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Therapeutic Potential of Fecal Microbiota Transplantation for Male Sexual Dysfunction: Evidence and Clinical Perspectives

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ABSTRACT

Fecal microbiota transplantation (FMT), a microbiome-based therapy, shows potential in treating male sexual dysfunction. Research into the influence of FMT on male sexual function has recently garnered increasing attention. This review aims to explore the impact of FMT on male sexual function and the underlying mechanisms, and to analyze the current research landscape, focusing on key findings and the challenges faced in this evolving field. By critically reviewing and synthesizing the available literature and research outcomes, we intend to provide foundational insights into FMT applications for male sexual health and to outline potential future research trajectories that could further elucidate its benefits and mechanisms.

1 | Introduction

Male sexual dysfunction, particularly erectile dysfunction (ED), represents a widespread condition that markedly affects quality of life in a significant proportion of men [1–3]. In a community-based survey across 30 provinces in China including 5210 men aged 40 years or older, the prevalence of ED was 40.56% as assessed by the 5-item version of the International Index of Erectile Function (IIEF-5) and increased steadily with age [4]. Another large Chinese survey reported an ED prevalence of 17.1% using the IIEF-5 and 12.0% by self-report, highlighting substantial variability depending on the assessment method [5]. ED is influenced by multifactorial determinants, including psychological status, physical health with vascular integrity and hormonal balance, and lifestyle factors. Major affecting factors include cardiometabolic and vascular risk profiles such as diabetes [6], hypertension [7], dyslipidemia [8], obesity and metabolic syndrome [8], as well as smoking [7] and medication exposures [9].

Recent studies suggest that gut microbiota composition is associated with male sexual function. In a Chinese pilot study, ED cases showed distinct gut microbial community patterns, with *Actinomyces* enriched and negatively correlated with erectile performance, whereas *Coprococcus_1*, *Lachnospiraceae_FCS020_group*, *Ruminiclostridium_5*, and *Ruminococcaceae_UCG_002* were depleted and correlated with erectile function measures [10]. Another recent study in Chinese patients reported a lower abundance of *Bacteroides intestinalis* and a higher abundance of *Ruminococcus gnavus* in ED, with functional signals suggesting links to atherosclerosis-related pathways and amino acid metabolism [11]. Genetic evidence also supports a microbiota contribution. Mendelian randomization analyses have identified taxa associated with

Highlights

- Gut microbiota dysbiosis is consistently associated with erectile dysfunction across human studies.
- Preclinical microbiota transfer studies suggest causal links via inflammation and endothelial nitric oxide (NO) signaling.
- Human intervention evidence for microbiota transplantation in male sexual dysfunction remains scarce.
- Neuroendocrine, immune, and metabolite pathways provide biologically plausible mechanistic frameworks.
- Rigorous, standardized trials with long-term safety monitoring are required before clinical translation.

higher ED risk, including *Lachnospiraceae*, *Lachnospiraceae_NC2004_group*, *Oscillibacter*, *Senegalimassilia*, and *Tyzzerella 3*, and a potentially protective association for *Ruminococcaceae_UCG_013* [12–16]. Across these lines of evidence, proposed pathways include systemic inflammation and endothelial dysfunction with impaired nitric oxide (NO) signaling, alongside metabolic and endocrine links that remain less directly tested in ED models [17].

Fecal microbiota transplantation (FMT) is a therapeutic intervention in which processed stool from a healthy donor is delivered into the gastrointestinal tract of a recipient to reestablish microbial balance and address conditions linked to dysbiosis [18]. FMT has shown therapeutic potential in treating *Clostridium difficile* infection and is currently being explored for its potential benefits in other medical conditions, such as metabolic syndrome and inflammatory bowel disease (IBD) [19, 20]. Given the established link between gut health and sexual function, FMT has been proposed as a potential microbiome-targeted intervention for male sexual dysfunction.

This review summarizes current evidence linking the gut microbiota to male sexual function, outlines plausible mechanisms grounded in the existing evidence, and discusses the current status and future prospects of FMT and related microbiome interventions for ED.

2 | Methods

This manuscript is a narrative review with a structured PubMed search to synthesize emerging evidence linking gut microbiota-related mechanisms and microbiota-targeted strategies with male sexual dysfunction, with a primary focus on ED. Given the heterogeneous study designs (animal experiments, observational microbiome studies, Mendelian randomization analyses, and limited intervention-related evidence) and the lack of sufficiently comparable interventional trials, we performed a qualitative synthesis rather than a formal meta-analysis.

A PubMed search was conducted from database inception to 11 January 2026 using a low-ambiguity query combining microbiota transplantation/microbiome terms with male sexual dysfunction/ED terms. Search results were exported and screened by title/abstract against predefined eligibility criteria; studies were included if they evaluated gut microbiota features or microbiota-targeted exposures/interventions in relation to male sexual function outcomes. The study identification and selection process is summarized in Figure 1. The included original studies are summarized by study type in Tables 1 to 4.

