FMT can improve liver function and the metabolic parameters in MASLD patients and animal models, restore microbial homeostasis, and alleviate hepatic steatosis and inflammation.¹⁴

AILD encompasses a group of inflammatory liver disorders caused by immune dysregulation, primarily including autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis (PSC). Patients with AILD often exhibit gut microbiota dysbiosis, which is closely linked to hepatic inflammation. Changes in the gut microbiota composition and function may exacerbate AILD through modulation of hepatic immune responses via the gut–liver axis.¹⁵ Experimental studies have shown that FMT can attenuate liver injury in autoimmune hepatitis models, restore the gut microbial composition, and rebalance T-cell subsets, thereby reducing hepatic inflammation.¹⁶ Clinically, FMT has been applied in the treatment of various autoimmune diseases, such as PSC, with PSC patients showing improvements in liver biochemical parameters and bile acid profiles.¹⁷

LC is a chronic liver disease resulting from persistent hepatocellular injury and regeneration, leading to hepatic fibrosis and nodule formation. Patients with LC exhibit characteristic alterations in gut microbiota, such as an increased proportion of *Escherichia coli* and *Klebsiella* species, and a decreased proportion of *Lactobacillus* and *Bifidobacterium* species.⁸ These microbial changes are closely associated with hepatic inflammation, liver failure, and complications such as HE. Clinical studies have demonstrated that FMT can effectively correct gut microbiota dysbiosis in LC patients, has a favorable safety profile, and is associated with a lower recurrence rate of HE.¹⁸

HE is a neuropsychiatric syndrome secondary to hepatic dysfunction, with a pathogenesis primarily involving hyperammonemia and inflammatory responses. Gut microbiota can influence the synthesis and absorption of ammonia, leading to elevated systemic ammonia levels and exacerbating HE symptoms.¹⁹ FMT can restore the gut microbial balance and reduce intestinal ammonia absorption and synthesis, thereby lowering blood ammonia levels and decreasing the risk of HE.²⁰ It was reported that FMT not only improved cognitive function in patients with HE but also alleviated HE-related clinical symptoms.²¹ This effect was mediated through enhancement of intestinal barrier integrity and a reduction of endogenous toxin translocation, thereby improving hepatic function and overall disease prognosis.^{22,23}

The development of liver cancer involves complex interactions with the gut microbiota. Intestinal microorganisms can modulate host immunity, metabolism, and inflammatory status, and are closely associated with the progression of chronic liver diseases such as CHB and MASLD, which themselves are major risk factors for HCC.²⁴ It was suggested that pathogenic gut bacteria, such as *Klebsiella pneumoniae*, might promote HCC development via the gut–liver axis.²⁵ It has also been shown that FMT can modulate host immune responses and enhance antitumor immunity, thereby potentially exerting beneficial effects in liver cancer treatment.²⁶

For other etiologies of chronic liver disease, such as drug-induced liver injury and hereditary liver diseases, careful evaluation is required to determine the role of the gut microbiota, as well as the necessity and safety of FMT in these diseases. Clinical evidence supporting the application of FMT in these types of chronic liver disease is currently lacking. Thus, it is not recommended as a first-line approach. In addition, hepatic failure, as the terminal stage of chronic liver disease and potentially resulting from various etiologies, also lacks sufficient evidence from clinical studies to support the use of FMT as a therapeutic intervention.

Issue 2: Contraindications and contraindicated populations for FMT in the treatment of chronic liver disease

Recommendation: Contraindications to FMT include unstable vital signs, severe impairment of the intestinal barrier, severe immunosuppression, and pregnancy. (A1)

Explanation: Although still an emerging therapeutic modality, FMT has been widely applied in the management of various diseases, particularly recurrent *Clostridioides difficile* (*C. difficile*) infection and antibiotic-associated diarrhea. However, FMT is not suitable for all patients. Based on relevant national and international expert consensus statements,^{27–29} the following list outlines the contraindications and contraindicated populations for FMT in clinical practice that should be noted.

