Jurnal Sosial dan Sains (SOSAINS)
p-ISSN 2774-7018 e-ISSN 2774-700x

Gut Microbiota on Erectile Dysfunction: A Systematic Review

Revantoro Artha Dwiprawira, Ariyo Sakso Bintoro
Naval Central Hospital Ramelan Departement of Surgery Sub-departement of Urology, Surabaya, Indonesia
revanartha@gmail.com

ABSTRACT

This study aims to evaluated relationship between gut microbiota and ED. A systematic review was conducted with PRISMA 2020 guidelines, with PICO framework to focus on individuals with ED. The intervention analyzed was gut microbiota compared to healthy controls, with the primary outcome being gut microbiota associated with ED. Search was performed across PubMed, Scopus, Web of Science, and Cochrane Library from 2020 to 2025 using keywords such as "gut microbiome," "gut microbiota," "intestinal microbiome," and "gut flora" combined with "erectile dysfunction." Inclusion and exclusion criteria were applied, and the risk of bias in studies was assessed using the Newcastle-Ottawa Quality Assessment Scale. The results show q total of 64 studies underwent screening, 7 were included in the final analysis. The results showed correlation between ED and changes in the gut microbiota. A higher risk of ED was associated with increased populations of Lachnospiraceae, Oscillibacter, Tyzzerella3, Senegalimassilia, and Actinomyces. On the other present, a lower risk of ED was related to Ruminococcaceae UCG013, Coprococcus 1, Lachnospiraceae FCS020, Prevotella, and Bifidobacterium. Moreover, ED patients had more species of Streptococcus, Subdoligranulum, Bacteroides, Fusobacterium, and Escherichia-Shigella genera compared to species Blautia, Roseburia, Ruminiclostridium 5, and Lactococcus. The role of gut microbiota in ED, with Lachnospiraceae, Oscillibacter, Tyzzerella3, and Senegalimassilia increasing risk, while Ruminococcaceae UCG013 is protective. However, further research is needed to understand microbial mechanisms and explore gut microbiota modulation as a potential therapeutic strategy.

Keywords: Dysfunction, Gut Microbiota, Systematic Review

INTRODUCTION

Erectile dysfunction (ED) is a widespread health issue that significantly impacts both the physical and psychological health of affected individuals and their partners. It can lead to conditions such as depression, anxiety, and other mental health issues, while also disrupting sexual relationships and family dynamics. According to epidemiological studies, approximately 150 million men across the globe are affected by varying levels of ED, with projections suggesting this number could increase to 300 million by 2025. Inflammation is a key factor in the development of ED. Damage to the endothelial cells triggers an inflammatory response in the vessel walls, resulting in higher production of inflammatory molecules and cell adhesion factors, which can lead to the formation of plaques in the penile blood vessels (Su et al., 2023).

The human gastrointestinal tract is home to a diverse array of microorganisms, collectively known as the *gut microbiota*. This microbiota functions as a natural barrier, playing a critical role in maintaining overall health and homeostasis (Sender et al., 2016). Based on their impact on human health, gut microorganisms can be categorized into three groups: beneficial bacteria, opportunistic bacteria, and pathogenic bacteria. A delicate balance between these groups is essential for the proper functioning of the intestinal environment. Beneficial

bacteria, such as *Bifidobacteria* and *Lactobacillus*, contribute to gut health, while harmful bacteria, such as *Escherichia coli* and *Enterococcus*, can lead to dysfunction. Disruptions in this balance due to both internal and external factors can result in a condition known as *dysbiosis*, which has been linked to a variety of diseases, including inflammatory bowel disease, irritable bowel syndrome, non-alcoholic fatty liver disease, viral hepatitis, and metabolic syndrome (Lin et al., 2018).

These imbalances not only contribute to the onset of these diseases but can also accelerate their progression. It has been suggested that *gut microbiota* plays a role in various factors such as endocrine function, psychological well-being, and metabolic health. Erectile dysfunction (ED) is commonly attributed to several causes, including vascular, neurological, psychological, and hormonal factors. ED is often linked with conditions such as diabetes, hypertension, hyperlipidemia, obesity, and testosterone deficiency. Psychological contributors, such as performance anxiety and relationship difficulties, are also frequently reported causes. Given these associations, it is plausible to hypothesize that *gut microbiota* composition may be related to ED. Furthermore, the *gut microbiota* distribution may differ between individuals with ED and healthy controls, suggesting a potential relationship between *gut microbiota* and the occurrence of ED (Geng et al., 2021).