3 | The Impact of FMT on Male Sexual Function

3.1 | Relevant Findings in Animal Experiments

Animal studies have provided critical insights into the mechanisms by which FMT may affect male sexual function. Current evidence from rodent models suggests that gut microbial dysbiosis is associated with significant alterations in sexual behavior and reproductive health. For instance, a study involving male Sprague–Dawley rats demonstrated that a high-fat diet (HFD) leads to significant impairments in ED and alterations in gut microbiota diversity. When fecal microbiota from healthy rats was transplanted into those affected by HFD-induced dysbiosis, improvements in ED were observed [21]. A study demonstrated that male mice receiving FMT from donors with a healthy gut microbiota exhibit improved testicular function, increased testosterone levels, and enhanced sexual activity compared to control groups [22]. These findings highlight the potential role of gut microbiota in regulating hormonal pathways associated with sexual health. Furthermore, the administration of specific bacterial strains via FMT has been linked to increased sperm counts and improved fertility parameters, suggesting that the intestinal microbiota may play a significant role in male reproductive health [23]. These effects may stem from the regulation of inflammatory pathways and hormonal balance, as it has been demonstrated that dysbiosis can trigger low-grade inflammation, negatively impacting reproductive organs [24].

In an HFD model, FMT was reported to mitigate diet-associated declines in male fertility while improving systemic and testicular metabolomic profiles, suggesting that microbiota transfer may influence spermatogenesis through metabolic remodeling [25]. In addition, FMT from alginate oligosaccharide-dosed donor mice has been reported to improve spermatogenesis and to rescue male fertility-related phenotypes in mouse models [26].

Microbiota transfer-based approaches have also been reported to influence female reproductive outcomes in animal settings. Fecal virome transfer increases commensal *Akkermansia muciniphila* and is unexpectedly associated with a higher fertility rate in co-housed female mice [27].

Taken together, these animal studies not only highlight the promise of FMT in improving male sexual function but also uncover the intricate relationship between gut microbiota and reproductive health.

3.2 | Recent Clinical Research Summary

Recent clinical research has increasingly focused on the potential role of FMT in improving male sexual function, particularly ED. A narrative review consolidating current research suggests a strong correlation between gut microbiota dysbiosis

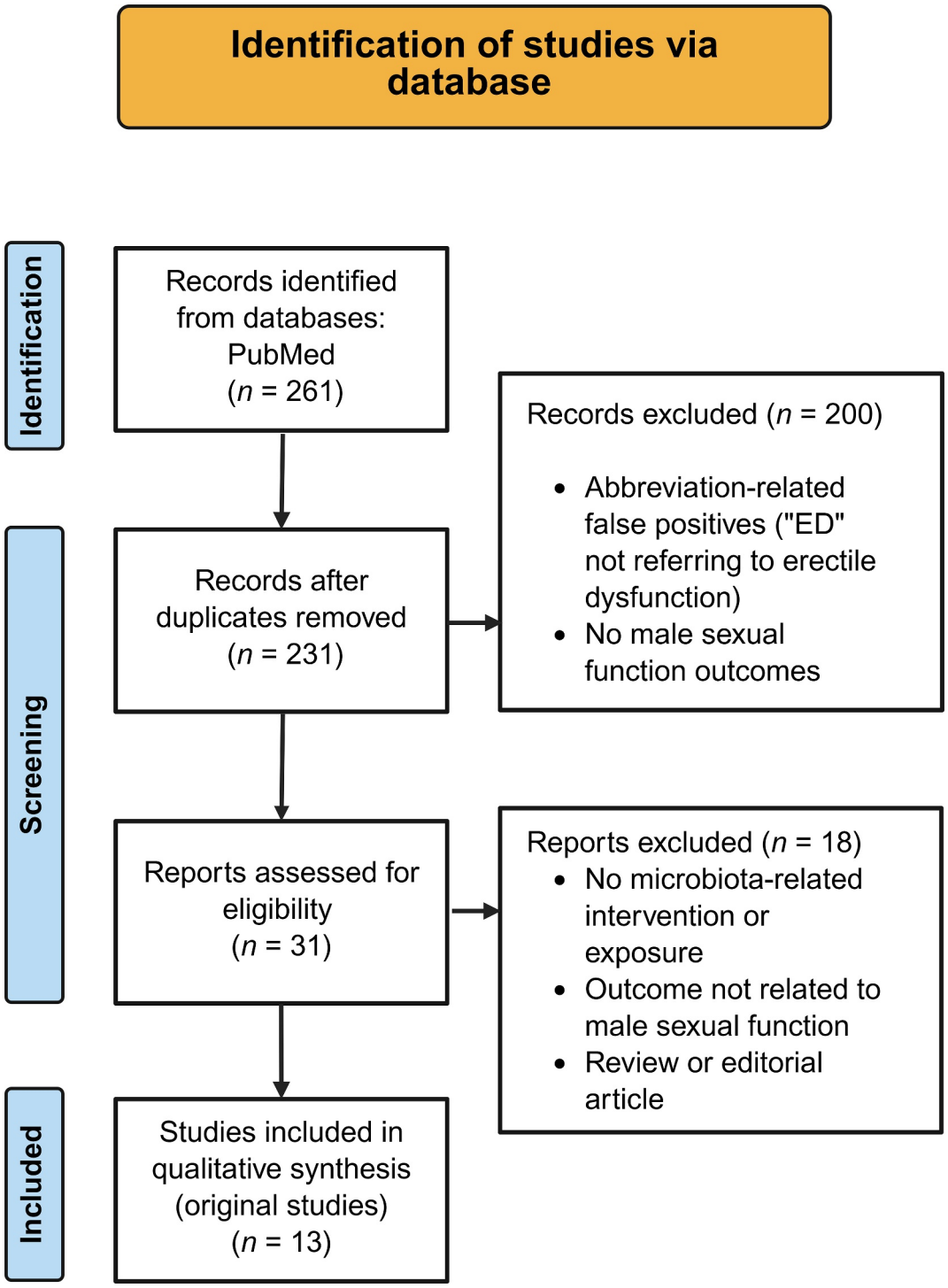

FIGURE 1 | PRISMA flow diagram of study identification, screening, eligibility assessment, and inclusion.

and ED pathogenesis [3]. This dysbiosis may result in endothelial dysfunction [28], hormonal imbalances [29], systemic inflammation [30], and altered neurotransmitter production [31], all of which appear to contribute to the maintenance of ED.

