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REVIEW OPEN ACCESS

The Feasibility of Using Fecal Microbiota Transplantation as a Treatment for Mental Health Conditions Among IBS/IBD Patients: A Literature Review

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Abstract

Introduction: The gut-brain axis has emerged as a crucial research area, emphasizing the intricate relationship between gastrointestinal health and mental well-being. Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD) are gastrointestinal disorders that not only affect digestive function but also frequently co-occur with psychiatric conditions, such as anxiety and depression. Research suggests that the gut microbiome may be a key factor in this gut-brain connection, with specific microbiota influencing brain function and behaviour via neurotransmitter production and inflammation modulation. Fecal matter transplantation (FMT), the transfer of healthy gut microbiota to treat gastrointestinal conditions by restoring healthy microbes, has shown promise for addressing comorbid psychological symptoms. This review evaluates the evidence on using FMTs as a potential concurrent treatment of both psychological comorbidities and gastrointestinal symptoms among IBS and IBD patients.

Methods: A review of the current literature was performed by searching for keywords using scientific electronic databases. Keywords used to search for articles included "fecal microbiota transplantation," "FMT", "comorbidity", "gut-brain axis," "mental health," "depression," "anxiety," "irritable bowel syndrome," "inflammatory bowel disease," and "gut dysbiosis". Articles were screened and selected based on quality and relevance.

Results: Animal IBS models demonstrate a significant effect of FMT for initiating and treating psychological symptoms. Similarly, clinical trials have proven FMT to alleviate psychological symptoms among IBS patients by restoring healthy microbiota, but long-term effects require further investigation. Preclinical IBD animal studies support a causal relationship between gut microbiota, inflammation, and symptoms of anxiety, depression. Clinical evidence further supports FMT for IBD mental health comorbidities, suggesting that gut alterations offer relief from symptoms.

Discussion: Results support the therapeutic potential of FMT in improving gastrointestinal and psychological symptoms among IBS and IBD patients. These conclusions remain preliminary due to a lack of homogeneity across studies, particularly in donor selection, administration route, and outcome measures, which limits the overall generalizability of results. Future research should address heterogeneous methodology to standardize protocols, as well as include larger and more diverse samples to inform clinical implementation.

Conclusion: This review suggests that FMT may be a potential treatment for both gastrointestinal and psychological symptoms.

Keywords: fecal microbiota transplantation; inflammatory bowel disease; irritable bowel syndrome; gut-brain-axis; anxiety; generalized anxiety disorder; depression; major depressive disorder; psychological comorbidities; gut microbiome

Introduction

Introduction to the Gut-Brain Axis (GBA)

In recent years, the relationship between the gut microbiome and the brain has received significant attention with respect to understanding the link between gastrointestinal (GI) disorders and mental health (MH) conditions. The gut-brain axis (GBA), the bidirectional communication network linking the enteric (ENS) and central nervous systems (CNS) through neural, hormonal, and immunological pathways, plays a central role in modulating GI function and the emotional and cognitive processes of the brain [1]. This complex gut-brain connection has emerged as a critical research area, particularly in understanding Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD), where microbiota disruptions likely contribute to GI symptoms and psychological comorbidities [2, 3].

The Gut-Brain Connection in IBS and IBD

IBD refers to a group of GI disorders that involve the inflammation and swelling of the GI tract, characterized by abdominal pain, interrupted bowel

movements (i.e., diarrhea, constipation, vomiting) and bloody stool [4]. IBS is a chronic functional GI disorder that shares many symptoms of IBD (i.e., abdominal pain, irregular bowel movements) but lacks an identifiable underlying cause, such as inflammation [5]. IBS and IBD exert significant socioeconomic burden on healthcare systems, and the individuals who live with them, particularly when psychological comorbidities are present [6-8], thus calling for effective interventions and systemic changes to care. Although the etiologies of both conditions are poorly understood, stress, MH disorders, infections, food intolerances, and microbial dysbiosis contribute to IBS, whereas IBD is an immune-mediated inflammatory disease likely driven by genetic and environmental factors [9, 10]. Numerous gaps remain in comprehending both conditions; however, the gut-brain connection has emerged as a valuable framework for elucidating symptom onset, severity, and treatment.

GBA disruptions are particularly pertinent among individuals with IBS and IBD, who experience disproportionately higher rates of anxiety and depression [11, 12]. Up to 60% of IBS patients, and twice as many IBD patients compared to the general population, experience anxiety and depression, often exacerbating physical symptoms and complicating treatment [13, 14]. Longitudinal human studies indicate that individuals with anxiety and/or depression without GI symptoms present at baseline will likely develop GI symptoms if psychological symptoms persist and vice versa [15]. Further, symptom severity in one domain (i.e., MH or GI) predicts corresponding outcomes in the other [11], and genetic studies suggest a shared susceptibility and pathophysiology between GI and psychological conditions, including anxiety and depression [16].

