Review Article

narra j

Review Article

Effective probiotic regimens for bacterial vaginosis treatment and recurrence prevention: A systematic review

Udjianto Udjianto[1,2*], Noorhamdani A. Sirat[3], Bambang Rahardjo[4] and Lilik Zuhriyah[5]

[1]Doctoral Program in Medical Science, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia; [2]Department of Obstetrics and Gynecology, Bhayangkara Hospital, Surabaya, Indonesia; [3]Department of Clinical Microbiology, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia; [4]Department of Obstetrics and Gynecology, Dr. Saiful Anwar Hospital, Malang, Indonesia; [5]Department of Environmental Health Sciences and Health Promotion, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

*Corresponding author: drudjianto@student.ub.ac.id

Abstract

Probiotics represent a promising alternative therapy for bacterial vaginosis; however, consensus on the most effective species, strains, and doses remains lacking, and long-term safety data are limited. The aim of this study was to evaluate the effectiveness of probiotics in managing bacterial vaginosis, considering species, strain, clinical outcomes, optimal dosage, duration, and side effects. This study included randomized-controlled trials (RCTs) published in English (2014–2024) on probiotic treatment for bacterial vaginosis, assessing species, strain, dose, duration, and efficacy. A systematic search was conducted on December 20, 2024, in Scopus, Web of Science, and PubMed using the keywords "vaginosis," "bacterial vaginosis," and "probiotic." Data were extracted and synthesized, and study quality was assessed using the Risk of Bias 2 tool, while NVivo 14 software facilitated thematic analysis. The systematic search yielded 1,560 initial records, of which 16 RCTs were included. The findings revealed that *Lactobacillus rhamnosus* TOM 22.8 (10×10^9 CFU/day for 10 days) was the most effective strain and dose, significantly improving Nugent scores, vaginal pH, and microbiota composition and reducing bacterial vaginosis recurrence rate. Alternative strains, including *L. crispatus, L. plantarum*, and *L. acidophilus*, showed therapeutic potential at doses of 1×10^8 to 5.4×10^9 CFU/day for treatment durations ranging from 6 days to 4 months. The reported side effects were mild and self-limiting. This study supports the use of probiotics as an adjunctive or alternative bacterial vaginosis treatment, emphasizing the need for a personalized approach based on patient characteristics. However, limitations such as small sample sizes and heterogeneous outcome measures necessitate further research. Larger, well-designed trials with standardized methodologies are required to refine probiotic recommendations.

Keywords: Bacterial vaginosis, probiotics, alternative therapies, vaginal diseases, women's health

https://narraj.org/

Introduction

Bacterial vaginosis is a common vaginal condition among women of reproductive age, with a global incidence of 23% to 29% [1]. The condition is characterized by dysbiosis, where the predominance of *Lactobacillus* sp. in the female reproductive tract is reduced or entirely supplanted by vaginal pathogens, primarily *Gardnerella* sp. [2]. Bacterial vaginosis is associated with significant morbidity and a high recurrence rate, affecting up to 50% of women of

Received: October 20, 2024 - Accepted: March 1, 2025 - Published online: March 10, 2025

reproductive age globally [3]. The lowest prevalence has been reported in Asia and Europe (4.5% to 24%), while the highest prevalence has been documented in Sub-Saharan Africa (6% to 58%) [4]. Therefore, bacterial vaginosis represents a significant global health concern due to its high prevalence, substantial morbidity, and frequent recurrence, particularly in regions with elevated incidence rates.

Bacterial vaginosis is diagnosed using Gram-stained smears (Nugent score 7–10), Amsel criteria, point-of-care diagnostics, or molecular tests [5,6]. Bacterial vaginosis is associated with pelvic inflammatory disease, late-trimester miscarriage, preterm birth, human immunodeficiency virus-1 transmission, and chorioamnionitis [7]. It adversely affects quality of life, job performance, and relationships, while increasing the risks of infertility, spontaneous abortion, and sexually transmitted infections [8,9]. Treatment for bacterial vaginosis involves oral or intravaginal antibiotics, such as metronidazole, clindamycin, or tinidazole, with initial efficacy of 50% to 80% [2]. However, relapse is common, affecting nearly 50% within 12 months, leading to repeated antibiotic use and drug-resistant bacteria [2,7]. Standard therapy with metronidazole often results in over 30% developing fungal vaginitis and more than 50% experiencing recurrence within three to six months [10].

Due to the reduced efficacy of antibiotics and high recurrence rate, probiotics are a promising alternative for preventing and treating bacterial vaginosis or as adjunctive therapy [11]. Both vaginal suppositories and oral ingestion have shown effectiveness, with oral ingestion also offering benefits for gastrointestinal health [12]. Several studies have explored probiotics for preventing and treating bacterial vaginosis [10,11,13]. A previous study highlighted the role of lactic acid bacteria in preventing bacterial vaginosis, fungal vaginitis, urinary tract infections, and sexually transmitted diseases [10]. Kyser *et al.* developed a three-dimensional-printed scaffold with *Lactobacillus crispatus* for gynecological use [1], while Lyu *et al.* selected viable female probiotic strains and established in vitro profiles for product characteristic [14]. Both studies highlight the potential of probiotics in treating bacterial vaginosis [1,14].

Despite numerous studies on bacterial vaginosis, gaps remain in understanding the optimal use of probiotics [3,15-17]. Most research focuses on specific strains or formulations, which limits the ability to make comparisons across studies [15,17,18]. Additionally, there is no consensus on the most effective species, strains, or doses, and long-term safety data remain scarce. Furthermore, comprehensive analyses of the efficacy and long-term safety of probiotics for preventing and treating bacterial vaginosis are lacking. Therefore, the aim of this study was to provide a comprehensive review of the effectiveness of probiotics in managing bacterial vaginosis, in particular clinical outcomes, species, strain, clinical outcomes, optimal dosage, duration, and side effects.

Methods

Study design and research question

Protocols for the present systematic review were designed in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline [19]. The present systematic review specifically analyzed probiotic species and strains, clinical outcomes, optimal dosage, treatment duration, and reported side effects. By systematically analyzing existing literature, the study aimed to provide comprehensive insights into the therapeutic potential of probiotics in the management of bacterial vaginosis.

Inclusion and exclusion criteria

Study selection followed the patient, intervention, comparison, outcome, and study design (PICOS) framework. The population included patients diagnosed with bacterial vaginosis, while the intervention assessed was probiotic administration, either orally or vaginally. No direct comparison was included, as the focus was solely on evaluating probiotics' effectiveness. The outcomes analyzed comprised probiotic species, strain, dose, duration, and treatment efficacy. Only randomized controlled trials (RCTs) published in English between 2014 and 2024 were included. Studies such as review articles, conference proceedings, and book chapters were excluded.

Search strategy

A systematic search was conducted on December 20, 2024, using Scopus, Web of Science (WoS), and PubMed databases. The search incorporated the following keywords and Medical Subject Headings (MeSH) terms: ″vaginosis," "bacterial vaginosis," and "probiotic″ (**Table 1**). Boolean operators (AND, OR) were applied to refine the search results.

Table 1. Combined keywords employed in each database

Database	Keyword string
Scopus	TITLE-ABS-KEY (("vaginosis" OR "bacterial vaginosis") AND "probiotic")
Web of Science	(("vaginosis" OR "bacterial vaginosis") AND "probiotic")(Topic)
PubMed	(("vaginosis" OR "bacterial vaginosis") AND "probiotic")

Data screening and selection

The systematic review was conducted using Parsifal (https://parsif.al/), which facilitated comprehensive screening of collected metadata. The screening protocol comprised two main phases: duplicate identification and eligibility assessment based on predefined inclusion and exclusion criteria. Eligible articles were those published in English between 2014 and 2024 that specifically addressed probiotic interventions for the treatment of bacterial vaginosis. Review articles, conference proceedings, and book chapters were excluded from the analysis. The screening process was conducted independently by four researchers (UU, NAS, BR and LZ). Only the approved articles by all four researchers were included in this systematic review. The platform's integrated tools systematically removed duplicates and applied the inclusion and exclusion criteria. Titles and abstracts were assessed for relevance, and articles were classified as "Accepted" or "Rejected." The selection process adhered to PRISMA guidelines [19], with a flow diagram documenting the number of duplicates identified and articles accepted or rejected. Full-text versions of accepted articles were subsequently retrieved for quality assessment.