Moreover, studies have shown that FMT can restore gut microbiota diversity and composition. This restoration may mitigate these adverse effects [32]. This suggests that FMT not only restores microbial balance but also has the potential to alleviate the physiological changes associated with ED.

In a case report, FMT was successfully administered to alleviate postorgasmic illness syndrome in a male patient [33]. Several recent human studies have reported alterations in gut microbiota composition in men with ED. A recent survey observed decreased *Bacteroides* and increased *Ruminococcus gnavus* in

TABLE 1 | Microbiota transplantation-based human intervention study.

Year	Authors	Title	Study type	Sample size	Primary assessment	Key findings	Limitations
2024	Quan et al.	Beneficial effects of the first case of washed microbiota transplantation for postorgasmic illness syndrome: a case report	Case report (WMT intervention)	1 patient	Symptom scores; gut microbiota profiling	WMT is associated with improvement in POIS-related symptoms accompanied by changes in gut microbial composition	Single case; no control; POIS rather than ED; findings not generalizable

TABLE 2 | Animal experimental studies.

Year	Authors	Title	Study type	Sample size	Primary assessment	Key findings	Limitations
2017	Li et al.	Relationship between gut microbiota and type 2 diabetic erectile dysfunction in Sprague–Dawley rats	Animal experiment	35 male Sprague–Dawley rats	Erectile function tests; 16S rRNA sequencing	Diabetic ED rats show altered gut microbiota composition compared with controls	Animal model; diabetes-specific ED; no causal manipulation
2025	Xu et al.	The role of gut microbiota in male erectile dysfunction of rats.	Animal experiment (FMT-related)	22 male Sprague–Dawley rats	Intracavernosal pressure; microbiota analysis	Transfer of dysbiotic microbiota is associated with impaired erectile function in recipient rats	Preclinical only; species differences; indirect relevance to humans

TABLE 3 | Human observational microbiome studies.

Year	Authors	Title	Study type	Sample size	Primary assessment	Key findings	Limitations
2020	Okamoto et al.	The association between gut microbiome and erectile dysfunction: a community-based cross-sectional study in Japan	Cross-sectional study	408 men	IIEF; gut microbiome profiling	Specific taxa are associated with ED status in a community cohort, with microbiome composition differing between low/high IIEF groups	Cross-sectional design cannot infer causality; possible confounding by diet/lifestyle factors
2024	Kang et al.	Characteristics of gut microbiota in patients with erectile dysfunction: a Chinese pilot study	Observational (pilot)	43 ED; 16 controls	IIEF; 16S rRNA sequencing	*Actinomyces* is enriched in ED, correlating with NPTR and yielding a classifier AUC of 0.72	Pilot study; limited sample; possible residual confounding; did not provide a 95% confidence interval
2024	Qiao et al.	Gut microbiota composition may be an indicator of erectile dysfunction	Observational study	53 ED; 32 controls	Microbiota profiling; ED assessment	*Bacteroides* abundance increases and *Bifidobacterium* abundance decreases in patients with ED	Association only; no causality
2025	Su et al.	Altered gut microbiota in erectile dysfunction patients: a pilot study	Observational (pilot)	19 ED; 15 controls	Gut microbiota analysis	The abundance of *Bacteroides intestinalis* is decreased while *Firmicutes* abundance increases in ED	Small sample; single center

Abbreviations: AUC, area under the curve; NPTR, nocturnal penile tumescence and rigidity.

TABLE 4 | Mendelian randomization studies.

Year	Authors	Title	Study type	Sample size	Primary assessment	Key findings	Limitations
2023	Zhang et al.	Genetically proxied intestinal microbiota and risk of erectile dysfunction	Mendelian randomization	6175 cases; 217,630 controls	Mendelian randomization study	Genetic proxies of specific taxa are associated with ED risk	Instrument strength; population specificity
2023	Zhang et al.	Causal effects of gut microbiota on erectile dysfunction: a two-sample Mendelian randomization study	Two-sample MR	6175 cases; 217,630 controls	Mendelian randomization study	There are potential causal links between taxa and ED	Pleiotropy; exposure definition
2023	Su et al.	Specific gut microbiota may increase the risk of erectile dysfunction: a two-sample Mendelian randomization study	Two-sample MR	18,340 cases; 223,805 controls	Mendelian randomization study	Certain taxa are genetically associated with higher ED risk	Genetic inference only
2024	Xu et al.	Causal effects of gut microbiota on the risk of erectile dysfunction: a Mendelian randomization study	Mendelian randomization	6175 cases; 217,630 controls	Mendelian randomization study	A possible causal contribution of microbiota to ED is supported	No functional validation
2024	Zhu et al.	The association between the gut microbiota and erectile dysfunction	Mendelian randomization-based genetic analysis	6175 cases; 223,805 controls	Mendelian randomization study	Genetic evidence linking gut microbiota to ED is provided	Indirect causal inference

patients with ED [11], and a 2024 cross-sectional study identified differences in genera such as *Bacteroides* and *Fusobacterium* between ED cases and controls [34]. A comparative study of taxonomic characteristics between patients with ED and healthy males identified distinct alterations in gut microbiota composition among patients with ED, including a negative correlation between *Actinobacteria* abundance and ED severity. [10]. Overabundance of Actinobacteria is correlated with indicators of gut barrier dysfunction, potentially exacerbating endothelial oxidative stress via the gut–vascular axis and impairing penile hemodynamics. Current evidence regarding FMT for the treatment of ED primarily derives from animal models, but there is a paucity of relevant clinical studies specifically investigating this intervention. Although direct clinical trials on FMT for ED are limited, indirect evidence suggests that gut microbiota modulation may improve sexual function. For example, a study of FMT in Crohn's disease reported improved sexual quality of life in 70% of patients [35]. FMT represents a promising therapeutic approach for men with sexual dysfunction associated with gut dysbiosis.