1. Unstable vital signs (temperature, heart rate, blood pressure, respiratory rate). Patients with concomitant unexplained infection or fever should undergo thorough evaluation to identify the infectious source; this is considered a relative contraindication.
2. Patients with severe intestinal barrier injury due to various causes, including sepsis, active gastrointestinal bleeding, or perforation.
3. Patients with fulminant colitis or toxic megacolon (excluding cases secondary to severe *C. difficile* infection).
4. Patients unable to tolerate enteral nutrition meeting $\geq 50\%$ of their caloric requirements due to severe diarrhea (relative contraindication if associated with *C. difficile* infection), significant fibrostenotic strictures, severe gastrointestinal bleeding, or high-output enteric fistula.
5. Patients with congenital or acquired immunodeficiency, or those with severe immunosuppression following recent high-risk immunosuppressive or cytotoxic therapy. Severe immunosuppression is defined as neutrophil count below the normal range (adults: $< 1,500$ cells/mm 3 , children: $< 1,000$ cells/mm 3) or CD4 $^+$ T-cell count < 200 cells/mm 3 .
6. Pregnant women.

Issue 3: Efficacy and safety of FMT in the treatment of chronic liver disease

Recommendation: In addition to standard treatment for the underlying disease, FMT may be used and is safe and effective for patients with CHB, AH, MASLD, PSC, LC, and HE. It may also be beneficial in enhancing tumor sensitivity to anticancer therapy in HCC. (B1)

Explanation: Clinical studies on the use of FMT in chronic liver diseases have been steadily increasing in recent years. For instance, Ren *et al.* conducted a study involving eighteen patients with HBeAg-positive CHB who remained HBeAg-positive despite receiving standard antiviral therapy for more than three years.³⁰ Among them, five patients underwent FMT, resulting in a significant reduction in HBeAg titers from baseline, with a progressive decline observed after each treatment. Notably, two patients achieved HBeAg clearance after a single FMT session, and one patient achieved clearance after two sessions. Chauhan *et al.* reported a 16.7% HBeAg clearance rate in their study's FMT group versus none in the antiviral-only group. These findings suggest that FMT may effectively promote the reduction and clearance of HBeAg in patients with CHB.³¹

For ALD, Philips *et al.* reported a case of steroid-nonresponsive SAH in which the patient received FMT, resulting in a marked improvement in clinical manifestations, biochemical parameters, and liver disease severity scores, along with a distinct shift in gut microbiota composition before and after the procedure.³² In another study, Philips *et al.* compared the outcomes of various treatment regimens (nutritional therapy, steroids, pentoxifylline, and FMT) in patients with SAH and found that FMT provided a greater survival benefit than the other approaches studied.³³ In a later study among patients receiving FMT, they found that the relative abundance of *Prevotella* was significantly reduced, whereas the abundance of *Bifidobacterium* was higher than in patients treated with steroids.³⁴

In a study on MASLD/NAFLD, He *et al.* divided patients with MASLD into an FMT group and a non-FMT group. Patients in the non-FMT group received oral probiotics, while those in the FMT group underwent three FMT procedures within three days.³⁵ All participants maintained a healthy diet and engaged in regular physical activity for more than 40 minutes daily. After one month of treatment, FMT was found to reduce liver fat attenuation by ameliorating gut microbiota dysbiosis, with a more pronounced effect compared with probiotic therapy. Other studies have also found that FMT can improve small intestinal permeability in patients with NAFLD.³⁶

Regarding AILD, Allegretti *et al.* investigated patients with PSC concomitant with inflammatory bowel disease and found that 30% of those who received FMT experienced a reduction in serum alkaline phosphatase levels by more than 50%.³⁷ In addition, Philips *et al.* reported a case of PSC with recurrent bacterial cholangitis. FMT markedly improved the patient's liver biochemical parameters, bile acids, and dysbiosis.³⁸ Furthermore, results from randomized controlled clinical trials have demonstrated that *Lactobacillus acidophilus* can improve cholestatic liver injury by inhibiting bile acid synthesis and promoting bile acid excretion,³⁹ suggesting a potential role for FMT in the treatment of PSC.