Data extraction

For each included study, the sample size, country of origin, mean participant age with standard deviation, severity of bacterial vaginosis, and outcome of interest were extracted by all four researchers (UU, NAS, BR and LZ). The present study evaluated key variables in probiotic interventions for bacterial vaginosis, with a focus on probiotic species, therapeutic dosage, treatment duration, side effects, and clinical effectiveness, as reported in the included studies. Identification of bacterial species and strains includes using scientific names complete with reference codes, while doses were expressed in colony-forming unit or CFU (generally 10^9–10^{10} CFU/day), and the duration of treatment varies with the specific frequency of administration. Side effects were extracted from reported documentation in the studies, while effectiveness was measured using a combination of Nugent score, vaginal pH, microbiological analysis, clinical symptom evaluation, cure rate, and other specific parameters.

Quality assessment

Quality assessment was carried out using the Cochrane Risk of Bias 2.0 (RoB 2.0) tool by four researchers (UU, NAS, BR and LZ). RoB 2.0 is a tool developed by Cochrane to assess the risk of bias in RCTs [20]. RoB 2.0 evaluates the risk of bias on five dimensions: (1) bias arising from the randomization process; (2) bias due to deviation from the intervention of interest; (3) bias due to missing outcome data; (4) bias in outcome measurement; and (5) bias in the selection of reported outcomes. Each of these dimensions was assessed using a structured set of signaling questions and scoring algorithms. The final assessment results for each study were categorized as low risk when all domains had a low risk of bias, some concerns when at least one domain presented potential bias, and high risk when one or more domains demonstrated a high risk of bias.

Data analysis

Data analysis was performed using NVivo v.14 software (Lumivero, Denver, Colorado, USA). In vivo coding was utilized to categorize content into key research domains, including probiotic species, side effects, effectiveness, dosage, and treatment duration. Thematic analysis was then applied to the coded segments, facilitating the development of sub-codes within each domain based on semantic similarities [21-23].

Results

Study selection

The literature selection process for the systematic review of probiotics in the treatment of bacterial vaginosis is outlined in the PRISMA flowchart (**Figure 1**). A total of 1,560 records were identified from Scopus, Web of Science, and PubMed, which was reduced to 1,209 after removing the duplicates. Following the screening, 954 records were excluded, leaving 255. Of these, six articles were inaccessible, resulting in 249 eligible for full-text screening. After the assessment, 232 records were excluded, and 16 articles were included for data extraction. These 16 articles [3,6-9,18,24-33] provide empirical evidence supporting the therapeutic efficacy of probiotic interventions in the treatment of bacterial vaginosis.

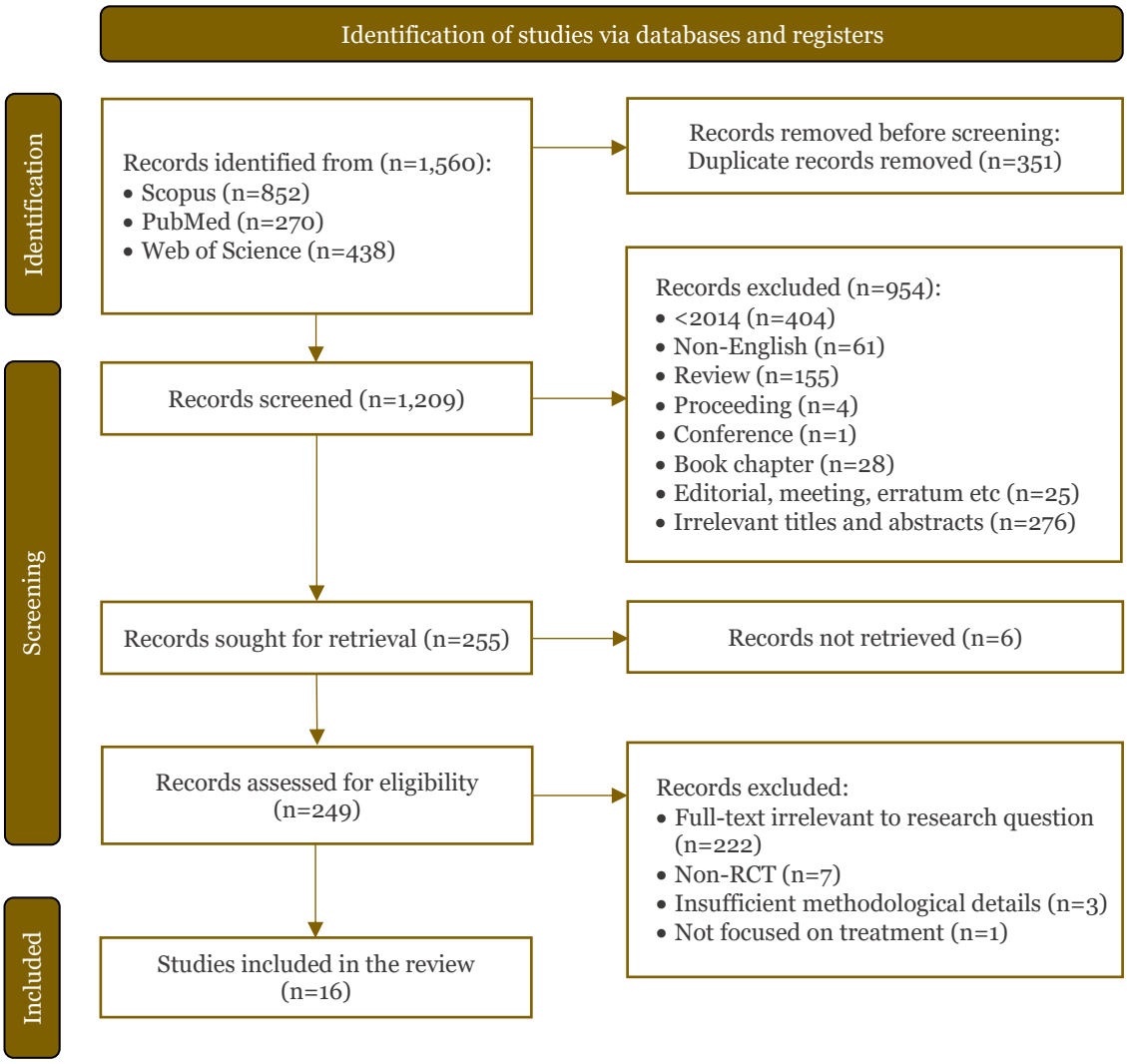

Figure 1. PRISMA flowchart illustrating the literature selection process.

Characteristics of the included studies

Study characteristics and outcomes are summarized in **Table 2**. Among the 16 studies included in this review, one was published in 2015 [24], two in 2016 [9,25], one in 2018 [26], three in 2020 [8,27,28], one each in 2021 [3] and 2022 [6], four in 2023 [7,18,29,30], and three in 2024 [31-33]. The studies were conducted in Italy [25,31,32], Poland [24], Germany [9,26], Rwanda [27], Canada [28], China [3,29], the United States [6], Estonia [18], the Republic of Korea [7], Thailand [30], Ukraine [8], and Iran [33]. Sample sizes ranged from 35 [25] to 340 participants [30], with an average age between 29 and 60 years. Bacterial vaginosis was primarily diagnosed using the Nugent score or Amsel criteria, with some studies [3,6,7,24,25,27-29,31,33] specifically including patients with intermediate (4–6) or high (7–10) Nugent scores.

Risk of bias

Among the 16 analyzed studies, the risk of bias assessment revealed variability in methodological quality (**Figure 2**). The outcome measurement bias domain and intervention deviation bias domain had the highest proportion of low-risk assessments, at approximately 85% and 80%, respectively. In contrast, the randomization bias domain showed a substantial proportion of studies categorized as "some concerns" or lacking information, accounting for approximately 40%. Overall, 10% of the studies had a low risk of bias, while 60% were categorized as having some concerns, with 30% lacking adequate data. Although most individual domains indicated a low risk of bias, the overall assessment was more conservative, with a predominance of the "some concerns" category, highlighting the need for cautious interpretation of findings (**Figure 2**).