It is noteworthy that a clinical report described improved fertility outcomes in patients with IBD after washed microbiota transplantation (WMT), suggesting that microbiota restoration may have reproductive implications in humans beyond male sexual function endpoints [36].

When interpreting the results of observational studies, caution must be exercised. For example, although the study by Okamoto et al. identified associations between specific taxa and ED status, this cross-sectional design precludes causal inference. It remains unclear whether gut dysbiosis drives ED or, conversely, whether metabolic disturbances, poor dietary habits, and psychological stress commonly seen in patients with ED shape a dysbiotic microbial profile. Moreover, many studies have failed to adequately control for key confounding factors—including lifestyle factors, dietary patterns, and smoking habits—that may jointly influence both gut microbiota composition and sexual function.

4 | The Potential Mechanisms Linking FMT and Male Sexual Function

To present the mechanistic evidence more systematically, we explicitly stratify evidence by strength (Table 5). Evidence level E1 denotes direct experimental findings in FMT–ED animal models, including changes in inflammatory profiles and erectile function-related vascular/NO signaling accompanied by erectile outcomes and penile/systemic readouts. E2 denotes supportive evidence from non-FMT–ED or related metabolic/vascular models and human observational studies. H denotes hypothesized mechanisms that are biologically plausible but not yet directly tested in FMT–ED models.

4.1 | Regulatory Mechanisms of Gut Microbiota on the Sex Hormone Axis

Sex hormone imbalances are associated with sexual dysfunction [43]. The relationship between gut microbiota and sex hormones has been increasingly reported and may be relevant to male sexual

TABLE 5 | Evidence stratification for FMT and gut microbiota-related pathways in erectile dysfunction.

Evidence level	Description	Details
Direct experimental evidence (E1)	Direct experimental evidence in FMT–ED animal models	1. In FMT–ED animal models, microbiota transfer has been associated with altered inflammatory profiles and erectile function-related vascular/NO signaling [21, 37] 2. ED outcomes reported in FMT–ED models include erectile function indices, penile vascular signaling, cavernous histology, and systemic inflammatory/oxidative stress markers [21, 37] 3. Systemic inflammation and oxidative stress markers are also reported in some FMT–ED studies as supportive endpoints [37]
Supportive evidence (E2)	Supportive evidence from non-FMT–ED or related models	1. Dysbiosis has been linked to impaired gut barrier function and endotoxin-related systemic inflammation in related ED/metabolic contexts [34] 2. Endotoxin-associated inflammatory signaling has been linked to elevated inflammatory mediators (TNF-α/IL-6) and endothelial dysfunction with reduced NO bioavailability in related models [17] 3. Human observational studies report altered gut microbiota composition in men with erectile dysfunction, whereas causal inference remains limited by study design [10, 38] 4. Gut microbiota–endocrine associations involving the HPG axis have been reported in non-FMT–ED/metabolic contexts [39]
Hypothesized mechanisms (H)	Hypothesized mechanisms without direct validation in FMT–ED models	1. Gut–brain axis: dysbiosis can influence serotonin/GABA levels, linked to ED via central pathways [40] 2. Neuroendocrine stress pathways may modulate sexual function and interact with gut–brain signaling [41] 3. Microbial metabolites (SCFAs and other bioactive metabolites) may modulate neuroinflammation and gut–brain communication [42]

Abbreviations: GABA, γ-aminobutyric acid; HPG, hypothalamic-pituitary-gonadal; NO, nitric oxide; SCFAs, short-chain fatty acids.

function. Available evidence—largely from preclinical studies and observational human data—suggests that gut microbial profiles are linked to endocrine pathways related to the hypothalamic-pituitary-gonadal (HPG) axis and testosterone homeostasis [29, 44]. Potential mechanisms proposed in the literature include microbial participation in steroid hormone metabolism and microbiota-derived metabolites that may influence hormone synthesis and secretion. For example, some gut bacteria have been reported to express enzymes capable of metabolizing androgens, which could alter their bioavailability and activity [45]. In addition, gut dysbiosis has been associated with alterations in hormonal regulation and ED-related phenotypes; however, causality cannot be inferred from observational associations due to potential residual confounding and reverse causation [3].

Research has also reported correlations between specific bacterial taxa and circulating testosterone levels. For instance, *Lactiplantibacillus plantarum* has been associated with higher testosterone levels in animal models, suggesting a hypothesis that microbiota modulation might influence reproductive endocrine outcomes under certain conditions [23]. Beyond *Lactiplantibacillus plantarum*, other *Lactobacillus* lineage probiotics have been linked to male reproductive endocrine phenotypes in preclinical studies. In aging mice, *Lactobacillus reuteri* has been reported to increase testicular size and serum testosterone, accompanied by increased Leydig cell numbers [46]. In diet-induced obese mice, *Lactobacillus rhamnosus* PB01 supplementation improves sperm kinematic parameters and increases serum testosterone, luteinizing hormone and follicle-stimulating hormone. Human evidence remains limited; a 12-week randomized, double-blind, placebo-controlled trial in healthy men aged 55–65 years evaluated *Limosilactobacillus reuteri* ATCC PTA 6475 but did not demonstrate an increase in testosterone levels [47].