Clinical and experimental research indicates that gut microbiota modifications not only influence the GI system, but also directly affect the CNS through neuroendocrine and metabolic pathways. Consequently, modifications to gut microbial composition have emerged as a potential treatment for MH symptoms, with specific microbiota influencing brain function and behaviour via neurotransmitter production and inflammation modulation [17]. Among individuals with IBS and IBD, treating psychological symptoms ameliorate GI symptoms and vice versa, emphasizing the GBA's bidirectional link [17]. Furthermore, emerging evidence suggests that multidisciplinary treatment that addresses both domains concurrently is best practice for IBS and IBD patients [11, 18].

There are several limitations to current treatment options for IBS and IBD. First, the uncertain pathophysiology of both conditions is compounded by variations in symptom presentation, rendering universal treatments insufficient. Thus, patients face difficulties in diagnosis and treatment due to inadequate etiological understanding and diagnostic tools for these conditions [19]. Additionally, patients and healthcare providers report dissatisfaction with the treatment options and outcomes for IBS and IBD [20]. Current treatments focus on GI symptom relief (i.e., stool softeners, fibre supplements, prescription medications), which may overlook dysbiosis and the GBA's psychological components. Selective Serotonin Reuptake Inhibitors (SSRIs) are occasionally prescribed to address neurotransmitters that modulate gut motility, visceral hypersensitivity, and GI transit speed, while demonstrating anti-inflammatory properties to regulate immunological pathways [21]. However, studies report impactful adverse events (AE) and uncertainty of the long-term treatment effects of SSRIs, highlighting the demand for diverse and integrated IBS/IBD treatments, particularly for those with comorbid psychological symptoms [21, 22].

Fecal Microbiota Transplants (FMTs) as an Intervention for IBS/IBD and Psychological Symptoms

Fecal microbiota transplants (FMTs) are a promising intervention for restoring microbial balance in IBS/IBD patients. FMTs involve the transfer of healthy fecal matter containing beneficial bacteria into the patient's GI tract via endoscopy, enema, and oral capsules. Randomized clinical trials have demonstrated that FMTs are effective methods to improve GI symptoms for IBS/IBD patients.

In addition to treating GI symptoms, FMTs have proven to address psychological symptoms. FMTs modulate the GBA by restoring healthy microbes, which influence microbiome-regulated connections to the CNS through several mechanisms, such as circulating metabolites and microbe-derived molecules to the brain, immune cell activation, and direct signalling via the vagus nerve [23]. These mechanisms modulate emotional behaviour, mood regulation, and stress response.

Research indicates that the gut composition of those with depression and anxiety differs from healthy controls, with the concentration of certain bacterial strains corresponding with symptom severity. For instance, reduced microbiota diversity, overgrowth of harmful bacteria, and fewer short chain fatty acid-producing bacteria, such as the butyrate producing *Faecalibacterium*, predicts increased depression and anxiety symptom severity [24-26]. The reduction in diversity indicates a dysbiotic state and a lack of beneficial bacteria, resulting in an inflammatory environment that influences mood regulation. These findings suggest that the gut microbiome may contribute to the severity, pathogenesis, and remission of anxiety and depression.

Preclinical research demonstrates that alterations to the microbiome can alleviate or exacerbate anxiety and depression symptoms [27-35]. For instance, FMTs from humans with depression into mice induce inflammation and behavioural features of depression [27]. Likewise, FMT reduces depressive symptoms in stressed mice, improving the expression of markers and neurotransmitters associated with mood regulation [28]. Similarly, FMT from humans to germ-free mice can induce behavioural features of

recipients' psychological conditions such as obsessive-compulsive disorder, anorexia nervosa, autism spectrum disorder, attention deficit hyperactivity disorder and substance use disorder [2, 29, 30]. Overall, FMTs modulate mood, cognition, pain, and motor function, offering potential for prevention and treatment of psychiatric illnesses. However, their use for treating MH comorbidities in conjunction with IBS/IBD symptoms warrants further investigation and discussion to better understand their efficacy and safety.