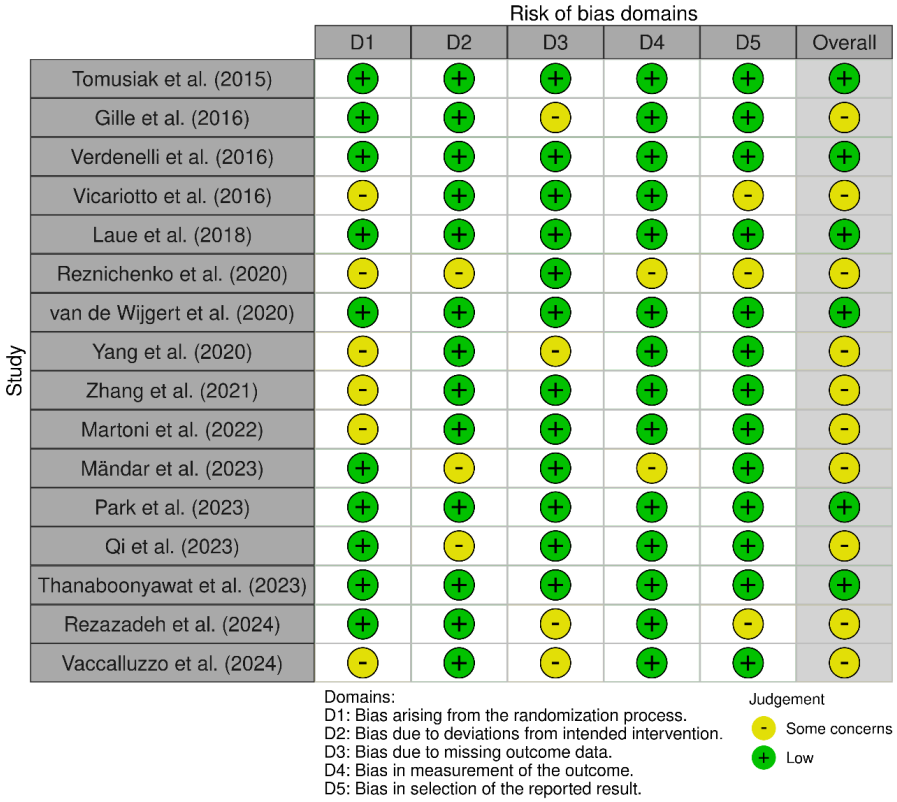

Figure 2. Risk of bias assessment for the included studies, evaluated using the Risk of Bias 2 (RoB 2) tool.

Probiotic treatment effectiveness in bacterial vaginosis management

The effectiveness of probiotics in treating bacterial vaginosis was typically assessed using the Nugent score, vaginal pH levels, microbiological analysis, clinical symptoms, cure rates, inflammatory biomarkers, and pregnancy rates in in vitro fertilization patients (**Table 3**). Most studies combined several of these criteria for a comprehensive evaluation. Several studies demonstrated the effectiveness of probiotics in treating bacterial vaginosis through improvements in clinical and microbiological parameters [7,24,32]. Significant reductions in Nugent scores and symptoms, such as vaginal discharge and burning sensation, were observed after probiotic use [7].

Probiotics also led to a decrease in vaginal pH and facilitated strain colonization in 82% of participants [24] (**Table 3**). A significant improvement was observed, with a 50% increase in vaginal health index scores and an 87.8% reduction in inflammatory cytokines [32]. Additionally, probiotics showed promise in preventing bacterial vaginosis recurrence and maintaining long-term vaginal health [8,18,26,27]. Lower recurrence rates (18.3% in the probiotic group compared to 32.1% in the placebo group) [8], reduced incidence [27], and increased vaginal *Lactobacillus* sp. populations were noted [18], with one study reporting complete resolution of symptoms in probiotic-treated groups [26].

Table 2. Characteristics of the included studies

Author, year	Study design	Country	Sample size, n	Age (years), mean±SD/median (min-max)	Severity	Probiotic species	Dosage	Duration
Tomusiak *et al.* (2015) [24]	RCT	Poland	160	29.14–31.12 (safety evaluation group); 29.30–30.95 (efficacy evaluation group)	• Before: Intermediate Nugent score (4–6) in both treatment group and placebo group • After: Lower Nugent score in treatment group (<1.0) and placebo group (<1.5)	*Lactobacillus fermentum* 57A, *L. plantarum* 57B, and *L. gasseri* 57C	One capsule (>10^9 CFU)	7 days
Gille *et al.* (2016) [9]	RCT	Germany	320 pregnant women (160 treatment, 160 placebo)	Treatment: 33±4 Placebo: 33±3.33	• Before: 2.8% in the treatment group and 5.4% in the placebo group • After: 2.2% in the treatment group and 1.8% in the placebo group	*L. rhamnosus* GR-1, *L. reuteri* RC-14	1×10^9 CFU	8 weeks
Verdenelli *et al.* (2016) [25]	RCT	Italy	35 women	29.8±7.1	• Before: Intermediate Nugent score (4–6) observed in 40% of women • After: Normal Nugent score in 20% of women	*L. rhamnosus* IMC 501®, *L. paracasei* IMC 502®	10^9 CFU	7 days
Laue *et al.* (2018) [26]	RCT	Germany	36 women	Verum: 32.6±11.2 Placebo: 39.0±12.3	Before: Based on Amsel criteria (3 out of 4): • Vaginal pH above 4.5 • Thin, homogeneous discharge • Release of amine ('fishy') odor after the addition of 10% KOH (whiff test) to vaginal smear • Clue cells on saline wet mount of vaginal smear (in phase contrast microscopy) After: • 100% bacterial vaginosis recovery rate in treatment group and 64.7% in placebo group	*L. crispatus* LbV 88, *L. gasseri* LbV 150N, *L. jensenii* LbV 116, *L. rhamnosus* LbV96	1×10^7 CFU/mL	4 weeks
Reznichenko (2020) [8]	RCT	Ukraine	166 women (82 verum, 84 placebo)	Placebo: 30.4±6.9 Verum: 31.1±7.0	• Before: All participants had four Amsel criteria before antibiotic therapy • After: 18.3% bacterial vaginosis recurrence in verum group and 32.1% in placebo group	*L. crispatus*, *L. brevis*, *L. acidophilus*	5.4×10^9 CFUs per capsule	The first 7 days are twice a day, then once a day until the 120th day (120 days in total)
van de Wijgert *et al.* (2020) [27]	RCT	Rwanda	68 women (17 per group ×4 groups)	Control: 29±3.22; Metronidazole:30±2.22 EF+ formula: 33±2.03 GynLP formula: 30±2.74	• Before: Nugent score 7–10 and/or vaginal pH >4.5, positive whiff test, or ≥20% clue cells in all patients • After: Lower percentage of Nugent score 7–10 in treatment group	*Lactobacillus* spp. (multi-strain), *Bifidobacterium bifidum* W28, *L. acidophilus* W70	1.5×10^9 CFU (EF+) 1.6×10^9 CFU (GynLP)	2 months