Regarding LC, Pringle *et al.* conducted a five-year prospective study showing that the oral administration of high-dose fecal microbiota capsules could help cure recurrent *C. difficile* infection in patients with advanced LC.⁴⁰ In a multi-

center study, Cheng *et al.* retrospectively analyzed 63 LC patients who underwent FMT for recurrent *C. difficile* infection and found that those treated with FMT had a lower incidence of serious adverse events and were less likely to develop infections.⁴¹

For treating HE, FMT was first applied in a patient with HE secondary to ethanol- and hepatitis C-related LC. After the first treatment, objective improvements were observed in reaction time, blood ammonia levels, and quality-of-life scores. These parameters continued to improve throughout the FMT treatment period but returned to baseline within seven weeks after discontinuation.⁴² Bajaj *et al.* found that FMT improved cognition and reduced the frequency of HE episodes,⁴³ and also decreased serum levels of interleukin-6 and lipopolysaccharide-binding protein.⁴⁴ In another study involving LC patients with recurrent HE, FMT improved cognitive function, reduced recurrence rates, and lowered rehospitalization rates.⁴⁵

Liver cancer is associated with end-stage liver diseases, including viral hepatitis, ALD, and MASLD. The application of FMT in the treatment of liver cancer has been primarily investigated as an intervention for certain precursor conditions of liver cancer. It has been reported that the composition of the gut microbiota is closely related to the response of liver cancer patients to immune checkpoint inhibitors, and specific microbial taxa may serve as biomarkers for predicting the efficacy of such therapies.⁴⁶ In clinical studies, FMT has shown potential therapeutic benefits in some liver cancer patients. When combined with immunotherapy, FMT may help enhance immune responses and improve treatment effectiveness.⁴⁷

Overall, according to existing research and reports, combining FMT with basic treatment for the primary disease is an effective approach for treating patients with CHB, AH, MASLD, PSC, LC, and HE. Increasing sensitivity to antitumor treatment for liver cancer may also be beneficial. FMT is relatively safe, with only short-term adverse reactions likely to occur, such as diarrhea, abdominal pain, and fever, which are generally mild and self-limiting. Indeed, a 2019 report from the U.S. Food and Drug Administration found only two serious adverse events related to FMT, which occurred due to the transmission of extended-spectrum β -lactamase-producing *Escherichia coli* from unscreened donors, one of which resulted in death.⁴⁸ Furthermore, in the context of the global COVID-19 pandemic, it was suggested that donor screening for SARS-CoV-2 should also be implemented.⁴⁹ For patients with chronic liver disease, special attention must be given to the safety of FMT. Donor selection should strictly adhere to established standards, with regular blood and stool testing, and comprehensive screening performed for multidrug-resistant organisms and potential pathogens.

Issue 4: How to select an appropriate fecal microbiota donor

Recommendation: Standard non-related donors should be prioritized for FMT, with mandatory comprehensive screening performed, including health history, psychological evaluation, and laboratory tests. (B2)

Explanation: While both standard non-related donors and related donors are acceptable for FMT, priority should be given to standard non-related donors when available.⁵⁰⁻⁵² Screening should encompass health information and history, physiological conditions, psychological status, laboratory testing, and imaging examinations.^{28,53}

Effective screening should cover the following:

- General information:
 1. Medical history: No gastrointestinal discomfort within the past two weeks; no use of antibiotics, acid suppressants, immunosuppressants, chemotherapeutic agents, or history of blood transfusion within the past three months; no chronic pain symptoms; no history of gastrointestinal surgery; no history of infectious diseases or contact with infectious disease cases; no allergic diseases, autoimmune diseases, metabolic disorders, cardiovascular or cerebrovascular diseases, neurological or psychiatric disorders; and no history of malignancy.
 2. Personal history: Regular lifestyle and healthy diet; no high-risk sexual behavior; no smoking, alcohol consumption, or illicit drug use; no drug dependence; no tattoos or severe skin injuries within the past six months; no travel or residence in tropical or epidemic areas within the past six months.
 3. Family history: No family history of gastrointestinal disorders, malignancy, or infectious diseases.
 4. Other: Not pregnant and not in the menstrual period.
- Psychological assessment: Mainly conducted through interviews and standardized questionnaires:
 1. Psychiatrist or psychological counselor interview confirming good psychological status.
 2. Scores within the normal range for the Self-Rating Scale of Mental Health, Self-Rating Depression Scale, Self-Rating Anxiety Scale, and Pittsburgh Sleep Quality Index.
- Laboratory tests:
 1. Hematology: Complete blood count, biochemical profile, liver and renal function, electrolytes, and C-reactive protein within normal ranges; negative for hepatitis viruses, human immunodeficiency virus, syphilis, Epstein–Barr virus, cytomegalovirus, nematodes, *Entamoeba histolytica*, and other pathogens.
 2. Stool tests: Normal routine stool examination; negative fecal occult blood test; negative for intestinal pathogens, including *C. difficile*, *Campylobacter*, *Salmonella*, *Shigella*, pathogenic *Vibrio*, and toxicogenic *Escherichia coli*; negative for helminth eggs, cysts, parasites, *Entamoeba*, spores, and other intestinal pathogens; negative for norovirus, rotavirus, and SARS-CoV-2; negative for multidrug-resistant organisms (Gram-negative bacilli, including extended-spectrum β-lactamase-producing *Enterobacteriaceae*, carbapenem-resistant *Enterobacteriaceae*, carbapenemase-producing *Enterobacteriaceae*; Gram-positive cocci, including vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus*). In addition, it is recommended that high-throughput sequencing be performed, such as 16S rRNA gene sequencing or metagenomic sequencing, depending on the institution's testing capabilities.
 3. Other tests: Urinalysis, chest radiography, electrocardiography, abdominal ultrasonography, urea breath test for *Helicobacter pylori*, and gastrointestinal endoscopy (optional for children under 14 years old) showing no significant abnormalities.

Issue 5: Donor management (daily management and dietary management)

Recommendation: FMT donors should undergo appropriate management to maintain the stability and sustainability of the donations, including regular health re-evaluations and the retention of stool sample test-

ing. Donors are advised to donate stools regularly, maintain a healthy diet, avoid high-fat, high-protein, and irritant foods, and are encouraged to adopt a varied diet and engage in moderate physical activity. (C2)

Explanation: FMT donors should be appropriately managed to ensure the stability and sustainability of donations. Given that donors' dietary habits can affect the characteristics and microbial composition of FMT products, dietary advice should be provided as appropriate and necessary. All donors should sign an informed consent form before donating feces. Daily management: (1) All screening evaluations should be repeated every six to twelve months to confirm continued eligibility (colonoscopy may be extended to every three years); (2) A sample from each stool donation should be retained for 16S rRNA gene sequencing or metagenomic sequencing (depending on the institutional testing capacity) to ensure the stability and diversity of the microbiota composition; (3) A sample from each stool donation should also be retained for metabolomic analysis (depending on the institutional testing capacity); (4) Donors should commit to long-term stool donation (at least six months), with a recommended frequency of once or twice per week, each time with stool samples weighing no less than 100 g. Once accepted as a donor, regular follow-up and health management should be conducted to ensure up-to-date information is maintained and available on the donor's health status. Weekly contact should be maintained to confirm any recent health conditions, and donors should be instructed to promptly report any physical discomfort. Donors in suboptimal health should undergo re-evaluation or be excluded based on the screening criteria. If a donor needs to leave their current location for an extended period, they should report in advance, with targeted measures taken as needed. Dietary recommendations: (1) Avoid animal-based foods, prioritize plant-based foods, particularly those rich in soluble dietary fiber; (2) Maintain a healthy and fresh diet, avoid unclean or spoiled food, abstain from snacks, minimize eating out, and avoid unfamiliar foods not previously consumed; (3) Avoid high-protein diets and limit the intake of seafood or other allergenic foods; (4) Avoid high-fat diets and limit the consumption of fatty meats, animal offal, and high-fat nuts; (5) Avoid the excessive intake of irritant foods and seasonings, such as chili, curry, ginger, onion, garlic, Sichuan peppercorn, and black pepper; (6) Avoid iron-rich or deeply pigmented foods, such as animal blood, pig liver, black fungus, kelp, seaweed, black sesame, tomatoes, chocolate, cocoa, cherries, mulberries, and foods containing artificial colorants, including certain cookies, candies, and beverages; (7) Avoid hard-to-digest foods, such as overly tough meat with tendons, unprocessed soy products, fried foods, glutinous rice, and its derivatives; (8) Increase dietary diversity, with a light and low-salt approach, particularly increasing the intake of grains, legumes, fruits, and vegetables rich in dietary fiber, such as oats, barley, peas, broad beans, lemons, citrus fruits, apples, pineapples, bananas, cabbage, and alfalfa; and (9) Undertake appropriate physical activity, ensuring a balance between food intake and energy expenditure.