Moreover, dysbiosis has been linked to systemic inflammation, and inflammatory signaling has been reported to suppress testosterone biosynthesis and adversely affect sexual function [48]. Chronic inflammation may increase proinflammatory cytokines that can impair Leydig cell function and thereby reduce testosterone synthesis [49].

Overall, clarifying the interactions among gut microbiota, sex hormones, and male sexual function will require more rigorous longitudinal and interventional studies. Nonetheless, these associative findings and preclinical mechanisms provide a rationale to further evaluate microbiome-targeted strategies in appropriately designed trials.

4.2 | Gut Microbiota-Mediated Immune Homeostasis and Sexual Dysfunction

The immune system is intricately linked to male sexual function. Gut microbiota dysbiosis has been significantly linked to the development of systemic inflammation, which is a key factor in the onset of ED [50, 51]. Gut dysbiosis disrupts intestinal barrier integrity, resulting in increased permeability that permits bacterial endotoxins, such as lipopolysaccharide (LPS), to enter the systemic circulation. LPS binds to Toll-like receptors (TLRs), especially TLR4, on immune cells, triggering the release of proinflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) [38]. Elevated levels of these cytokines exacerbate oxidative stress and impair endothelial NO production. NO plays a central role in vasodilation, and its deficiency plays a central role in ED pathophysiology. Elevated TNF-α levels are inversely correlated with ED scores, underscoring their pivotal role in the pathophysiology of ED [52].

Additionally, the gut microbiota impacts the immune system by producing metabolites that can modulate immune responses. Short-chain fatty acids (SCFAs), produced through the fermentation of dietary fiber by gut microbes, exhibit anti-inflammatory properties and help strengthen the integrity of the gut barrier [53]. SCFAs inhibit the release of proinflammatory cytokines such as IL-6 and TNF-α and promote the production of anti-inflammatory mediators by activating G protein-coupled receptors (GPCRs) [54]. Maintaining a healthy gut barrier is essential for preventing the translocation of pathogens and inflammatory mediators into the bloodstream, as this process can worsen systemic inflammation and adversely affect sexual function.

Critically, FMT has been designed to restore microbial composition, which may influence host immune responses. Specific beneficial bacterial taxa introduced via FMT can promote anti-inflammatory responses by stimulating the production of cytokines such as IL-4, IL-10, IL-11, and IL-13, while simultaneously reducing proinflammatory mediators such as IL-1, IL-6, and TNF-α. By modulating regulatory T cells (Tregs) and T helper cells (Th cells) [55], this modulation fosters a systemic anti-inflammatory state. Given the established role of chronic inflammation and endothelial dysfunction in conditions such as ED, a key component of male sexual dysfunction, this immune rebalancing has been proposed as a potential mechanism linking gut microbiota modulation to male sexual health.

In conclusion, the regulation of the immune system by the gut microbiota appears to be a significant factor in male sexual health. By affecting systemic inflammation and immune responses, the gut microbiota can significantly influence ED and overall reproductive well-being. Future studies should aim to investigate the therapeutic potential of modifying gut microbiota through dietary interventions and FMT to enhance sexual health outcomes in men.

4.3 | Gut–Brain Axis-Mediated Psychosocial Mechanisms and Microbial Modulation in ED

The reciprocal relationship between mental health and ED is strongly shaped by the gut–brain axis, a crucial pathway that connects intestinal homeostasis with neurological and endocrine regulation. This intricate two-way communication system integrates neural pathways, hormonal regulation, immune responses, and metabolic cross-talk. Microbial imbalance impairs this connectivity, triggering disturbances in neurochemical synthesis, immune system dysregulation, and hyperactivity of stress–response pathways [56]. Anxiety and depressive states frequently associated with ED may be partially mediated by gut microbiota interactions [3]. Intestinal microorganisms synthesize neuroactive compounds, including approximately 90% of the body's serotonin and substantial γ-aminobutyric acid (GABA), both essential for emotional regulation. Dysbiosis-induced depletion of these metabolites correlates with affective disorder development [2]. Concurrently, compromised intestinal barrier function permits systemic translocation of bacterial endotoxins, initiating cytokine cascades involving IL-6 and TNF-α. Such chronic low-grade inflammation promotes neuroinflammatory pathways implicated in depressive pathophysiology [57].

The hypothalamic-pituitary-adrenal (HPA) axis, a primary stress regulation mechanism, demonstrates microbiota-dependent modulation. Dysbiotic conditions enhance HPA axis sensitivity, resulting in sustained cortisol elevation that amplifies psychological distress and impairs sexual performance [58]. Clinical evidence identifies protective microbial genera (*Lactobacillus* and *Bifidobacterium*) associated with HPA axis stabilization and stress adaptation, whereas elevated populations of *Bacteroides* and *Escherichia-Shigella* correlate with heightened anxiety metrics and sexual dysfunction severity [59]. Although these links are biologically coherent and supported by broader gut–brain literature, direct experimental validation within FMT–ED models remains limited.

4.4 | Impact of Microbial Metabolites on Male Sexual Function

Metabolites produced by the gut microbiota serve as important regulators of nervous system health and gut–brain communication and may, therefore, be relevant to sexual health. These microbial metabolites, particularly SCFAs, indoles, and neurotransmitters, can affect neuroinflammation, neuronal health, and communication between the gut and the brain, all of which are critical for maintaining sexual health [60].