Author, year	Study design	Country	Sample size, n	Age (years), mean±SD/median (min-max)	Severity	Probiotic species	Dosage	Duration
Yang *et al.* (2020) [28]	RCT	Canada	Initial: 86 women (43 per group) Final: 66 women (32 probiotic, 34 placebo)	Probiotic: 33.8±4.2 Placebo: 34.4±3.3	• Before: Intermediate Nugent score (4–6) or bacterial vaginosis (Nugent score 7–10) • After: 34.4% with normal Nugent score in probiotic group and 32.3% in placebo group	*L. rhamnosus* GR-1, *L. reuteri* RC-14	2.5×10^9 of GR-1 and 2.5×10^9 RC-14	12 weeks
Zhang *et al.* (2021) [3]	RCT	China	126 women (probiotic: 52, metronidazole: 47, dropout: 27).	Probiotic: 34.2±7.0 Metronidazole: 33.3±7.5	• Before: All participants had a Nugent score ≥7 at baseline, confirming a bacterial vaginosis diagnosis • After: Normal Nugent score in both groups	*L. rhamnosus* GR-1, *Limosilactobacillus reuteri* RC-14	Oral for 30 days $\geq1\times10^9$ CFU per day	30 and 90 days
Martoni *et al.* (2022) [6]	Clinical trial	USA	43 women (36 completed)	Subgroup 1: 35.7±8.16 Subgroup 2: 34.9±6.57	• Before: Intermediate Nugent score (4–6) or vaginal pH >4.5 • After: Reduced vaginal pH, but no significant changes in Nugent score	8 Lactobacilli and 2 *Bifidobacteria* strains (*L. acidophilus* DDS-1, *L. gasseri* UALg-05, *L. plantarum* UALp-05, *L. rhamnosus* UALr-06, *L. reuteri* UALre-16, *L. paracasei* UALpc-04, *L. crispatus* UALcr-35, *L. brevis* UALbr-02, *B. longum* subsp. *longum* UABl-14, and *B. animalis* subsp. *lactis* UABla-12)	2.5×10^{10} CFU	28–42 days
Mändar *et al.* (2023) [18]	RCT	Estonia	182 women (89 with bacterial vaginosis, 93 with vulvovaginal candidiasis as placebo)	Oral capsule: 39.09±21.04 Vaginal capsule: 39.23±9.04 Placebo: 40.37±13.33	• Before: Diagnosed according to Amsel criteria (amount and smell of discharge, high vaginal pH, overgrowth of *Gardnerella*/*Bacteroides* and *Mobiluncus*), high Nugent score • After: Decreased Nugent score, improvement in amount and smell of discharge	*L. crispatus* DSM32717, DSM32720, DSM32718, DSM32716	3×10^{10} CFU per capsule	3 months
Park *et al.* (2023) [7]	RCT	Republic of Korea	101 women (76 completed)	Treatment: 39.56±6.58 Placebo: 37.03±7.15	• Before: Nugent score 4–6. • After: Nugent score 0–3 in 25.6% of treatment group and 13.5% of placebo group	*Ligilactobacillus salivarius* MG242, *Limosilactobacillus fermentum* MG901, *Lactiplantibacillus plantarum* MG989, *Lacticaseibacillus*	5.0×10^9 CFU	12 weeks

Author, year	Study design	Country	Sample size, n	Age (years), mean±SD/median (min-max)	Severity	Probiotic species	Dosage	Duration
						paracasei MG4272, and *Lacticaseibacillus rhamnosus* MG4288		
Qi *et al.* (2023) [29]	RCT	China	67 women	Probiotic group: 34.3±7.7 Control group: 32.1±6.8	• Before: Nugent score ≥7 • After: Nugent Score <4	*L. gasseri* TM13, *L. crispatus* LG55	Daily intake ≥5×10^9 CFU	30 days
Thanaboonyawat *et al.* (2023) [30]	RCT	Thailand	340 infertile women	Intervention: 35.10±3.38 Control: 35.51±3.25	• Before: Intervention 17.7% prevalence, control 14.1% prevalence • After: Higher live birth rate in control group	*L. acidophilus*	100 million (10^8) CFU per tablet	6 days
Vaccalluzzo *et al.* (2024) [31]	RCT	Italy	80 women (60 treatment, 20 control)	Treatment group: 34.7±6.96 Non-treatment group: 33.2±7.02	• Before: At least 3 Amsel criteria, a Nugent score ≥7, and an abnormal Lactobacillary Grade (LBG III) • After: Nugent score between 0 and 3 and a normal Lactobacillary Grade (LBG I)	*Lacticaseibacillus rhamnosus* TOM 22.8 (DSM 33500)	10×10^9 CFU per capsule per day	10 days
Vicariotto *et al.* (2024) [32]	Clinical trial	Italy	50 postmenopausal women	59.80±6.41	• Before: Vaginal pH ≥5 • After: Reduction in vaginal pH	*Lactiplantibacillus plantarum* PBS067, *Bifidobacterium animalis* subsp. *lactis* BL050, and *Lacticaseibacillus rhamnosus* LRH020	3B (3×10^9) CFU/day	28 days
Rezazadeh *et al.* (2024) [33]	RCT	Iran	55 women (20 vaginal group, 35 oral group)	Vaginal group: 35.20±7.19 Oral group: 38.11±8.57	• Before: Nugent score 7–9 in oral group and 8–9 in vaginal group • After: Nugent score decreased from 8.5 to 3 (vaginal) and from 9 to 3 (oral)	Lactovage® (vaginal group): *Lactobacillus* strains with maltodextrin; Lactofem® (oral group): *Lactobacillus* strains with fructooligosaccharide	• Vaginal group: 1 capsule nightly • Oral group: 2 capsules daily	• Vaginal group: 2 weeks • Oral group: 4 weeks

SD: standard deviation; CFU: colony-forming unit

Table 3. Effectiveness of probiotics in bacterial vaginosis management

Author, year	Effectiveness
Tomusiak *et al.* (2015) [24]	• Significant decrease (p<0.05) in vaginal pH (5.03 to 4.71 between visits 1 and 3; 5.03 to 4.66 between visits 1 and 4) and Nugent score • Significant increase (p<0.05) in Lactobacillus count in the probiotic group, with 82% of women at visit 3 and 47.5% at visit 4
Gille *et al.* (2016) [9]	Nugent score indicated a decrease in normal microbiota: • Treatment group: 82.5% to 77.8% • Placebo group: 79.1% to 74.3%

Author, year	Effectiveness
Verdenelli *et al.* (2016) [25]	• No significant post-intervention difference between groups (p=0.297) • Normal Nugent score in 50% of participants after 7 days; one additional participant normalized by day 28 • Lactobacilli count increased by 0.8 log10 after 7 days, maintaining 0.4 log10 at 28 days post-treatment • Probiotic strain colonization: 100% at 7 days, 34% at 28 days • IMC 501® recovery: 22.86% (day 7), 14.29% (day 28) • IMC 502® recovery: 23.81% (day 7), 9.35% (day 28)
Laue *et al.* (2018) [26]	• Cure rates: 0/17 in the probiotic group vs 6/17 in the control group (p=0.018) • Amsel score reduction: 4.0 to 2.0 (p=0.038) • Vaginal discharge symptom reduction: 2.0 to 1.0 (p=0.010) • Nugent score reduction: 5.5 in the probiotic group vs 3.0 in the control group (p=0.158)
Reznichenko (2020) [8]	Recurrence rate: • Probiotic group: 18.3% (15/82) • Placebo group: 32.1% (27/84) (p=0.014) Time to recurrence (mean): • Probiotic group: 97.3 days • Placebo group: 74.7 days (p=0.014)
van de Wijgert *et al.* (2020) [27]	Bacterial vaginosis incidence (Nugent score 7–10): • Metronidazole group: 1.41/person-year (p=0.004) • Ecologic Femi+ group: 3.58/person-year (p=0.043) • Gynophilus LP group: 5.36/person-year (p=0.220) Bacterial vaginosis-associated anaerobe expansion: • Significantly lower in oral metronidazole users (relative abundance; p=0.023) • Significantly lower in Ecologic Femi+ users (estimated concentration; p=0.041)
Yang *et al.* (2020) [28]	• Nugent score: 30% of women in both groups achieved normalization at 28 weeks, maintained up to 35 weeks • Microbial diversity: No significant difference in Shannon Diversity Index between the groups at 13, 28, and 35 weeks • Cytokine and chemokine levels: No significant differences between the groups • Safety: No safety concerns associated with probiotic use during pregnancy
Zhang *et al.* (2021) [3]	The cure rate of bacterial vaginosis did not improve with adjunctive treatment compared to metronidazole alone at either 30 days (57.69% vs 59.57%, p=0.04) or 90 days (36.54% vs 48.94%, p=0.213)
Martoni *et al.* (2022) [6]	A significant decrease in vaginal pH was observed from baseline to day 28 (MD: -0.19; p=0.047)
Mändar *et al.* (2023) [18]	• Improvement in Nugent score • Reduction in discharge amount, odor, and itching/irritation • Increased vaginal Lactobacilli counts • Decreased proportion of bacteria associated with bacterial vaginosis
Park *et al.* (2023) [7]	• Nugent score decreased in the treatment group (-0.36±1.72) compared to an increase in the placebo group (0.19±1.85) (p=0.041) • Significant reduction in vaginal discharge, dysuria, and burning sensation • Increased proportion of beneficial Lactobacilli • Decreased bacterial vaginosis-causing pathogens (confirmed by quantitative polymerase chain reaction (qPCR))
Qi *et al.* (2023) [29]	Cure rates: • Day 14: Probiotics 72.73% vs control 84% • Day 30: Probiotics 57.14% vs control 60% • Day 90: Probiotics 32.14% vs control 48.39%