Issue 6: How to select an appropriate route for transplantation

Recommendation: FMT can be applied via different routes, including the upper gastrointestinal tract (oral

fecal microbiota capsules), mid-gastrointestinal tract (gastroscopy, nasoduodenal/nasojejunal tube), and lower gastrointestinal tract (colonoscopy, endoscopic colonic transendoscopic enteral tubing, enema). The most appropriate transplantation route should be determined through a comprehensive evaluation, with patients fully informed of the associated risks, and patient tolerance closely monitored during the procedure. (B1)

Explanation: FMT delivery routes can be categorized into upper gastrointestinal routes, mid-gastrointestinal routes, and lower gastrointestinal routes. Upper gastrointestinal routes primarily involve the intake of oral fecal microbiota capsules; mid-gastrointestinal routes include gastroscopy and nasoduodenal/nasojejunal tube placement; and lower gastrointestinal routes include colonoscopy, colonic transendoscopic enteral tubing, sigmoidoscopy/rectoscopy, and transanal retention/high-volume enemas. For chronic liver disease patients with a reduced tolerance for colonoscopy or a poor appetite, the optimal FMT route should be determined through comprehensive evaluation by an FMT multidisciplinary team in accordance with the appropriate clinical guidelines and operational standards. The procedure should only be performed after obtaining informed consent with the full disclosure of potential complications and adverse effects. Pretreatment preparation should be tailored based on individual patients' characteristics and disease type. For the upper and mid-gastrointestinal routes, proton pump inhibitors or prokinetic agents may be administered as needed. For the lower gastrointestinal route, bowel preparation should be performed when indicated. During the procedure, the patient's tolerance must be closely monitored, and any adverse reactions should be promptly managed.

Relative indications for each major FMT route: (1) Oral fecal microbiota preparations: Suitable for patients with normal swallowing function who are unsuitable for or refuse hospitalization. (2) Gastroscopy/colonoscopy: Mainly used for single-session transplantation. (3) Nasoduodenal/nasojejunal tube or colonic transendoscopic enteral tubing: Suitable for multiple repeated transplants. (4) Enema: Suitable for multiple repeated transplants, especially when lesions are localized to the rectum/sigmoid colon. In decompensated liver cirrhosis patients with reduced endoscopic tolerance, enema and oral fecal microbiota capsules are the most preferable choices.²⁸

Issue 7: Pre-transplant preparation

Recommendation: Antibiotic use should be avoided whenever possible, as it could negatively impact the overall success rate of FMT. Specifically, while antibiotics could enhance the engraftment of certain bacterial species, overall microbiota restoration and diversity could be compromised. (B2)

Explanation: The relationship between antibiotic use and the success rate of FMT is complex. Studies have shown that antibiotic pretreatment does not significantly improve overall engraftment rates and may even hinder the establishment of specific bacterial communities.⁵⁴ It has been reported that while antibiotic pretreatment may increase the engraftment of certain bacteria, such as *Bifidobacterium*, the overall similarity between the recipient's post-transplant microbiota and that of the donor was not significantly increased.⁵⁵ Further-

more, antibiotic use can lead to incomplete microbiota recovery after FMT, potentially affecting the clinical outcome.⁵⁶ Although FMT has demonstrated good efficacy in treating recurrent *C. difficile* infection, prior antibiotic use may reduce its therapeutic effect, especially regarding the restoration of microbial diversity.⁵⁷