Objective of Review

This narrative review evaluates evidence on the use of FMTs as a potential concurrent treatment for MH comorbidities and GI symptoms among IBS and IBD patients. The review assesses the types of interventions, and the effect of the interventions on mental and GI symptoms, identifies literature gaps, and discusses the potential clinical implications and feasibility of implementing microbiome-targeted FMT treatments. These findings offer valuable insights for healthcare providers and researchers, supporting the growing body of research on these treatments and their potential feasibility in clinical practice.

Methods

To conduct this study, a comprehensive review of the present literature was performed to synthesize current knowledge on using FMT as treatment for psychological conditions among IBS and IBD patients. The review was completed using electronic scientific databases, including PubMed, Google Scholar and Ovid Medline. Main search terms included "fecal microbiota transplantation," "FMT", "comorbidity", "gut-brain axis," "mental health," "depression," "anxiety," "irritable bowel syndrome," "inflammatory bowel disease," and "gut dysbiosis". Relevant synonyms were included. Boolean operators (AND, OR) were used to ensure a comprehensive coverage of existing literature. Recent publications from 2015 onward were included to ensure the literature was up-to-date. The search criteria were limited to primary research, and preclinical and clinical trials when concluding the efficacy of FMTs as a treatment option. 24 peer-reviewed articles written in English were included in the review. Eligible studies examined FMT as a treatment for MH and GI symptoms or transfer of behavioural phenotypes via FMT. See Appendix Table 1 for full methodological details.

Results

IBS Evidence

Preclinical Studies

Preclinical rodent studies provide strong evidence that altering gut microbiome composition with FMTs can modulate GI and MH symptoms [2, 27, 28, 33-36]. De Palma et al. [2] found that when germ-free (GF) mice received FMT from IBS patients, they exhibited decreased intestinal motility, increased intestinal permeability, and anxiety-like behaviours. Similarly, Li et al. [35] transplanted the fecal matter of mice exposed to chronic unpredictable mild stress (CUMS), a commonly used model for stress-induced IBS, to recipient mice following antibiotics. Compared to controls, recipients had significant increases in the anxiety- and depression-like behaviour and increased dysbiosis and neuroinflammation. These findings suggest that FMT influences the GBA, which influences GI function, MH, and inflammatory responses.

In addition to FMTs initiating MH and GI symptoms, FMTs from healthy donors have reversed these symptoms. Cai et al. [28] found that FMTs from healthy rodents improved depressive behaviours and colonic motility in CUMS rats. Following stress exposure, mice demonstrated depressive behaviours, heightened inflammatory markers, and dysbiosis. After FMT, appetite, colonic function, brain-derived neurotrophic factor, glutamate, and gamma-aminobutyric acid levels were restored. Similarly, Rao et al. [36] reported that FMTs from healthy rodents improved depression-like behaviours, intestinal inflammation, intestinal barrier damage, neuroinflammation, and restored gut microbiota imbalance in stressed rats. These findings support the use of FMTs for antidepressant effects and GI improvements, particularly for dysbiosis, an initiating factor in IBS. See Appendix Table 2 for detailed results.

Clinical Studies

Clinical studies on treating IBS patients' psychological symptoms show promising but varied results [37, 39-49]. Kurokawa et al. [37] were the first to evaluate the effect of FMTs on anxiety and depression in IBS patients, reporting significant improvements in GI, anxiety, depression, and insomnia symptoms, without AEs. Notably, even those without GI improvements demonstrated psychological improvements following FMT. Subsequent studies have assessed quality of life (QoL) in IBS patients following FMTs using the IBS-QoL measure, assessing dysphoria, body image, activity interference, food avoidance, health worry, sexual dysfunction, social reaction, and relationships [38]. Although it remains unclear if QoL improvements are due to relief of GI or MH symptoms, psychological distress and QoL appear to improve following FMT interventions. El-Salhy et al. [39] found that among 165 patients, half had significant improvements in GI, fatigue, and QoL symptoms over three months following colonoscopic FMT. Likewise, Huang et al. [40] assessed IBS-QoL, depression and anxiety symptoms over six months following endoscopic FMT. Significant improvements were seen across all measures at the one- and three-month mark. Treatment effects and microbiota diversity peaked at one month, but by six months, effects did not significantly differ from baseline, suggesting that the treatment effect is initially efficacious but may diminish over time.

Although findings are promising, not all evidence favours FMT for addressing psychological comorbidities [46, 47, 50]. Mazzawi et al. [41] reported increased QoL among 13 IBS patients within three weeks of endoscopic FMT, lasting six months. However, depression and anxiety symptoms only improved within the first month. A follow-up study by Mazzawi et al. [42] found no significant differences in depression nor anxiety symptoms of 11 IBS patients in the 24 weeks following endoscopic FMT. Lahtinen et al. [43] assessed GI and MH symptoms at five intervals over one year following FMT, reporting no significant changes in GI or MH symptoms, QoL, or microbial diversity. See Appendix Table 3 for detailed results.