SCFAs such as acetate, propionate, and butyrate are produced when gut bacteria ferment dietary fibers, and these molecules have been shown to exert neuroprotective effects. They are capable of crossing the blood–brain barrier, where they can affect brain function by modulating inflammation and supporting the health of neuronal cells [61]. Butyrate inhibits the phosphorylation of the inhibitor of nuclear factor KappaB (NF-κB) isoform α (IκBα) and nuclear translocation of NF-κB p65 via the G-protein-coupled receptor 43 (GPR43)/β-arrestin-2 signaling pathway, thereby suppressing the NF-κB-mediated inflammatory response [62]. In the context of sexual function, SCFAs may help mitigate the effects of stress and anxiety, which are known to impair ED [63, 64]. By fostering a healthy gut environment and lowering systemic inflammation, SCFAs can indirectly enhance sexual health in men.

Indoles, another category of microbial metabolites, originate from the amino acid tryptophan and have been shown to affect neurotransmitter production and mood regulation [65]. Excessive production of indoles in the gut may reduce tryptophan availability to the central nervous system, thereby decreasing serotonin synthesis in the brain. Low levels of serotonin are directly linked to mood disorders, including depression and anxiety [66]. Modulating gut microbiota to regulate indole synthesis may improve mental health, thereby enhancing sexual function.

Moreover, the gut–brain axis forms a communication pathway that links the gut microbiota to the central nervous system, permitting microbial metabolites to affect brain activity and behavior [67]. Dysbiosis can disrupt this communication, leading to altered neurotransmitter levels and increased neuroinflammation, both of which can negatively impact sexual health.

Studies indicate that FMT can help reestablish a balanced gut microbiota and boost the synthesis of beneficial metabolites, which may contribute to improved sexual function [68, 69]. Overall, metabolite-mediated pathways remain plausible, but their causal contribution to erectile outcomes requires more direct testing.

4.5 | Microbiota-Targeted Intervention Strategies for Metabolic Disorders

Metabolic conditions such as obesity, Type 2 diabetes mellitus (T2DM), hypertension, and hyperlipidemia exhibit a robust correlation with ED. Key contributors to this relationship include insulin dysregulation, chronic low-grade inflammation, and impaired endothelial function, which collectively underpin both metabolic dysregulation and ED development [70].

Current studies indicate that the risk of ED increases with body weight [71]. Obesity has been associated with an altered microbial composition characterized by increased Firmicutes and decreased Bacteroidetes, which may enhance dietary energy harvest and promote weight gain [72].

Diabetes is a major contributor to sexual dysfunction in men [73, 74]. The prevalence of ED is higher in diabetic patients compared to the normal population, with an earlier onset age in diabetics than in nondiabetics [73]. In various animal models of diabetes, alterations in gut microbiota, known as gut dysbiosis, have been associated with low-grade inflammation. This dysbiosis has been linked to several metabolic disturbances, including impaired glucose tolerance, increased weight gain, and accumulation of fat mass. Additionally, it plays a role in the infiltration of macrophages into visceral adipose tissue, further exacerbating inflammatory responses and metabolic dysfunction [75]. High-fat, high-sucrose diet-induced T2DM rats showed restored gut microbiota composition and improved insulin sensitivity after FMT treatment [76]. FMT can enhance insulin signaling pathways by boosting the population of butyrate-producing bacteria and facilitating the generation of SCFAs [77]. WMT refers to a modified form of FMT in which fecal microbiota are processed using repeated washing, filtration, and suspension steps to enrich microbial components while removing a substantial proportion of fecal debris and soluble impurities before infusion. Compared with standard FMT, WMT primarily differs in the preparation process, with the intended goal of improving product consistency and potentially reducing procedure-related contaminants. A WMT trial conducted in a southern Chinese population demonstrated that it significantly reduces glycemic variability and fasting blood glucose levels [78].

Hypertension is acknowledged as a potential risk factor that can influence human sexual behavior. Both men and women with hypertension have a higher prevalence of sexual dysfunction [79]. Existing studies also indicate that gut microbiota dysbiosis contributes to hypertension [80]. This robust correlation may help elucidate how genetic, epigenetic, and nutritional factors affect the composition of gut microbiota and regulate blood pressure. Analyzing bacterial genomes from fecal samples collected from hypertensive rats and humans has shown notable decreases in bacterial richness, diversity, and evenness [81]. Minocycline, an antibiotic with anti-inflammatory properties, can improve hypertension-associated dysbiosis by modulating the Firmicutes-to-Bacteroidetes ratio in the gut microbiota, thereby exerting antihypertensive effects [82]. Thus, modulating the gut microbiota seems to offer substantial promise in the management of sexual dysfunction induced by hypertension.

The gut microbiota plays a significant role in the metabolism and modification of bile acids, and any imbalance within this microbial community can result in irregularities in bile acid production and circulation, ultimately influencing cholesterol metabolism. *Faecalibaculum* and *Ruminococcaceae_UCG_010* reduce serum cholesterol levels by modulating bile acid metabolic enzyme activity [83]. The SCFAs produced by gut microbiota through dietary fiber fermentation can regulate lipid synthesis and breakdown via GPR activation [83]. Microbial dysbiosis leads to reduced SCFA production, thereby exacerbating lipid accumulation. Furthermore, dysbiotic microbiota may inhibit lipoprotein lipase (LPL) activity, slowing triglyceride (TG) hydrolysis and contributing to hypertriglyceridemia [84]. Clinical research has shown that WMT is effective over the long term in Chinese individuals diagnosed with hyperlipidemia. This treatment has been associated with significant decreases in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and TGs while also maintaining a positive

safety record [85]. Furthermore, FMT delays the progression of glucose intolerance by enhancing the bile acid metabolic capacity of gut microbiota, thereby indirectly ameliorating lipid metabolism disorders [69].