In addition, the assessment of gastrointestinal motility before FMT is important for determining the optimal delivery route, as well as the volume and form of the fecal material to be transplanted. Pre-transplant bowel preparation is recommended to clear the bowel, remove retained stools, and residual antibiotics, thereby improving contact between the transplanted microbiota and the intestinal mucosa and facilitating engraftment.^{58,59}

Issue 8: Determination of the transplantation dose, frequency, and form

Recommendation: Higher doses and more frequent administrations can effectively restore the balance of the intestinal microbiota, reduce recurrence rates, and decrease the need for endoscopic transplantation. Additionally, the use of fresh fecal samples yields better outcomes than other approaches. The dose and frequency of FMT should be flexibly adjusted according to the patient's response. (B2)

Explanation: A study on recurrent *C. difficile* infection found a positive correlation between the FMT dose and clinical efficacy, with higher doses more effectively restoring the intestinal microbiota balance and thereby reducing the recurrence rate. However, the frequency of FMT needs to be adjusted for different disease conditions. For example, in the treatment of antibiotic-associated diarrhea, it was reported that multiple FMT sessions could significantly improve cure rates.⁶⁰ Several clinical studies on FMT for recurrent *C. difficile* infection have shown that endoscopic delivery has a higher success rate than enema or oral capsule administration, and fresh fecal samples are more effective than frozen samples.⁶¹ Also, higher doses (total fecal mass > 275 g) were found to be associated with greater clinical symptom relief.⁶² Currently, there are no studies that define the optimal FMT dose for patients with chronic liver disease, with only a study protocol reported for HE.⁶³ Therefore, decisions regarding repeated FMT should be based on the patient's initial treatment response and subsequent follow-up to determine whether multiple administrations are beneficial for microbiota engraftment and ensuring a sustained response.

Issue 9: Follow-up principles for FMT

Recommendation: A combination of short-term follow-up (within 24 h to observe tolerance) and long-term follow-up (evaluation of the patient's symptoms and relevant test results at four weeks) should be adopted to comprehensively assess the efficacy of the FMT treatment. Donor selection should be reconsidered, or repeat FMT performed if necessary. Follow-up should last at least eight weeks. (B1)

Explanation: Studies have shown that after the first FMT treatment, the median duration of clinical efficacy is 125 days, while after the second treatment, the median duration is 176.5 days.⁶⁴ Therefore, adopting both short- and long-

term follow-up after FMT is recommended to fully evaluate its therapeutic effect.

Short-term follow-up: The patient's tolerance should be closely monitored within 24 h after each infusion of the bacterial suspension. If an adverse reaction occurs, this should be promptly managed and reported.

Long-term follow-up: Within four weeks after the completion of the first treatment course, patients should undergo symptom assessment, and gut microbiota analysis may be performed if necessary. The follow-up and efficacy evaluation indicators for diseases treated with FMT should mainly follow the treatment guidelines for the primary disease. If there is no improvement three weeks after the first course of FMT, a donor change may be attempted, followed by another course of FMT. If this is effective, treatment may then continue; if this is still ineffective, the patient should be considered a non-responder to FMT, and further FMT should be avoided to prevent delays in alternative treatment. If the patient's symptoms improve significantly after FMT, multiple repeated treatments may be considered. The follow-up endpoint should be at least eight weeks after the final FMT, and, if feasible, long-term follow-up for over one year is recommended.