Previous studies have examined the connection between *gut microbiota* and various diseases, including metabolic disorders and inflammation (Lin et al., 2018; Sender et al., 2016). Geng et al. (2021) further investigated the potential relationship between *gut microbiota* and erectile dysfunction, proposing that the composition of *gut microbiota* could influence the development of ED through its effect on inflammation and endocrine function. These studies laid the groundwork for understanding how microbiota imbalances might contribute to ED, though the relationship has not been fully explored. Our research aims to address this gap by systematically reviewing existing literature and synthesizing findings on how *gut microbiota* composition influences ED, offering a broader understanding of this link.

To prove this hypothesis, several case studies have been conducted regarding *gut microbiota* and erectile dysfunction, which have shown significant results related to *gut microbiota* and erectile dysfunction. Therefore, the purpose of this study is to systematically review several studies related to *gut microbiota* in the context of erectile dysfunction. The findings could benefit clinicians by providing a more holistic understanding of ED and suggesting the inclusion of *gut microbiota* management in therapeutic approaches. For researchers, it will serve as a reference for future studies exploring microbiota-based interventions in managing ED.

RESEARCH METHOD

This paper follows the PRISMA guidelines for systematic reviews (Page, McKenzie, et al., 2021; Page, Moher, et al., 2021). A comprehensive search was conducted across PubMed, Scopus, Web of Science, and the Cochrane Library for studies published between 2020 and 2025. The search terms included *"gut microbiome," "gut microbiota," "intestinal microbiome,"* and *"gut flora"* combined with *"erectile dysfunction"* to identify relevant literature. Restricting the search to the last five years ensured the inclusion of current and clinically relevant findings.

The inclusion criteria prioritized international, English-language, open-access articles with full-text availability to minimize bias and facilitate analysis. Selected studies examined the association between *gut microbiota* and erectile dysfunction (ED), including its effects, microbial characteristics in ED patients, comparative microbiome analyses, and potential causal relationships. Case-control and Mendelian randomization studies were emphasized due to their methodological strength in establishing associations.

Exclusion criteria removed studies unrelated to the *gut microbiota*-ED connection, as well as case reports and animal studies, which were deemed outside the scope of this review. Following article selection, data extraction focused on study methodologies and the taxonomic classification (*e.g.*, genus, family) of *gut microbiota* linked to ED.

Risk of Bias

The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS), which was employed to evaluate the risk of bias in the seven studies included in this review. Based on the NOS scores, two studies were rated with a score of six out of maximum nine , four studies received a score of seven out of maximum nine, while one study achieved a score of at the maximum which is nine (Hartling *et al.*, 2013; Lo, Mertz and Loeb, 2014).

Data Analysis

In the articles reviewed, bacterial taxa were extracted from the gut microbiome, analyzed, and then compared to those from control groups. The aim was to determine whether there were significant differences between the gut microbiota taxa of ED patients and those of healthy controls. Following the analysis, comparisons were made with previous studies to validate the findings. Several studies included in the review shared the same patient populations, but investigated different aspects, such as the causal effect of gut microbiota on ED, the causal relationship between gut microbiota and ED, and the specific gut microbiota that may increase the risk of ED. Despite these different focuses, the studies generally indicated similar results regarding the bacterial taxa found in ED patients compared to the control group.

RESULTS AND DISCUSSION

The search in the databases, the results were as follows 64 articles. 64 articles underwent screening, 7 were included in the final analysis. This can be seen in Figure 1 for further explanation regarding the article search strategy (Geng et al., 2021; Su et al., 2023; Zhang et al., 2023; Chen et al., 2024; Kang et al., 2024; Qiao et al., 2024; Zhu et al., 2024).

Based on data obtained from seven studies, a total of 217,009 participants were included, comprising 6,301 patients diagnosed with erectile dysfunction (ED) and 210,708 healthy controls. Of the reviewed studies, four utilized a European population of patients with ED, while three focused on patients from China. Diagnostic criteria for ED varied across studies; some utilized the International Index of Erectile Function (IIEF-5), while others relied on the International Classification of Diseases (ICD-10) codes (N48.4 and F52.2), medical intervention history for ED (including surgical codes [OPCS-4: L97.1 and N32.6]), oral medications (vardenafil/Levitra, tadalafil/Cialis, or sildenafil/Viagra), or self-reports from participants(Geng et al., 2021; Su et al., 2023; Zhang et al., 2023; Chen et al., 2024; Kang et al., 2024; Qiao et al., 2024; Zhu et al., 2024).