Author, year	Effectiveness
	Full recovery (Nugent score <4) in cured participants: • Day 14: Probiotics 87.5% vs control 71.43% • Day 30: Probiotics 93.75% vs control 88.89% • Day 90: Probiotics 77.78% vs control 66.67% Probiotic colonization in feces: • Day 14: *L. crispatus* and *L. gasseri* significantly increased (p<0.001) • Day 30: Only *L. crispatus* remained elevated (p=0.0037) • Day 90: Colonization significantly decreased
Thanaboonyawat *et al.* (2023) [30]	• Clinical pregnancy rate was higher in the study group than in the control group (42.3% vs. 34.8%, p=0.590) • Live birth rate was 1.5 times higher in the study group than in the control group (42.3% vs. 26.1%, p=0.230)
Vaccalluzzo *et al.* (2024) [31]	• Amsel criteria significantly decreased after 10 days of treatment and remained stable at 30 days • Nugent score (0–3) observed in 96.7% of participants after 10 days and in 100% at 30 days • Lactobacillary Grade normalized after treatment
Vicariotto *et al.* (2024) [32]	• Vaginal health index improved by 50% after 28 days • Vaginal pH reduced from >6.0 to 5.1–6.0 • Inflammatory cytokines decreased: interleukin-6 (87.8%), tumor necrosis factor-alpha (57.6%), interleukin-1β (40.8%) • Vaginal ecosystem improved in five subjects, with one showing inverse behavior
Rezazadeh *et al.* (2024) [33]	Both groups showed significant improvement: Nugent score decreased from 8.5 to 3 (vaginal) and 9 to 3 (oral), with no significant difference between groups (p=0.053)

Nevertheless, some studies reported mixed or insignificant results [3,9,29] (**Table 3**). One study found no substantial difference in the cure rate between the probiotic group (57.69%) and the metronidazole-only group (59.57%) [3]. Another study observed no increase in the proportion of normal vaginal microbiota, with a slight decrease from 82.6% to 77.8% [9]. Additionally, while the addition of probiotics did not improve the overall cure rate, a higher proportion of recovery was noted in the probiotic group [29].

Innovations in probiotic formulations and delivery systems showed promise in improving treatment effectiveness [30,31]. *L. rhamnosus* TOM 22.8 restored physiological pH and reduced pathogens [31] (**Table 3**). Another study highlighted the benefits of probiotics in specific subpopulations, noting improved clinical pregnancy rates in in vitro fertilization patients with vaginal dysbiosis [30]. These findings emphasized the importance of developing tailored probiotic formulations to address individual patient needs.

Probiotic species and strains in the management of bacterial vaginosis

Various studies identified the most commonly used probiotic species and strains in managing bacterial vaginosis. Among these, *L. rhamnosus* was one of the most frequently used and extensively studied species, with eight distinct strains (GR-1, LbV96, MG4288, TOM 22.8, IMC 501, UALr-06, LRH020, and Lcr35) evaluated across ten studies [3,6,7,9,25-28,31,32] (**Table 4**). The GR-1 strain demonstrated consistent efficacy, particularly in combination with *L. reuteri* RC-14 [3,28]. The TOM 22.8 strain significantly restored normal vaginal pH and alleviated clinical symptoms [31]. Strains Lcr35 and IMC 501 were effective in various formulations, both as monotherapies and in combination therapies [25,27]. The diversity of strains highlighted the versatility of *L. rhamnosus* in different treatment approaches for bacterial vaginosis.

Table 4. Probiotic species used in bacterial vaginosis management

Species	Strain	Supporting studies
Lactobacillus rhamnosus	GR-1; IMC 501®; LbV96; MG4288; TOM 22.8 (DSM 33500); LRH020; UALr-06	[3,6,7,9,25-28,31,32]
Lactobacillus crispatus	LbV 88; DSM32717; DSM32720; DSM32718; DSM32716; LG55; UALcr-35	[6,8,18,26,29]
Lactobacillus plantarum	57B; MG989; PBS067; UALp-05	[6,7,24,27,32]
Lactobacillus acidophilus	W70; DDS-1	[6,8,27,30]
Lactobacillus gasseri	57C; LbV 150N; TM13; UALg-05	[6,24,26,29]
Lactobacillus reuteri	RC-14; UALre-16	[3,6,9,28]
Lactobacillus paracasei	IMC 502®; MG4272; UALpc-04	[6,7,25]
Lactobacillus brevis	UALbr-02; W63;	[6,8,27]
Lactobacillus fermentum	57A; MG901	[7,24]
Lactobacillus salivarius	MG242; W24	[7,27]
Bifidobacterium animalis subsp. *lactis*	BL050 (DSM 25566); UABla-12	[6,32]

L. crispatus demonstrated effectiveness in reducing bacterial vaginosis symptoms and preventing recurrence through strains DSM and LMG S-29995 [8,18] (**Table 4**). *L. plantarum* strains 57B, MG989, and PBS067 significantly reduced vaginal pH and enhanced *Lactobacillus sp*. colonization [7,24,32]. Similarly, *L. acidophilus* strains W70, KS400, and DDS-1 effectively increased *Lactobacillus* sp. colonization and lowered vaginal pH [6,27,30], while *L. gasseri* strains TM13, 57C, LbV 150N, and UALg-05 contributed to vaginal health restoration [24,29]. *L. paracasei* strains MG4272, IMC 502, and UALpc-04 demonstrated efficacy, particularly in multi-strain formulations [6,7,25]. *L. reuteri* strains RC-14 and UALre-16 were frequently combined with *L. rhamnosus* GR-1 to optimize therapeutic outcomes [3,6,9,28].

L. fermentum, L. brevis, L. salivarius, and *Bifidobacterium animalis* subsp. *lactis* were moderately studied in bacterial vaginosis research [6-8,24,27,32] (**Table 4**). *L. brevis*, consistently used as part of multi-strain formulations, has demonstrated positive demonstrated positive outcomes in bacterial vaginosis management; however, its individual efficacy remained unassessed due to frequent combination with other probiotic strains [6,8,27]. *L. fermentum* (strains MG901 and 57A) and *L. salivarius* (strains MG242 and W24) showed promise in multi-strain formulations [7,24,27]. Similarly, *Bifidobacterium animalis* subsp. *lactis* (strains UABla 12 and BL050) demonstrated potential as an adjunctive therapy for bacterial vaginosis management [6,32].

Probiotic dosage in bacterial vaginosis management

The treatment of bacterial vaginosis with probiotics at various doses yielded mixed results regarding effectiveness [9,25-27,30]. The low-dose group showed variable outcomes in treating bacterial vaginosis (**Table 2**). One study using 1×10^7 CFU/mL in yogurt form found that after four weeks of intervention, none of the 17 participants in the probiotic-treated group had bacterial vaginosis, compared to 6 of 17 in the control group [26]. Another study using 1×10^8 CFU in vaginal tablet form showed no significant effect in the overall population but reported an increased clinical pregnancy rate in the subgroup with bacterial vaginosis (42.3% vs 34.8%) [30]. A dose of $1.5–1.6\times10^9$ CFU significantly reduced bacterial vaginosis incidence [27], while 1×10^9 CFU per strain orally had no significant impact on vaginal microbiota [9]. Despite the relatively low doses, some studies reported positive outcomes, particularly with vaginal administration [25,27,30].