Issue 10: Potential adverse reactions of FMT, and principles for their prevention and management

Recommendation: The most common adverse reactions to FMT are mild gastrointestinal responses, most of which are self-limiting. Strict donor screening and thorough assessment of the patient's health status can reduce the risk of adverse reactions. In addition, dietary advice should be provided, and patients should be fully informed of the risk of potential adverse reactions to enhance treatment compliance. (B1)

Explanation: Adverse reactions to FMT can be categorized as mild (e.g., abdominal discomfort, diarrhea, abdominal distension, nausea), moderate (e.g., fever), and severe (e.g., severe infection). Within 24 to 48 h after FMT, the main adverse reactions may be gastrointestinal symptoms, such as diarrhea, abdominal discomfort, abdominal distension, and nausea. These symptoms are generally mild and self-limiting, and may be associated with immune stress responses induced by FMT or with the primary disease itself. In patients with chronic liver disease, it is particularly important to distinguish between symptoms caused by the primary disease and those related to FMT. A meta-analysis that included FMT-related data from 4,241 patients in 129 studies reported that 19% of cases experienced adverse reactions associated with FMT.⁶⁵ The most common were diarrhea (10%) and abdominal discomfort/pain/cramping (7%). Notably, the incidence of severe adverse reactions was 1.4%, including infections and deaths, with 0.99% microbiologically related. Among the five reported FMT-related deaths, four occurred in patients who underwent the procedure via the upper gastrointestinal route, and all the reported severe adverse reactions occurred in patients with mucosal barrier injury. This highlights the need for special attention to safety in these high-risk patients when performing FMT.

To reduce the incidence of adverse reactions, rigorous donor screening to ensure the absence of pathogenic microorganisms is essential. Patients should undergo a comprehensive clinical evaluation before FMT to confirm the absence of other underlying diseases or risks. Dietary and lifestyle modifications tailored to the primary disease may also help

reduce the occurrence and extent of adverse reactions. For mild adverse reactions, clinicians may advise dietary adjustments and appropriate symptomatic medications. In cases of fever, close monitoring of the body temperature and relevant laboratory tests should be conducted to exclude infection and other complications. Moreover, patient education (the principle of FMT, its efficacy, safety, possible adverse reactions, postoperative precautions, etc.) and informed consent are crucial. Given that FMT is a relatively novel technique, patients may have concerns and uncertainties. Therefore, clinicians should explain in detail the potential adverse reactions and their management strategies in order to improve patient knowledge, engagement, and adherence.

Issue 11: Precautions for FMT in special populations with chronic liver disease (children, pregnant women)

Recommendation: For special populations with chronic liver disease, such as children and pregnant women, the application of FMT should be approached with caution, and careful evaluation is required to ensure safety. There have been no reports yet of FMT in children with chronic liver disease, while FMT is not recommended for pregnant women. In dealing with these special populations, physician-patient trust, informed consent, and transparent communication are essential. (C2)

Explanation: Special caution should be exercised when performing FMT in special populations, such as children and pregnant women. Due to their unique physiological characteristics and immune status, FMT in children and pregnant women faces unique challenges and potential risks. In recent years, an increasing number of clinical trials and case reports have shown that FMT has good efficacy in the treatment of refractory diarrhea in children. FMT has also been explored for the treatment of autism spectrum disorder in children, with preliminary results indicating both its efficacy and safety; however, the necessity of implementation should still be fully evaluated.⁶⁶ For pregnant women, at the time of writing this consensus, only a single report of a pregnant woman with recurrent *C. difficile* infection receiving FMT could be found, which suggested the possibility of intergenerational transfer.⁶⁷ Therefore, the implementation of FMT in pregnant women requires careful consideration and balancing the benefits and risks. Notably, current expert consensus does not recommend performing FMT in pregnant women. For children or pregnant women with chronic liver disease, a multidisciplinary medical team, which should include a pediatrician, gynecologist, and obstetrician, should comprehensively assess the necessity, safety, and potential risks of performing FMT. In addition, when dealing with special populations, particular attention should be paid to building physician-patient trust, the provision of thorough informed consent, and maintaining transparent communication regarding the expected therapeutic effects and potential risks, all of which are key to the successful implementation of FMT.

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Conflict of interest

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Author contributions

All authors contributed to the study conception, design and draft. All authors have read and approved the final version and publication of the manuscript.

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