Additionally, the genome-wide association study (GWAS) statistics for ED were extracted from the study by Bovijn et al., which included data from the Partners HealthCare Biobank, the Estonian Genome Center at the University of Tartu, and the UK Biobank. The study encompassed 223,805 participants of European ancestry, of whom 6,175 were diagnosed

with ED (Bovijn et al., 2019). Further details regarding study design, data analysis methods, and population characteristics are presented in Table 1.

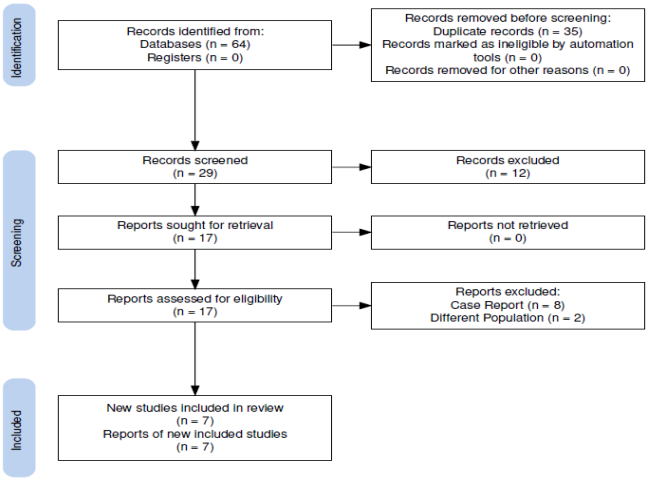

Figure 1. Flow diagram on article selection process
(Page, McKenzie, et al., 2021; Page, Moher, et al., 2021)

Table 1. Results of articles analysis, guts microbiota on ED

Bacterial Genus/Family	First Author, Year	Study Design	Country /Continent	Causal Relationship	Odds Ratio (OR)	95% Confidence Interval (CI)	Method	p-value	Study Population
Lachnospiraceae (Family)	Chen et al. (2024)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.265	1.060 – 1.509	IVW	0.008	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Lachnospiraceae NC2004	Chen et al. (2024)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.189	1.028 – 1.374	IVW	0.019	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Oscillibacter	Chen et al. (2024)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.200	1.035 – 1.393	IVW	0.016	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Tyzzerella3	Chen et al. (2024)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.134	1.018 – 1.262	IVW	0.023	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)

Ruminococcaceae UCG013	Chen et al. (2024)	Mendelian Randomization (MR)	Europe	Negative (Decreased in ED)	0.761	0.626 – 0.926	IVW	0.023	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Streptococcus	Geng et al. (2021)	Case-Control	China	Positive (Increased in ED)	-	-	t-test	0.043	30 ED patients, 30 healthy donors
Subdoligranulum	Geng et al. (2021)	Case-Control	China	Positive (Increased in ED)	-	-	t-test	0.036	30 ED patients, 30 healthy donors
Prevotella	Geng et al. (2021)	Case-Control	China	Negative (Decreased in ED)	-	-	t-test	0.025	30 ED patients, 30 healthy donors
Blautia	Geng et al. (2021)	Case-Control	China	Negative (Decreased in ED)	-	-	t-test	0.048	30 ED patients, 30 healthy donors
Lachnospiraceae NK4A136	Geng et al. (2021)	Case-Control	China	Negative (Decreased in ED)	-	-	t-test	0.006	30 ED patients, 30 healthy donors
Roseburia	Geng et al. (2021)	Case-Control	China	Negative (Decreased in ED)	-	-	t-test	0.017	30 ED patients, 30 healthy donors
Actinomyces	Kang et al. (2023)	Case-Control	China	Positive (Enriched in ED)	-	-	LEfSe, Spearman	<0.05	43 ED patients, 16 healthy controls
Coprococcus 1	Kang et al. (2023)	Case-Control	China	Negative (Depleted in ED)	-	-	LEfSe, Spearman	<0.05	43 ED patients, 16 healthy controls
Ruminiclostridium 5	Kang et al. (2023)	Case-Control	China	Negative (Depleted in ED)	-	-	LEfSe, Spearman	<0.05	43 ED patients, 16 healthy controls
Lachnospiraceae FCS020	Kang et al. (2023)	Case-Control	China	Negative (Depleted in ED)	-	-	LEfSe, Spearman correlation	<0.05	43 ED patients, 16 healthy controls
Ruminococcaceae UCG 002	Kang et al. (2023)	Case-Control	China	Negative (Depleted in ED)erectile function)	-	-	LEfSe, Spearman correlation	<0.05	43 ED patients, 16 healthy controls
Lactococcus	Kang et al. (2023)	Case-Control	China	Negative (Depleted in ED)	-	-	LEfSe, Spearman correlation	<0.05	43 ED patients, 16 healthy controls
Bacteroides	Qiao et al. (2023)	Case-Control	China	Positive (Increased in ED)	-	-	LEfSe, Spearman	<0.05	53 ED patients, 32 healthy controls