The medium-dose range provided more consistent results in treating bacterial vaginosis [7,8,29,32]. A 3×10^9 CFU dose improved menopausal symptoms and reduced inflammatory cytokine levels [32] (**Table 2**). A 5×10^9 CFU dose lowered Nugent scores and alleviated symptoms such as vaginal discharge, dysuria, and burning [7]. A 5.4×10^9 CFU dose reduced recurrence rates (18.3% vs 32.1% in the placebo group) [8], while $\geq5\times10^9$ CFU resulted in a higher complete recovery rate compared to the control group [29].

High-dose treatments showed promising results, though with some notable considerations regarding effectiveness [6,18,31]. A dose of 10×10^9 CFU of a single strain effectively restored physiological pH and reduced potential pathogens, including bacteria and yeast responsible for vaginal dysbiosis [31] (**Table 2**). A dose of 2.5×10^{10} CFU significantly lowered vaginal pH and increased *Lactobacillus* sp. abundance [6]. The highest dose of 3×10^{10} CFU, administered via both oral and vaginal capsules, reduced signs and symptoms, with a significant increase in *Lactobacillus* sp. colonization [18]. Importantly, no serious side effects were reported in any of these studies, suggesting a favorable safety profile. Overall, while low-dose treatments yielded mixed results, medium and high doses provided more consistent effectiveness. However, the route of administration (oral or vaginal) and the specific probiotic strain used may have influenced treatment outcomes.

Duration of probiotic treatment in bacterial vaginosis management

Short-term treatment (1–2 weeks) showed mixed effectiveness [24,25,31,33]. A 7-day vaginal probiotic treatment resulted in significant reductions in vaginal pH and Nugent scores [24] (**Table 2**). Another study confirmed that seven days of treatment were sufficient to restore 50% of patients to normal conditions, with effects lasting up to 28 days [25]. A 10-day treatment effectively restored physiological pH and reduced pathogens [31], while two weeks of vaginal probiotic treatment led to significant improvement [33].

Intermediate treatment durations (1–2 months) provided more sustained benefits [3,6,9,26,27,32]. A four-week treatment resulted in a 50% improvement in vaginal health index scores [32] (**Table 2**). Another study found that a 30-day treatment with probiotics as an adjunct to metronidazole therapy had positive effects [3]. Two months of probiotic administration significantly reduced the incidence of bacterial vaginosis [27], while four weeks of probiotic yogurt consumption effectively prevented it [26].

Long-term treatment durations (>2 months) showed potential for preventing recurrence [7,8,18,28] (**Table 2**). A 12-week treatment resulted in a significant reduction in Nugent scores [7], and a 20-day-per-month protocol over three months effectively reduced symptoms [18]. Another study demonstrated that 120 days of treatment significantly reduced recurrence rates [8]. Twelve weeks of treatment was also confirmed to be safe for pregnant women [28]. Long-term evaluations after discontinuation of treatment provided insight into the persistence of probiotic effects [25,29,32]. One study observed benefits up to 90 days after a 30-day treatment [29], while another detected probiotics up to 21 days after a one-week course [25]. These findings emphasized the importance of considering both the optimal treatment duration and the long-term effects.

Side effects of probiotics use for bacterial vaginosis management

Probiotic use for managing bacterial vaginosis was associated with gastrointestinal side effects, including gas, bloating, abdominal distension, nausea, constipation, dyspepsia, abdominal cramps, pain, and decreased appetite [6] (**Table 5**). These symptoms were associated with strains such as *L. plantarum* P17630, as well as with oral and vaginal probiotic formulations [6-8]. Local discomfort and genitourinary symptoms, such as vaginal discharge, itching, and hypogastric pain, were also common side effects [24]. Strains involved in these effects included combinations of *Lactobacillus sp.* in products such as inVag® (containing *L. fermentum* 57A, *L. plantarum* 57B, *L. gasseri* 57C) and LACTIN-V (containing *L. crispatus* CTV-05) [9,24]. Although these symptoms caused discomfort, the severity was generally mild to moderate, with no reported discontinuations of treatment. Certain probiotic strains, including *L. rhamnosus* IMC 501® and *L. paracasei* IMC 502®, as well as *L. rhamnosus* GR-1 and *L. reuteri* RC-14, were not associated with adverse effects [3,25,28,30,32]. Additionally, one study that did not specify the species or strains of probiotics used reported no adverse effects in either vaginal or oral probiotic groups [33].

Table 5. Side effects of probiotics use for bacterial vaginosis management

Author, year	Side effects
Tomusiak *et al.* (2015) [24]	No serious side effects (genitourinary tract symptoms including vaginal discharge, pruritus, and hypogastric pain)
Gille *et al.* (2016) [9]	None
Verdenelli *et al.* (2016) [25]	None
Laue *et al.* (2018) [26]	None
Reznichenko (2020) [8]	Not mentioned
van de Wijgert *et al.* (2020) [27]	None
Yang *et al.* (2020) [28]	None
Zhang *et al.* (2021) [3]	Not mentioned
Martoni *et al.* (2022) [6]	Two participants reported mild side effects (abdominal cramping, bloating, stomach pain, decreased appetite and increased energy)
Mändar *et al.* (2023) [18]	None
Park *et al.* (2023) [7]	None
Qi *et al.* (2023) [29]	Not mentioned
Thanaboonyawat *et al.* (2023) [30]	Not mentioned
Vaccalluzzo *et al.* (2024) [31]	None
Vicariotto *et al.* (2024) [32]	None
Rezazadeh *et al.* (2024) [33]	No serious complications reported in either group

Discussion

Probiotic treatment for bacterial vaginosis showed significant potential, with efficacy influenced by probiotic species, dosage, and treatment duration. This systematic review identified *L. rhamnosus, L. crispatus, L. plantarum, L. acidophilus, L. gasseri,* and *L. reuteri* as commonly used strains [3,6-9,18,24-32]. Probiotic dosages ranged from 1×10^7 to 3×10^{10} CFU per day, with treatment durations spanning from 6 days to 4 months. Efficacy was primarily assessed using Nugent scores, alongside vaginal pH measurements, microbiological analyses, clinical symptom evaluation, cure rates, inflammatory biomarker levels, and pregnancy outcomes [3,6,7,9,18,24-27,29-32]. Reported adverse effects were generally mild to moderate, including gastrointestinal symptoms and localized discomfort [6-8,24].

The effectiveness of probiotic species and strains in bacterial vaginosis treatment depends on multiple factors. *L. rhamnosus*, the most frequently used probiotic species, was administered both as a single strain [31] and in combination with other species [3,7,9,26-28,32]. Most studies employed a multi-strain approach, suggesting a preference for leveraging the synergistic benefits of probiotic strains in bacterial vaginosis management [34]. The dosage of *L. rhamnosus* varied significantly, ranging from 10^7 to 10^{10} CFU per day, while treatment duration spanned from 7 days to 12 weeks, highlighting the lack of consensus on the optimal regimen. Oral administration was the predominant route [3,6-9,26,28,31,32], with one study utilizing a yogurt-based medium [26] and two studies employing vaginal administration [25,27]. Although the vagina is the primary therapeutic target, oral administration remains preferred due to its convenience and the potential for vaginal colonization via translocation from the gastrointestinal tract.

A key finding was the variability in outcomes associated with the combination of *L. rhamnosus* GR-1 and *L. reuteri* RC-14, which was evaluated in three distinct studies [3,9,28]. Despite differences in dosage and treatment duration, these studies produced inconsistent results. However, previous studies demonstrated the efficacy of this probiotic combination, suggesting that its effectiveness depends on multiple factors, including vaginal microbiota composition, route of administration, dosage, and patient lifestyle [9,24,28,35-38]. In contrast, other strains, such as TOM 22.8, LRH020, and MG4288, yielded more consistent and favorable outcomes [7,31,32]. *L. rhamnosus* TOM 22.8 (10×10^9 CFU per day, orally) reduced Nugent scores in 96.7% of participants after 10 days of treatment, with this effect maintained at 30 days. Additionally, this strain significantly improved Amsel criteria and restored normal Lactobacillary Grades [31]. Clinical symptoms also improved, with no reported side effects, making *L. rhamnosus* TOM 22.8 one of the most promising strains for bacterial vaginosis management.