IBD Evidence

Preclinical Studies

Animal studies demonstrate a causal link between microbiota alterations and MH symptoms for IBD. Yoo et al. [51] found that FMTs from IBD patients increase depressive behaviours and colitis symptoms in mice, as well as hippocampal and colonic inflammation. However, when treated with healthy donor FMT, GI and psychological outcomes significantly improved, supporting the use of FMTs for symptom improvement.

Likewise, Jang et al. [52] found that FMTs from IBD patients induced both colitic symptoms and neuroinflammation in GF mice, alongside anxious and depressive behaviours. Importantly, the severity of depressive symptoms in the donor had corresponding effects on the rodent's behavioural phenotype, suggesting that symptom severity may transmit via FMT. Conversely, FMTs from healthy individuals significantly reduced anxiety and depression-like behaviours and neuroinflammatory markers in mice. These preclinical findings highlight the therapeutic potential of FMTs for MH symptoms in IBD patients by restoring the microbiome and reducing inflammation. See Appendix Table 4 for detailed results.

Clinical Studies

Clinical studies demonstrate strong evidence for FMT as a treatment for IBD symptoms, but few studies have assessed psychological comorbidities [53-55]. Ding et al. [53] determined FMT for ulcerative colitis (UC) to be a highly effective and safe method for improving GI symptoms and QoL after a follow-up of 1–5 years. Similarly, Kilincarslan and colleagues [54] followed UC and Crohn's disease (CD) patients for one month following FMT, reporting a significant decrease in depression and anxiety symptoms, suggesting that FMT improves MH outcomes by restoring the microbial environment and reducing neuroinflammation related to dysbiosis. See Appendix Table 5 for detailed results.

Discussion

This review assessed the potential of using FMT as a treatment for psychological symptoms in IBS and IBD patients. Preclinical IBS evidence demonstrates a causal link between gut microbiota and MH symptoms, with FMT relieving both GI and psychological symptoms by restoring healthy microbiota. Although preclinical studies provide instrumental insights, their controlled environments limit generalizability. While clinical evidence further supports FMT for ameliorating anxiety and depression in IBS patients, treatment durability appears transient and inconsistent. A lack of standardized methodology and insufficient long-term data limit conclusions on duration of efficacy. Furthermore, FMT's therapeutic mechanism remains unclear, specifically whether observed improvements are directly attributed to microbiota shifts or mediated by other factors such as symptom relief. Despite these shortcomings, FMT is an effective and promising intervention for addressing psychological symptoms in IBS patients.

Preclinical IBD studies support a causal relationship between gut microbiota, inflammation, and symptoms of anxiety, depression, and IBD, suggesting that gut alterations offer MH symptom relief. Likewise, clinical studies support that FMT improves GI symptoms and QoL for IBD patients, but the effect on MH symptoms remains unclear due to few clinical studies utilizing direct psychological measures. Although research has shown that QoL, typically measured by the IBS-QoL [39, 40], may correspond with MH symptoms [56], the use of QoL as a proxy for psychological outcomes is insufficient for capturing clinical features of anxiety and depression. However, one clinical study found reductions in anxiety and depression using direct measures, but its generalizability was limited by an insufficient sample size and follow-up duration. Although FMT shows promise for addressing well-being, these gaps hinder the comprehensive understanding of FMT's effects on specific psychological symptoms among IBD patients, as it is unclear whether improvements are due to symptom relief or GBA-modulated psychological improvements.

Importantly, these findings indicate that the GBA plays a significant role in the comorbid nature of psychological and GI symptoms. Although FMT offers a promising, albeit experimental, alternative to traditional treatments, its support for MH symptoms requires further investigation, particularly in less controlled settings and among diverse populations.

Limitations

Of the 24 studies reviewed, most included small sample sizes, heterogeneous methodology, and mixed methodological quality. As such, these results should be considered preliminary. Further, this review was limited to studies written in English, subjecting it to publication bias and reducing generalizability to global populations.

Additionally, most studies relied on clinician-reported measures and excluded patient input or follow-up, which may reduce the accuracy and completeness of results. Finally, this review did not involve a quantitative synthesis of effect sizes nor pooled estimates, limiting its inferential conclusions.