Fusobacterium	Qiao et al. (2023)	Case-Control	China	Positive (Increased in ED)	-	-	LEfSe, Spearman	<0.05	53 ED patients, 32 healthy controls
Lachnoclostridium	Qiao et al. (2023)	Case-Control	China	Positive (Increased in ED)	-	-	LEfSe, Spearman	<0.05	53 ED patients, 32 healthy controls
Megamonas	Qiao et al. (2023)	Case-Control	China	Positive (Increased in ED)	-	-	LEfSe, Spearman correlation	<0.05	53 ED patients, 32 healthy controls
Escherichia-Shigella	Qiao et al. (2023)	Case-Control	China	Positive (Increased in ED)	-	-	LEfSe, Spearman correlation	<0.05	53 ED patients, 32 healthy controls
Bifidobacterium	Qiao et al. (2023)	Case-Control	China	Negative (Decreased in ED)	-	-	LEfSe, Spearman	<0.05	53 ED patients, 32 healthy controls
Lachnospiraceae (Family)	Su et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.265	1.054 – 1.519	IVW	0.012	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Senegalimassilia	Su et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.320	1.064 – 1.638	IVW	0.012	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Lachnospiraceae NC2004	Su et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.197	1.018 – 1.407	IVW	0.030	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Tyzzerella3	Su et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.138	1.017 – 1.273	IVW	0.024	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Oscillibacter	Su et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.201	1.035 – 1.393	IVW	0.016	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Ruminococcaceae UCG013	Su et al. (2023)	Mendelian Randomization (MR)	Europe	Negative (Decreased in ED)	0.770	0.615 – 0.965	IVW	0.023	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)

Lachnospiraceae (Family)	Zhu et al. (2021)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.265	1.060 – 1.509	IVW	0.008	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Lachnospiraceae NC2004	Zhu et al. (2021)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.189	1.028 – 1.374	IVW	0.019	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Oscillibacter	Zhu et al. (2021)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.200	1.035 – 1.393	IVW	0.016	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Senegalimassilia	Zhu et al. (2021)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.355	1.113 – 1.651	IVW	0.002	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Tyzzerella3	Zhu et al. (2021)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.133	1.018 – 1.262	IVW	0.022	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Ruminococcaceae UCG013	Zhu et al. (2021)	Mendelian Randomization (MR)	Europe	Negative (Decreased in ED)	0.761	0.626 – 0.926	IVW	0.023	223,805 participants ED Cases: 6,175 ED patients ED Controls: 217,630 non-ED participants (ED GWAS), 18,340 participants (microbiota GWAS)
Lachnospiraceae (Family)	Zhang et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.265	1.054 – 1.519	IVW	0.012	223,805 participants (ED GWAS), 18,340 participants (microbiota GWAS)
Senegalimassilia	Zhang et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.320	1.064 – 1.638	IVW	0.012	223,805 participants (ED GWAS), 18,340 participants (microbiota GWAS)
Lachnospiraceae NC2004 group	Zhang et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.197	1.018 – 1.407	IVW	0.030	223,805 participants (ED GWAS), 18,340 participants (microbiota GWAS)
Tyzzerella3	Zhang et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.138	1.017 – 1.273	IVW	0.024	223,805 participants (ED GWAS), 18,340 participants (microbiota GWAS)

Oscillibacter	Zhang et al. (2023)	Mendelian Randomization (MR)	Europe	Positive (Increased in ED)	1.201	1.035 – 1.393	IVW	0.016	223,805 participants (ED GWAS), 18,340 participants (microbiota GWAS)
Ruminococcaceae UCG013	Zhang et al. (2023)	Mendelian Randomization (MR)	Europe	Negative (Decreased in ED)	0.770	0.615 – 0.965	IVW	0.023	223,805 participants (ED GWAS), 18,340 participants (microbiota GWAS)

Quality Score

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS) to evaluate risk of bias. Among the seven studies reviewed, two scored 6/9, four scored 7/9, and one achieved the maximum score of 9/9. Three studies utilized representative samples of ED patients, while the remaining two were considered higher risk due to less representative ED populations. The study population demonstrated potential bias with its predominantly European demographic, limiting global generalizability due to insufficient diversity.