4.6 | Interplay Among Sexlessness, Autism Spectrum Disorder Traits, and Gut Microbiota in Male Sexual Dysfunction

Recent large-scale studies have revealed significant associations between a life without sexual activity and specific phenotypic characteristics [86]. Research indicates that sexlessness in males is correlated with higher educational attainment and certain cognitive advantages, yet it is also accompanied by increased unhappiness and a greater tendency towards social isolation. These findings suggest that sexlessness may not solely result from personal choice but could be closely linked to neurodevelopmental traits, as well as underlying biological mechanisms. Core symptoms commonly seen in individuals with autism spectrum disorder (ASD)—including reduced social interaction, communication challenges, and a strong preference for routine—may pose significant challenges to establishing and maintaining intimate relationships, thereby increasing the likelihood of a sexless life [87].

This behavior pattern, influenced by neurodevelopmental traits, interacts profoundly with the gut microbiota. Studies have shown that individuals with ASD possess a gut microbiota composition that differs markedly from that of neurotypical individuals, often displaying reduced microbial diversity, abnormal levels of *Clostridium* and *Bacteroides*, and distinct shifts in microbial metabolite profiles [88]. Such dysbiosis can affect the balance of neurotransmitters such as serotonin and GABA, exacerbate systemic low-grade inflammation, and modulate the stress response of the HPA axis via the bidirectional communication pathway of the gut–brain axis [89]. Collectively, these physiological changes may intensify social anxiety, sensory processing overload, and behavioral inflexibility in individuals with ASD, thereby undermining the motivation and capacity to initiate or respond to sexual intimacy [90]. These observations are derived primarily from ASD-related literature and should not be interpreted as direct evidence for ED or FMT-related mechanisms.

At the level of male sexual function, this complex interplay becomes even more apparent. Neuroinflammation driven by gut microbiota dysbiosis can disrupt the normal function of the HPG axis, potentially suppressing testosterone synthesis and directly reducing libido, a core driver of sexual function [29, 91]. Concurrently, anxiety and mood states influenced by aberrant microbial metabolism can further exacerbate performance anxiety and psychological discomfort in sexual contexts. Although direct research on FMT for improving ASD-related sexlessness or sexual dysfunction is currently lacking, preliminary evidence indicates that FMT can significantly ameliorate gastrointestinal symptoms and some core behavioral manifestations in patients with ASD [92]. This provides a theoretical foundation and prospective perspective for future exploration of microbiata-targeted interventions to indirectly improve social function and sexual health in neurodiverse individuals.

4.7 | Safety Considerations for FMT in Non-*Clostridioides difficile* Indications

Although FMT is increasingly explored beyond recurrent *Clostridioides difficile* infection (CDI), safety issues in non-CDI indications warrant explicit discussion, particularly immunogenicity and long-term metabolic sequelae. In a meta-analysis of nine high-quality randomized/prospective studies (756 FMTs), the pooled overall adverse-event (AE) rate was 39.3%, whereas serious AEs (SAEs) occurred in 5.3%; placebo arms reported 36.3% AEs and 2.96% SAEs, suggesting substantial background procedural/host contributions and attribution heterogeneity [93]. In a large systematic review and meta-analysis, the pooled rate of SAEs related to FMT was 0.65%, with specific SAEs including sepsis or sepsis-like conditions (0.19%), aspiration pneumonia (0.27%), and bowel perforation (0.20%) [94].

Regarding immunogenicity, a meta-analysis in IBD populations reported an overall pooled rate of IBD worsening after FMT of 14.9%, underscoring the need to prespecify immune-mediated endpoints and standardized flare definitions in non-CDI trials [95]. Long-term metabolic effects remain incompletely characterized. A case report described new-onset obesity after FMT from an overweight donor [96]. Besides, donor metabolic phenotype may influence recipient insulin sensitivity [96].

Therefore, future FMT studies targeting ED should incorporate structured safety monitoring, including infectious, immune-mediated, and metabolic endpoints. These quantitative estimates are cited to contextualize safety signals rather than to provide a formal pooled efficacy or risk assessment.

5 | Future Research Directions and Challenges

Although FMT shows preliminary potential in improving male sexual function, its clinical application faces multiple challenges. Currently, clinical translation of FMT and other gut microbiota-targeted interventions in sexual medicine remains constrained by limited high-quality evidence. Most existing studies lack rigorous randomization and allocation concealment, potentially introducing selection bias. Achieving a perfect double-blind design is challenging due to the specificity of the procedure, which may lead to performance and detection biases. Furthermore, significant variations in donor screening, dosage, administration routes, and the absence of standardized placebo controls limit the comparability of findings across studies [97]. Rigorous donor screening is fundamental to the safety and efficacy of FMT. Future strategies could include the use of engineered probiotics or phage therapies to achieve targeted modulation of specific microbial populations, thereby enabling precision treatments for ED-associated dysbiosis [97]. Additional research is necessary to confirm their long-term safety and effectiveness.