Despite these limitations, these results contribute to the growing literature on the role of GBA in MH, reinforcing the use of integrative treatment frameworks for comorbidities. Additionally, findings highlight the need to standardize protocols and align methodology. This review informs both the public and clinical professionals on the most recent findings of a rapidly evolving research sphere.

Future Directions

Despite FMT's promise for addressing MH symptoms, particularly among IBS and IBD patients, the treatment remains in its infancy due to numerous unanswered questions. FMT is generally safe, with most adverse reactions being relatively mild (e.g., abdominal pain, diarrhea, constipation), though more severe AEs (infections, worsening of symptoms) do occur and remain underexplored [57]. High attrition rates and inconsistent AE reporting emphasize need for standardized and rigorous safety protocols, including improved patient-clinician agreement on the severity of AEs experienced [58]. Furthermore, donor and patient selection criteria were highly heterogeneous across studies, with most focusing on infectious disease and GI health, excluding psychiatric history or traits, ultimately limiting the generalizability of treatment. "Superdonors" are normobiotic donors with beneficial bacteria, the absence of disease, and healthy behaviours, and are particularly effective in restoring microbial balance for positive GI outcomes [39]. However, insufficient research has assessed which donor characteristics optimize MH outcomes. Given the evidence of transferring behavioural phenotypes to the receiving organism, a thorough evaluation of the donor's psychological history is critical, as well as assessing behavioural side effects in recipients.

Methodological heterogeneity further limits understanding of FMTs efficacy and safety, particularly in generalizing to a broader patient population. Most studies exclude participants with comorbidities or previous health conditions, which may lead to inaccurate conclusions due to oversimplified or overly restrictive sample populations. Additionally, condition subtypes should be analyzed separately to better interpret varied outcomes and standardize protocols, as many studies pool participants' results. Clear, standardized inclusion criteria and stratified analyses are required to determine treatment efficacy and safety across populations. Likewise, inconsistencies in FMT preparation and administration further complicates conclusions, as these incongruent methods lead to varied GI outcomes and AEs [61, 62]. Few studies compare methodologies, leaving unanswered questions for implementing treatment. Research suggests that anaerobically prepared pooled FMT offers longer lasting results for GI symptoms due to more viable bacteria and greater diversity [57], but its effect on psychological symptoms remains unknown.

Finally, considerations of accessibility, cost, and integration into care are not yet defined, since FMT for MH symptoms is experimental and expensive [29]. The economic burden of IBS, IBD and MH conditions is highly impactful, but the conceptualization of FMT as a solution to this burden is insufficiently understood. Additionally, adjunct methods, such as probiotics and diet, to supplement treatment retention remain underexplored but may enhance retention and lower economic barriers.

Conclusions

These results support the efficacy of FMT to treat MH symptoms, specifically anxiety and depression, in IBS and IBD patients. Overall, the heterogeneity of studies remains a limiting factor in implementing these treatments, highlighting the need for standardized procedures and shared databases of FMT procedures. Further research is required to understand the optimal methodology for FMT treatment, including patient criteria, risk and reduction of AEs, and donor criteria. Therefore, an open science framework is suggested for subsequent studies to address methodological inconsistencies, centralize findings, and improve globalized conceptualizations of FMT by integrating cross-cultural differences into practice.

List of Abbreviations

AE: adverse events
CNS: central nervous system
ENS: enteric nervous system
GBA: gut-brain-axis
GI: gastrointestinal
IBD: inflammatory bowel disease
IBS: irritable bowel syndrome
MH: mental health
SSRI: selective serotonin reuptake inhibitors

Conflicts of Interest

The author declares no conflicts of interest.

Ethics Approval and/or Participant Consent

No ethics approval or participant consent was required for this review, as it was completed using only pre-existing literature.

Authors' Contributions

MMM: Made contributions to the design of the study, collected and analysed data, drafted the manuscript, and gave final approval of the version to be published.

Acknowledgements
The author would like to acknowledge their mentor, Mikayla Hall-Bruce, for providing writing assistance, feedback, and support throughout the review process.

Funding
This study was not funded.

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Article Information
Managing Editor: Jeremy Y. Ng
Peer Reviewers: Mikayla Hall-Bruce, Samara Baum
Article Dates: Received Apr 27 25; Accepted Jun 13 25; Published Aug 12 25

Citation
Please cite this article as follows:
Mifsud MM. The feasibility of using fecal microbiota transplantation as a treatment for mental health conditions among IBS/IBD patients: A literature review. URNCST Journal. 2025 Aug 12: 9(6).
https://urncst.com/index.php/urncst/article/view/905
DOI Link: https://doi.org/10.26685/urncst.905