All studies derived their control groups from the same population base. Four studies obtained data from secure medical records, while three relied on participant self-reports. Six studies reported similar exposure levels between ED cases and healthy controls, whereas one study showed slight exposure differences that may introduce bias (Hartling et al., 2013; Lo, Mertz & Loeb, 2014). Overall risk of bias was generally low, with only two studies exhibiting medium risk. The complete comparative assessment is presented in Table 2.

Table 2. Quality assessment using New Castle-Ottawa Scale for risk of bias

Study ID	New-Castle Ottawa Scale									
	Selection				Comparability	Exposure			Total Score	Overall
	Is the case definition adequate? (Maximum : ★)	Representative of The Cases (Maximum : ★)	Selection of Controls (Maximum : ★)	Definition of Controls (Maximum : ★)	Comparability of cases and controls on the basis of the design or analysis (Maximum : ★★)	Ascertainment of exposure (Maximum : ★)	Same method of ascertainment for cases and controls (Maximum : ★)	Non-Response rate (Maximum : ★)		
Chen, 2024	★	★	★	★	Gut Microbiomes on ED ★★	★	-	-	★★★★ ★★★(7)	Low Risk Of Bias
Geng, 2021	★	★	★	★	Gut Microbiomes on ED ★★	-	★	-	★★★★ ★★★(7)	Low Risk Of Bias
Kang, 2023	★	-	★	★	Gut Microbiomes on ED ★★	-	★	-	★★★★ ★★(6)	Medium Risk Of Bias

Su, 2023	★	-	★	★	Gut Microbiomes on ED ★★	-	★	-	★★★★ ★★(6)	Medium Risk Of Bias
Zhang, 2023	-	-	★	★	Gut Microbiomes on ED ★★	★	★	★	★★★★ ★★★ (7)	Low Risk Of Bias
Zhu, 2021	★	-	★	★	Gut Microbiomes on ED ★★	★	★	-	★★★★ ★★★ (7)	Low Risk Of Bias
Qiao, 2023	★	★	★	★	Gut Microbiomes on ED ★★	★	★	★	★★★★ ★★★★ ★ (9)	Low Risk Of Bias

Outcome

Based on the results of the studies reviewed, a total of seven articles were examined to assess the relationship between gut microbiota and the occurrence of erectile dysfunction (ED) in patients. The articles reviewed presented varying findings regarding the influence of different gut microbiota taxa on ED, although not all bacterial taxa identified were identical. However, they all belonged to the same genus. The accumulated evidence from these studies revealed common trends, particularly the genus Ruminococcaceae, which consistently showed a reduction in abundance in ED patients. In contrast, the genus or family Lachnospiraceae tended to show an increase in abundance in ED patients when compared to control groups (Geng et al., 2021; Su et al., 2023; Zhang et al., 2023; Chen et al., 2024; Kang et al., 2024; Qiao et al., 2024; Zhu et al., 2024).

Multiple studies have demonstrated significant associations between gut microbiota composition and erectile dysfunction (ED). Increased abundance of the Lachnospiraceae family (OR: 1.265; 95% CI: 1.060–1.509; p=0.008) and genera such as Lachnospiraceae NC2004 (OR: 1.189; 95% CI: 1.028–1.374; p=0.019), Oscillibacter (OR: 1.200; 95% CI: 1.035–1.393; p=0.016), Tyzzerella3 (OR: 1.134; 95% CI: 1.018–1.262; p=0.023), Senegalimassilia (OR: 1.320; 95% CI: 1.064–1.638; p=0.012), and Actinomyces ($p<0.05$) were consistently linked to a higher risk of ED. Conversely, decreased abundance of Ruminococcaceae UCG013 (OR: 0.761; 95% CI: 0.626–0.926; p=0.023) was associated with a reduced risk of ED (Geng et al., 2021; Su et al., 2023; Zhang et al., 2023; Chen et al., 2024; Kang et al., 2024; Qiao et al., 2024; Zhu et al., 2024).