However, biomarkers predictive of donor therapeutic efficacy remain elusive, and current screening criteria continue to rely on empirical exclusion rather than positive selection strategies. Moreover, in existing studies, FMT materials are typically quantified based on fecal weight or suspension volume, lacking standardized conversion to viable bacterial counts or microbial diversity indices. The complexity and interindividual variability

of gut microbiota complicate research. Future studies must elucidate the specific roles of microbial taxa and metabolites in regulating sex hormones, immune responses, and neural signaling to clarify their direct links to sexual function. Additionally, existing research predominantly focuses on short-term outcomes, whereas long-term safety concerns, such as potential metabolic disturbances or immune dysregulation, require extended follow-up studies.

The development of personalized therapeutic strategies is another critical direction. Given the significant influence of host genetics, diet, and lifestyle on gut microbiota composition, future research should integrate multidimensional data to design precision interventions. Interdisciplinary collaboration is equally essential, combining microbiome science, endocrinology, and neuroscience to systematically unravel the molecular mechanisms of the "gut–gonadal axis."

Importantly, treating sexual dysfunction via gut microbiota interventions can create interdisciplinary friction among traditional clinical specialties, particularly when evidence is still emerging and indications remain investigational. Recently published principles and practice guidelines of microbiota medicine provide a structured framework for multidisciplinary communication and coordinated decision-making, which may help resolve such controversies. Accordingly, future clinical translation of FMT or other microbiota-targeted therapies for sexual dysfunction should be embedded within guideline-informed, integrative care models supported by multidisciplinary teams and shared decision-making. In addition, these guidelines emphasize that microbiome testing should be interpreted cautiously, and consumer-grade microbiome reports should not be used as standalone bases for diagnosis or therapeutic decisions [98].

Finally, ethical and regulatory issues must be addressed. As FMT applications expand, strict donor screening protocols, informed consent processes, and long-term monitoring frameworks must be established to balance therapeutic innovation with risk mitigation. Where applicable, standardized evaluation and reporting frameworks should be followed to improve transparency and comparability across studies.

Addressing these challenges through rigorously designed clinical trials and mechanistic studies will advance FMT from experimental therapy to evidence-based practice in sexual medicine.

6 | Conclusions and Perspectives

Based on preliminary findings, FMT represents a potential microbiome-targeted therapeutic strategy for male sexual dysfunction, particularly ED. Observational studies have reported that gut dysbiosis is associated with ED and ED-related phenotypes, with proposed links involving systemic inflammation, endothelial dysfunction, altered sex hormone profiles, and metabolic comorbidity. However, these associations do not establish causality and may be influenced by residual confounding and reverse causation. Preclinical studies and early clinical observations suggest that FMT can be accompanied by changes in microbial diversity and host immune–metabolic pathways, which may be relevant to penile hemodynamics and neuroendocrine regulation, although definitive mechanistic pathways in humans require confirmation. *Actinomyces* enrichment and *Ruminococcaceae_UCG_013* depletion correlate with impaired ED, offering diagnostic potential [10]. Furthermore, the abundance of *Alistipes* and *Clostridium XVIII* shows notable correlations with the severity of ED, indicating their potential role as biomarkers for disease progression [38]. Clinical observations and preclinical studies corroborate that FMT alleviates sexual dysfunction associated with gut dysbiosis and exhibits synergistic therapeutic effects in ED comorbid with metabolic disorders such as diabetes and obesity. Notably, *Actinobacteria* may exacerbate oxidative stress via the gut–gutvasculature axis, whereas FMT intervention effectively reverses these pathological alterations, underscoring the critical role of precise microbial modulation in therapeutic outcomes.

Nevertheless, translating microbiome research in ED into clinical practice remains difficult. The current evidence base is limited by small cohorts and substantial heterogeneity across studies, including differences in participant selection, microbiome profiling workflows, and outcome measurement. In human observational work, several factors that affect both the gut microbiome and erectile function are not consistently captured or adjusted in the analysis. These include recent antibiotic exposure, proton-pump inhibitor use, diet, obesity and metabolic comorbidity, and obstructive sleep apnea. As a result, many reported microbiome associations should be interpreted cautiously and not treated as proof of causality. Mendelian randomization studies offer supportive signals for specific taxa, but they do not replace interventional evidence.

Mechanistic links also remain incomplete. Inflammation, endothelial dysfunction, and NO signaling currently have the most coherent support across the available data, whereas the roles of microbial metabolites and neuroendocrine pathways are still largely inferential and need direct testing in standardized models. Because ED is a non-CDI indication, FMT should be viewed as an investigational approach. Any move towards clinical use will require well-designed trials and clearer standardization of donor screening, product preparation, administration route, dosing, and follow-up. Long-term safety must be addressed with particular care, including the risks of infection transmission and unintended metabolic effects, supported by larger longitudinal studies with consistent AE reporting.

Future research should prioritize more robust prospective designs with predefined covariates and standardized outcomes, along with deeper mechanistic experiments connecting microbial function to host pathways. Equally important is the development of clinically meaningful, microbiome-informed subtypes that can guide precision prevention and treatment.

Author Contributions

Junyi Chen: writing – original draft, methodology, validation, investigation, visualization. **Chenfeng Bu:** methodology, validation, investigation, visualization. **Xia Li:** methodology, validation, visualization. **Lei Wu:** conceptualization, methodology, writing – review and editing, funding acquisition, resources, supervision, project administration. **Xingxiang He:** conceptualization, methodology,

writing – review and editing, funding acquisition, resources, supervision, project administration.

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Conflicts of Interest

Xingxiang He is the Associate Editor of *Microbiota Medicine Research*. To minimize bias, he was excluded from all editorial decision-making related to the acceptance of this article for publication. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during this study.

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