At the molecular level, *L. rhamnosus* exerted antimicrobial effects through multiple mechanisms to combat bacterial vaginosis. It produced lactic acid, which maintained an acidic vaginal pH, creating an environment unfavorable for the proliferation of pathogenic bacteria [16,31]. Additionally, *L. rhamnosus* synthesized bacteriocins—antimicrobial peptides that inhibited the growth of bacterial vaginosis-associated pathogens [16,31]. Its ability to adhere to the vaginal epithelium further enhanced its therapeutic efficacy by competing with pathogenic bacteria for nutrients and attachment sites, thereby preventing colonization and infection [39].

Other probiotic species and strains that demonstrated efficacy in bacterial vaginosis treatment included *L. crispatus* (strains DSM and LMG S-29995), *L. plantarum* (strains 57B, MG989, and PBS067), and *L. acidophilus* (strains W70, KS400, and DDS-1), with doses ranging from 1×10^8 to 5.4×10^9 CFU per day and treatment durations varying from 6 days to 4 months [6-8,18,24,27,30,32]. *L. crispatus* exerted antimicrobial effects by producing lactic acid, hydrogen peroxide, and bacteriocins, in addition to forming a protective biofilm over the vaginal mucosa [8,18,40]. *L. plantarum* enhanced epithelial barrier integrity while modulating immune responses through increased production of anti-inflammatory cytokines and inhibition of pro-inflammatory cytokines [7,24,32,41,42]. Meanwhile, *L. acidophilus* contributed to vaginal health by producing lactic acid and hydrogen peroxide, inhibiting pathogen adhesion, and regulating immune responses [6,27,30].

The therapeutic efficacy of probiotics in bacterial vaginosis is influenced by multiple factors, including age (most effective in individuals aged 25–45 years), disease severity (optimal outcomes observed at Nugent scores of 4–6), ethnicity, lifestyle, and geographical differences affecting baseline microbiota composition [3,6-9,18,24-32]. More advanced stages of bacterial vaginosis may necessitate higher probiotic doses or prolonged treatment durations [6,8,25,29]. Ethnic variations may impact the composition of the vaginal microbiota and the response to probiotic therapy [3,9,28,29,36-38]. Lifestyle factors, such as sexual activity, vaginal douching, and smoking, can disrupt the vaginal microbiota and potentially reduce probiotic efficacy [27,43-45]. Additionally, geographical differences may influence the prevalence of bacterial vaginosis and the distribution of pathogenic strains [3,29,46].

Probiotics may serve as an adjunctive or alternative therapy for bacterial vaginosis, particularly in individuals with mild to moderate disease or recurrent episodes [3,6,7,9,18,24-32]. *L. rhamnosus* is broadly applicable, whereas *L. crispatus* may be more effective in cases of recurrent bacterial vaginosis. *L. plantarum* and *L. acidophilus* could be beneficial for older individuals or those with a suboptimal response to other strains [3,8,9,18,28]. When selecting probiotic therapy, patient preference, adherence, and tolerability should be considered. Additionally, patient education is essential, emphasizing the avoidance of factors that may disrupt the vaginal microbiota, such as vaginal douching and smoking.

The primary limitations of this systematic review were small sample sizes, short follow-up durations, and a lack of standardization in inclusion criteria, probiotic dosage, and administration methods [3,6-9,18,24-32]. Further research is required to assess the long-term efficacy and safety of various probiotic strains and to determine the optimal dosage and treatment duration. Future research should focus on elucidating the molecular mechanisms of probiotic action, assessing long-term efficacy and safety in diverse populations, and developing personalized treatment strategies based on patient-specific factors for bacterial vaginosis

management. Additionally, larger and more diverse study populations are needed to evaluate the impact of factors such as ethnicity, age, and geographic location on probiotic effectiveness.

Conclusion

This study highlights the efficacy and safety of *L. rhamnosus* TOM 22.8 (10×10^9 CFU/day for 10 days) in managing bacterial vaginosis, with *L. crispatus*, *L. plantarum*, and *L. acidophilus* also showing therapeutic potential. Probiotics help alleviate symptoms, reduce recurrence, and support vaginal health through antimicrobial production, pH modulation, and immune regulation. Despite certain limitations, current evidence supports their use as adjunctive or alternative therapy. Further research is needed to refine strain selection, optimize dosing, and assess long-term efficacy, particularly in diverse populations.

Ethics approval

Not required.

Acknowledgments

The authors would like to thank the Library of Universitas Brawijaya for its support in providing relevant scientific materials and assisting with qualitative data analysis software, which greatly contributed to the successful completion of the present study.

Competing interests

All the authors declare that there are no conflicts of interest.

Funding

This study received no external funding.

Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

This study utilized artificial intelligence (AI) tools and methodologies to support various aspects of manuscript preparation. AI-based language models, including Claude 3.5 Sonnet (Anthropic, San Francisco, USA) and DeepL (DeepL SE, Cologne, Germany), were employed for language refinement, content summarization, and technical writing assistance. Language refinement involved improving grammar, sentence structure, and readability, while content summarization facilitated concise presentation of findings and conclusions. Additionally, AI-assisted technical writing provided suggestions for structuring complex descriptions more effectively. We confirm that all AI-assisted processes were critically reviewed by the authors to ensure the integrity and reliability of the results. The final decisions and interpretations presented in this article were solely made by the authors.

How to cite

Udjianto U, Sirat NA, Rahardjo B, Zuhriyah L. Effective probiotic regimens for bacterial vaginosis treatment and recurrence prevention: A systematic review. Narra J 2025; 5 (1): e1671 - http://doi.org/10.52225/narra.v5i1.1671.

References

1. Kyser AJ, Masigol M, Mahmoud MY, *et al.* Fabrication and characterization of bioprints with *Lactobacillus crispatus* for vaginal application. J Controlled Release 2023;357:545-560.
2. Minooei F, Kanukunta AR, Mahmoud MY, *et al.* Mesh and layered electrospun fiber architectures as vehicles for Lactobacillus acidophilus and *Lactobacillus crispatus* intended for vaginal delivery. Biomater Adv 2023;154:213614.