Other findings revealed that genera such as Streptococcus (p=0.043), Subdoligranulum (p=0.036), Bacteroides ($p<0.05$), Fusobacterium ($p<0.05$), Lachnoclostridium ($p<0.05$), Megamonas ($p<0.05$), and Escherichia-Shigella ($p<0.05$) were significantly more abundant in ED patients, indicating a positive association with ED. In contrast, genera such as Prevotella (p=0.025), Blautia (p=0.048), Lachnospiraceae NK4A136 (p=0.006), Roseburia (p=0.017), Coprococcus 1 ($p<0.05$), Ruminiclostridium 5 ($p<0.05$), Lachnospiraceae FCS020 ($p<0.05$), Ruminococcaceae UCG 002 ($p<0.05$), Lactococcus ($p<0.05$), and Bifidobacterium ($p<0.05$) were significantly less abundant in ED patients, suggesting a protective effect against ED

(Geng et al., 2021; Su et al., 2023; Zhang et al., 2023; Chen et al., 2024; Kang et al., 2024; Qiao et al., 2024; Zhu et al., 2024).

Discussion

The results of this systematic review demonstrate a significant association between gut microbiota composition and the occurrence of erectile dysfunction (ED). Among the seven analyzed studies, a consistent pattern was observed regarding alterations in specific bacterial taxa in patients with ED. In general, a decreased abundance of the genus Ruminococcaceae, particularly the sub-genus Ruminococcaceae UCG013, was correlated with a reduced risk of ED. Conversely, an increased abundance of the genus or family Lachnospiraceae, including sub-genera such as Lachnospiraceae NC2004, Lachnospiraceae NK4A136, and Lachnospiraceae FCS020, was associated with an elevated risk of ED. Additionally, other genera that were significantly more abundant in ED patients included Oscillibacter, Tyzzerella3, Senegalimassilia, Actinomyces, Streptococcus, Subdoligranulum, Bacteroides, Fusobacterium, Lachnoclostridium, Megamonas, and Escherichia-Shigella, indicating a positive association with ED. In contrast, several genera such as Prevotella, Blautia, Roseburia, Coprococcus 1, Ruminiclostridium 5, Ruminococcaceae UCG002, Lactococcus, and Bifidobacterium were found to be less abundant in ED patients and are presumed to exert a protective effect against the development of ED (Geng et al., 2021; Su et al., 2023; Zhang et al., 2023; Chen et al., 2024; Kang et al., 2024; Qiao et al., 2024; Zhu et al., 2024). These findings indicate that gut microbiota imbalance, or gut dysbiosis, may contribute to the pathogenesis of erectile dysfunction.

The gut microbiota is primarily located within the gastrointestinal tract and constitutes a vital component of the human microbiome. It is characterized by extensive species diversity and substantial abundance, with the functional potential of various gut microbiota increasingly recognized. Beyond its role in the breakdown and storage of lipids, the gut microbiota contributes to the regulation of immune, endocrine, metabolic, and neurological functions through immunological, neuroendocrine, and vagal mechanisms(Zang et al., 2023). Several hypotheses have been proposed to underscore the critical role of the gut microbiota within these interconnected systems, including the gut-brain axis, gut-liver axis, gut-muscle axis, and gut-kidney axis. Recently, the influence of gut microbiota on the male reproductive system has garnered significant attention, particularly in relation to androgens. In male rodents and other mammals, Leydig cells located in the testicular interstitium are responsible for producing the majority of androgens under the regulation of the hypothalamic-pituitary-gonadal (HPG) axis. Androgens represent key hormones that bridge the endocrine and reproductive systems, exerting widespread effects on multiple organs and tissues. Their active forms, primarily testosterone and dihydrotestosterone (DHT), play essential roles in the development and maintenance of masculinization, normal sexual function, and spermatogenesis (Li et al., 2022).

Erectile dysfunction (ED) is a common male sexual disorder, defined as the inability of an adult male to achieve or maintain a penile erection sufficient for satisfactory sexual intercourse. This condition can result in both psychological and physiological distress. The pathogenesis of ED involves multiple contributing factors, encompassing both physiological and psychological domains. The primary mechanisms include endocrine dysfunction,

neurological impairment, and vascular abnormalities. Additionally, metabolic diseases, cardiovascular disorders, neurological conditions, structural abnormalities, pharmacological agents, and lifestyle-related factors may also contribute to the development of ED (Zhu et al., 2024).

Erectile function is primarily under parasympathetic control, with the vagus nerve being the largest parasympathetic nerve in the body considered a critical component of the broader brain–microbiome–gut axis. Parasympathetic signal transmission via the vagus nerve can influence gastrointestinal function, including the composition of the gut microbiota. Alterations in the gut microbiota may, in turn, affect vagal signaling and potentially impact erectile function. Furthermore, the gut microbiota can regulate glucose and lipid metabolism, thereby influencing endothelial function within the penile vasculature. Additionally, the gut microbiota may exert modulatory effects on neurotransmitters, testosterone, and thyroid function, ultimately contributing to the onset and progression of erectile dysfunction(Zhu et al., 2024).

Zhu et al. reported that increased abundance of the family Lachnospiraceae, and the genera Lachnospiraceae_NC2004_group, Oscillibacter, Senegalimassilia, and Tyzzerella_3 was associated with an elevated risk of erectile dysfunction, whereas increased abundance of Ruminococcaceae_UCG-013 was associated with a reduced risk of erectile dysfunction (Zhu et al., 2024). Su et al. in their study reported that the genera Oscillibacter, Tyzzerella_3, and Senegalimassilia were associated with an increased risk of erectile dysfunction progression (Su et al., 2023). Qiao et al. observed differences in gut microbiota composition between the control group and the erectile dysfunction (ED) group, demonstrating distinct microbial community structures (β-diversity) between the two groups. LEfSe analysis identified gut microecological disturbances in ED patients. Specifically, Bifidobacterium exhibited a higher relative abundance in the control group, whereas Bacteroides, Megamonas, Escherichia-Shigella, Lachnoclostridium, Roseburia, Fusobacterium, and Coprococcus showed higher relative abundance in the ED group (Qiao et al., 2024).

Kang et al. identified significant alterations in gut microbiota composition in patients with erectile dysfunction (ED). Specifically, Actinomyces showed a significant increase, whereas Coprococcus_1, Lachnospiraceae_FCS020_group, Lactococcus, Ruminiclostridium_5, and Ruminococcaceae_UCG_002 were decreased in ED patients. Spearman correlation analysis revealed a significant negative association between Actinomyces abundance and Nocturnal Penile Tumescence and Rigidity (NPTR) test results, indicating that higher Actinomyces levels were associated with worse erectile function. Conversely, Coprococcus_1, Lachnospiraceae_FCS020_group, Ruminiclostridium_5, and Ruminococcaceae_UCG_002 demonstrated positive correlations with both International Index of Erectile Function-5 (IIEF-5) scores and NPTR results. Furthermore, random forest classification based on relative taxonomic abundance showed good diagnostic efficacy with an AUC of 0.72. These findings suggest that gut microbiota profiling may serve as a potential biomarker for distinguishing ED patients from healthy individuals, indicating a promising diagnostic utility for ED(Kang et al., 2024).

Chen et al. reported a positive causal relationship between the genera Lachnospiraceae_NC2004_group, Oscillibacter, Tyzzerella_3, and the family Lachnospiraceae with erectile dysfunction (ED) in men. Conversely, a negative causal

relationship was observed between the genus Ruminococcaceae_UCG-013 and ED. These findings indicate that distinct gut microbiota communities may exert differential effects on the occurrence of ED in the male population (Chen et al., 2024). Zhang et al. evaluated the potential causal relationship between gut microbiota and erectile dysfunction (ED) by utilizing large-scale genome-wide association study (GWAS) data for both microbiota and ED. The analysis identified six microbial features as essential contributors to the pathogenesis of ED. Increased abundance of Lachnospiraceae, Senegalimassilia, Lachnospiraceae_NC2004_group, Tyzzerella_3, and Oscillibacter (odds ratio [OR] >1, $P < 0.05$) was associated with a higher risk of ED, while increased abundance of Ruminococcaceae_UCG-013 (OR <1, $P < 0.05$) appeared to exert a protective effect against ED (Zhang et al., 2023).

Conditions influenced by the gut microbiome exhibit significant correlations with the incidence of erectile dysfunction (ED), which is primarily driven by vascular, hormonal, and psychological factors. Based on these theoretical frameworks, disturbances in gut microbiota can be rationally associated with an increased risk of ED (Zhang et al., 2023). Normal erection is the result of a complex sequence of processes influenced by metabolic diseases, neurological and psychological disorders, vascular conditions, metabolic dysregulation, and inflammatory factors. Metabolism-related diseases, including diabetes mellitus, hypertension, dyslipidemia, and obesity, are all closely associated with erectile dysfunction (ED). Emerging evidence underscores the crucial role of the gut microbiota in the regulation of energy intake and glucose and lipid metabolism. Salonen et al. reported that increased abundance of Lachnospiraceae may lead to lipid metabolic dysregulation. Diabetes mellitus can induce neuropathy accompanied by decreased testicular hormone levels, ultimately resulting in ED. Furthermore, Que et al. found that increased abundance of Tyzzerella was also closely correlated with impaired glucose tolerance. Research on Senegalimassilia remains limited, with only a few studies indicating its association with hypertension. The abundance of Senegalimassilia in the gut has been positively correlated with blood pressure (diastolic blood pressure, systolic blood pressure, and mean arterial pressure). Hypertension may lead to endothelial cell damage, impairing vasodilation and blood flow, thereby affecting erectile function. Oscillibacter may exacerbate vascular disease, with its increased abundance showing a strong correlation with atherosclerotic damage. Atherosclerosis causes narrowing and occlusion of small arteries in the corpus cavernosum of the penis, thereby impairing penile blood flow and erectile function (Defeudis et al., 2022; Zhu et al., 2024).