3. Zhang Y, Lyu J, Ge L, *et al.* Probiotic *Lacticaseibacillus rhamnosus* GR-1 and *Limosilactobacillus reuteri* RC-14 as an adjunctive treatment for bacterial vaginosis do not increase the cure rate in a Chinese cohort: A prospective, parallel-group, randomized, controlled study. Front Cell Infect Microbiol 2021;11:1-13.
4. Happel AU, Jaumdally SZ, Pidwell T, *et al.* Probiotics for vaginal health in South Africa: What is on retailers' shelves? BMC Womens Health 2017;17:1-10.
5. Yang L, Zhang H, Shen H, *et al.* Quality assessment in systematic literature reviews: A software engineering perspective. Inf Softw Technol 2021;130:106397.
6. Martoni CJ, Frederiksen AKS, Damholt A, *et al.* Effects of a 10-strain oral probiotic on parameters of vaginal health and microbial community: A pilot clinical study. Int J Womens Health 2022;14:29-39.
7. Park SH, Lee ES, Park ST, *et al.* Efficacy and safety of MED-01 probiotics on vaginal health: A 12-week, multicenter, randomized, double-blind, placebo-controlled clinical trial. Nutrients 2023;15:331.
8. Reznichenko H, Henyk N, Maliuk V, *et al.* Oral intake of Lactobacilli can be helpful in symptomatic bacterial vaginosis: A randomized clinical study. J Low Genit Tract Dis 2020;24:284-289.
9. Gille C, Böer B, Marschal M, *et al.* Effect of probiotics on vaginal health in pregnancy. EFFPRO, a randomized controlled trial. Am J Obstet Gynecol 2016;215:608.e1-608.e7.
10. Borges S, Silva J, Teixeira P. The role of Lactobacilli and probiotics in maintaining vaginal health. Arch Gynecol Obstet 2014;289:479-489.
11. Almeida MO, do Carmo FLR, Gala-García A, *et al. Lactobacillus crispatus* protects against bacterial vaginosis. Genet Mol Res 2019;18:GMR18475.
12. Balzaretti S, Taverniti V, Rondini G, *et al.* The vaginal isolate *Lactobacillus paracasei* LPC-S01 (DSM 26760) is suitable for oral administration. Front Microbiol 2015;6:1-13.
13. Ehrström S, Daroczy K, Rylander E, *et al.* Lactic acid bacteria colonization and clinical outcome after probiotic supplementation in conventionally treated bacterial vaginosis and vulvovaginal candidiasis. Microbes Infect 2010;12:691-699.
14. Lyu J, Gao M, Zhao S, *et al.* From whole genomes to probiotic candidates: A study of potential Lactobacilli strains selection for vaginitis treatment. Heliyon 2024;10:e30495-e30495.
15. Pino A, Rapisarda AMC, Vitale SG, *et al.* A clinical pilot study on the effect of the probiotic *Lacticaseibacillus rhamnosus* TOM 22.8 strain in women with vaginal dysbiosis. Sci Rep 2021;11:1-12.
16. Recine N, Palma E, Domenici L, *et al.* Restoring vaginal microbiota: Biological control of bacterial vaginosis. A prospective case–control study using Lactobacillus rhamnosus BMX 54 as adjuvant treatment against bacterial vaginosis. Arch Gynecol Obstet 2016;293:101-107.
17. Webb L. Probiotics for preventing recurrent bacterial vaginosis. J Am Acad Physician Assist 2021;34:19-22.
18. Mändar R, Sõerunurk G, Štšepetova J, *et al.* Impact of *Lactobacillus crispatus*-containing oral and vaginal probiotics on vaginal health: A randomised double-blind placebo controlled clinical trial. Benef Microbes 2023;14:143-152.
19. Page MJ, McKenzie JE, Bossuyt PM, *et al.* The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372.
20. Sterne JAC, Savović J, Page MJ, *et al.* RoB 2: A revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:1-8.
21. Alinani K, Liu D, Zhou D, *et al.* Service composition and optimal selection in cloud manufacturing: State-of-the-art and research challenges. IEEE Access 2020;8:223988-224005.
22. Khaslavskaya A, Roso V. Dry ports: Research outcomes, trends, and future implications. Marit Econ Logist 2020;22:265-292.
23. Tumpa RJ, Skaik S, Ham M, *et al.* A holistic overview of studies to improve group-based assessments in higher education: A systematic literature review. Sustainability 2022;14:9638.
24. Tomusiak A, Strus M, Heczko PB, *et al.* Efficacy and safety of a vaginal medicinal product containing three strains of probiotic bacteria: A multicenter, randomized, double-blind, and placebo-controlled trial. Drug Des Devel Ther 2015;9:5345-5354.
25. Verdenelli MC, Cecchini C, Coman MM, *et al.* Impact of probiotic SYNBIO®Administered by vaginal suppositories in promoting vaginal health of apparently healthy women. Curr Microbiol 2016;73:483-490.
26. Laue C, Papazova E, Liesegang A, *et al.* Effect of a yoghurt drink containing *Lactobacillus* strains on bacterial vaginosis in women - a double-blind, randomised, controlled clinical pilot trial. Benef Microbes 2018;9:35-50.

27. van de Wijgert JHHM, Verwijs MC, Agaba SK, *et al.* Intermittent *Lactobacilli*-containing vaginal probiotic or metronidazole use to prevent bacterial vaginosis recurrence: A pilot study incorporating microscopy and sequencing. Sci Rep 2020;10:1-15.
28. Yang S, Reid G, Challis JRG, *et al.* Effect of oral probiotic *Lactobacillus rhamnosus* GR-1 and lactobacillus reuteri RC-14 on the vaginal microbiota, cytokines and chemokines in pregnant women. Nutrients 2020;12:1-17.
29. Qi F, Fan S, Fang C, *et al.* Orally administrated *Lactobacillus gasseri* TM13 and *Lactobacillus crispatus* LG55 can restore the vaginal health of patients recovering from bacterial vaginosis. Front Immunol 2023;14:1-12.
30. Thanaboonyawat I, Pothisan S, Petyim S, *et al.* Pregnancy outcomes after vaginal probiotic supplementation before frozen embryo transfer: A randomized controlled study. Sci Rep 2023;13:1-10.
31. Vaccalluzzo A, Pino A, Grimaldi RL, *et al. Lacticaseibacillus rhamnosus* TOM 22.8 (DSM 33500) is an effective strategy for managing vaginal dysbiosis, rising the Lactobacilli population. J Appl Microbiol 2024;135:lxae110.
32. Vicariotto F, Malfa P, Viciani E, *et al.* Efficacy of *Lactiplantibacillus plantarum* PBS067, *Bifidobacterium animalis* subsp. lactis BL050, and *Lacticaseibacillus rhamnosus* LRH020 in the amelioration of vaginal micro. Nutrients 2024;16:402.
33. Rezazadeh MB, Zanganeh M, Jarahi L, *et al.* Comparative efficacy of oral and vaginal probiotics in reducing the recurrence of bacterial vaginosis: A double-blind clinical trial. BMC Womens Health 2024;24(1).
34. Russo R, Karadja E, De Seta F. Evidence-based mixture containing Lactobacillus strains and lactoferrin to prevent recurrent bacterial vaginosis: A double blind, placebo controlled, randomised clinical trial. Benef Microbes 2019;10:19-26.
35. Jespers V, van de Wijgert J, Cools P, *et al.* The significance of *Lactobacillus crispatus* and *L. vaginalis* for vaginal health and the negative effect of recent sex: A cross-sectional descriptive study across groups of African women. BMC Infect Dis 2015;15:1-14.
36. Anukam K, Osazuwa E, Ahonkhai I, *et al.* Augmentation of antimicrobial metronidazole therapy of bacterial vaginosis with oral probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14: Randomized, double-blind, placebo controlled trial. Microbes Infect 2006;8:1450-1454.
37. Liu P, Lu Y, Li R, *et al.* Use of probiotic Lactobacilli in the treatment of vaginal infections: In vitro and in vivo investigations. Front Cell Infect Microbiol 2023;13:1-12.
38. Vujic G, Jajac KA, Despot SV, *et al.* Efficacy of orally applied probiotic capsules for bacterial vaginosis and other vaginal infections: A double-blind, randomized, placebo-controlled study. Eur J Obstet Gynecol Reprod Biol 2013;168:75-79.
39. Mashatan N, Heidari R, Altafi M, *et al.* Probiotics in vaginal health. Pathog Dis 2023;81:1-12.
40. De Almeida MO, Carvalho R, Aburjaile FF, *et al.* Characterization of the first vaginal *Lactobacillus crispatus* genomes isolated in Brazil. PeerJ 2021;9:1-24.
41. Zhao W, Peng C, Sakandar HA, *et al.* Meta-analysis: Randomized trials of *Lactobacillus plantarum* on immune regulation over the last decades. Front Immunol 2021;12:1-8.
42. Hao R, Liu Q, Wang L, *et al.* Anti-inflammatory effect of Lactiplantibacillus plantarum T1 cell- free supernatants through suppression of oxidative stress and NF-κB- and MAPK-signaling pathways. Appl Environ Microbiol 2023;89:1-15.
43. Abbe C, Mitchell CM. Bacterial vaginosis: A review of approaches to treatment and prevention. Front Reprod Health 2023;5:1-13.
44. Barrientos-Durán A, Fuentes-López A, de Salazar A, *et al.* Reviewing the composition of vaginal microbiota: Inclusion of nutrition and probiotic factors in the maintenance of eubiosis. Nutrients 2020;12:1-30.
45. Saraf VS, Sheikh SA, Ahmad A, *et al.* Vaginal microbiome: Normalcy vs dysbiosis. Arch Microbiol 2021;203:3793-3802.
46. Peebles K, Velloza J, Balkus JE, *et al.* High global burden and costs of bacterial vaginosis: A systematic review and meta-analysis. Sex Transm Dis 2019;46:304-311.