Multiple studies have demonstrated that the pathogenesis of erectile dysfunction (ED) is associated with inflammatory responses. Streptococcus, predominantly pro-inflammatory, includes Group A Streptococcus (GAS), a Gram-positive pathogen capable of causing various diseases, including severe invasive infections. Studies have observed increased expression of Streptococcus and decreased abundance of Rothia, both of which are associated with inflammatory responses. Given that ED involves inflammatory processes, Streptococcus and Rothia exhibit correlations with the occurrence of ED (Geng et al., 2021). Actinomyces, as an opportunistic pathogen, primarily colonizes the upper gastrointestinal tract. Forbes et al. analyzed the gut microbiome composition across various inflammatory diseases, including inflammatory bowel disease (IBD), multiple sclerosis, and rheumatoid arthritis. The findings demonstrated a significant increase in Actinomyces abundance in disease groups compared to

healthy controls, indicating a critical role of this genus in the pathogenesis of inflammation-related disorders. Inflammatory responses are hypothesized to underlie endothelial dysfunction in erectile dysfunction (ED). Scientific evidence shows that elevated levels of systemic inflammatory cytokines and endothelial prothrombotic compounds correlate with the progression of ED (Kang et al., 2024).

Coprococcus, classically regarded as a common commensal bacterium, possesses the ability to metabolize dietary fibers consumed by humans. Previous studies have demonstrated that higher Coprococcus abundance is associated with a lower prevalence of metabolic diseases such as type 2 diabetes mellitus, dyslipidemia, and obesity. Wei et al. reported a reduction in Coprococcus abundance in cases of hyperuricemia. These metabolic conditions, as risk factors for erectile dysfunction (ED), may contribute to its development through modulation of gut microbiota. The biological function of the Lachnospiraceae_FCS020_group remains incompletely understood; however, recent studies have reported its correlation with cognitive function in middle-aged adult populations. Lactococcus is recognized as a commensal gut bacterium with probiotic properties that play a vital role in human health. In patients with nephrolithiasis, a decrease in _Ruminiclostridium_5 abundance has been observed, while administration of specific prebiotics has been shown to improve gut ecological homeostasis by increasing _Ruminiclostridium_5 abundance. Ruminococcaceae, in general, are considered to be associated with disease, with reductions observed in patients with inflammatory bowel disease (IBD). However, the specific role of Ruminococcaceae_UCG_002 remains to be fully elucidated (Kang et al., 2024).

Erectile dysfunction (ED) shows a significant correlation with gut microbial diversity in men. The gut microbiota is capable of modulating erectile function through the regulation of hormone levels, inflammatory mediators, and various other physiological factors. Modulation of the gut microbiota has emerged as a potential therapeutic approach for the prevention and management of ED in the future(Geng et al., 2021). The limitations of this systematic review include the predominance of observational studies, which precludes the establishment of a causal relationship between gut microbiota composition and the incidence of erectile dysfunction (ED). Furthermore, taxonomic inconsistencies were observed across studies, despite referring to the same genera or families, indicating potential bias in microbial identification.

CONCLUSION

This systematic review highlights the significant association between gut microbiota composition and the pathogenesis of erectile dysfunction (ED). Our analysis identifies distinct microbial signatures associated with ED risk, including elevated levels of *Lachnospiraceae*, *Oscillibacter*, and *Tyzzerella_3*, while *Ruminococcaceae_UCG-013* appears to exert protective effects. The findings suggest that gut microbiota may influence erectile function through multiple interconnected pathways, including metabolic regulation, endocrine modulation, inflammatory responses, and neurovascular mechanisms. These results position gut microbiota modulation as a promising therapeutic target for ED management. Future research should prioritize longitudinal studies to establish causal relationships between specific microbial profiles and ED development. Additionally, clinical investigations into microbiota-

targeted interventions—including probiotics, prebiotics, and dietary modifications—could yield valuable insights for both preventive and therapeutic strategies. Such efforts may pave the way for novel, microbiome-based approaches to ED treatment.

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