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PROBIOTICS IN THE PREVENTION AND TREATMENT OF UROGENITAL INFECTIONS IN POSTMENOPAUSAL WOMEN: A SYSTEMATIC REVIEW

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ABSTRACT

Background. Postmenopausal women are prone to recurrent urinary and vaginal infections due to estrogen decline, epithelial atrophy, elevated pH, and loss of Lactobacillus-dominated microbiota. Antibiotics reduce recurrences but promote resistance. Probiotics may restore vaginal homeostasis, inhibit pathogens, and modulate immunity.
Aim. To review randomized controlled trials (RCTs) on probiotics for prevention and treatment of urogenital infections in postmenopausal women.
Materials and methods. PubMed, Scopus, and Web of Science were searched to, in line with PRISMA. Eligible RCTs investigated probiotic interventions reporting clinical or microbiological outcomes. Risk of bias was assessed with the Cochrane RoB 2.0 tool. Results were synthesized narratively due to heterogeneity.
Results. Six RCTs were included. Vaginally derived strains such as L. rhamnosus GR-1, L. reuteri RC-14, L. crispatus, L. gasseri, and L. jensenii improved Nugent scores and vaginal microbiota. Oral GR-1/RC-14 achieved meaningful changes even after short treatment, whereas L. rhamnosus GG was ineffective due to poor colonization. Large-scale trials showed probiotics less effective than antibiotics for UTI prevention but without inducing resistance. All regimens were well tolerated, with no serious adverse events.
Conclusion. Probiotics are safe and may improve vaginal microbiota in postmenopausal women. Efficacy is strain- and route-dependent, with GR-1/RC-14 showing the most consistent results. While not a replacement for antibiotics, probiotics represent a promising adjunct in non-hormonal management of urogenital health. Further high-quality trials are needed to establish optimal use.

KEYWORDS

Probiotics; Urogenital Infections; Postmenopausal Women; Vaginal Microbiota

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1. Introduction

Postmenopausal women are at increased risk of urogenital infections and dysbiosis-related conditions, including recurrent urinary tract infections (rUTIs) and abnormal vaginal microbiota patterns resembling bacterial vaginosis. Estrogen deficiency following menopause leads to epithelial thinning, reduced glycogen availability within vaginal epithelial cells, and increased vaginal pH, which together impair the ecological dominance of Lactobacillus species and facilitate colonization by opportunistic and uropathogenic bacteria (Raz, 2011; Stapleton, 2016; Jung and Brubaker, 2019). These alterations are central to the pathophysiology of the genitourinary syndrome of menopause (GSM), in which vaginal symptoms frequently coexist with microbiota instability and increased susceptibility to infection (Portman and Gass, 2014; Stabile et al., 2023).

Antibiotic prophylaxis is effective in reducing rUTI recurrence; however, its long-term use is limited by adverse effects, disruption of commensal microbiota, and the rapid emergence of antimicrobial resistance (Wagenlehner et al., 2013; Gupta and Trautner, 2013). Consequently, non-antibiotic interventions aimed at restoring mucosal and microbial homeostasis have gained increasing attention. Among these, probiotics - particularly selected Lactobacillus strains - have been investigated for their ability to re-establish a Lactobacillus-dominant vaginal ecosystem, lower vaginal pH, inhibit pathogen growth through competitive exclusion and antimicrobial metabolite production and modulate local immune responses (Reid and Burton, 2014; Andrews et al., 2025).

Clinical studies conducted in postmenopausal women indicate that the effectiveness of probiotic interventions is highly dependent on strain selection, formulation, and route of administration. A multicenter, randomized, double-blind, placebo-controlled trial evaluating a vaginal medicinal product containing three Lactobacillus strains (Lactobacillus fermentum 57A, Lactobacillus plantarum 57B, and Lactobacillus gasseri

57C) demonstrated that intravaginal administration promoted Lactobacillus colonization and was associated with significant improvements in vaginal pH and Nugent score among women with abnormal or intermediate vaginal microbiota (Tomusiak et al., 2015). These findings support the concept that direct vaginal delivery may be particularly relevant in postmenopausal women, in whom natural colonization resistance is compromised.

In addition to intravaginal formulations, oral probiotic supplementation has also been explored in hypoestrogenic conditions. Clinical trials conducted in women experiencing menopause or menopause-like states, including oncology-related hypoestrogenism, have reported improvements in vaginal microbiota composition and Nugent scores following oral administration of selected Lactobacillus strains (Marschalek et al., 2017).

More recent interventional studies have expanded the range of probiotic strategies evaluated in pre- and postmenopausal populations. Randomized trials assessing Lactobacillus-containing feminine products have reported improvements in vaginal microbiota parameters and genitourinary symptoms, with the most pronounced benefits observed in women presenting with baseline dysbiosis (Yoshikata et al., 2022). Additional clinical investigations focusing specifically on postmenopausal women have demonstrated favorable effects of targeted probiotic combinations on vaginal well-being and microbiota composition (Vicariotto et al., 2024).

Systematic reviews and meta-analyses examining probiotic use during the menopausal transition consistently report beneficial shifts toward a healthier vaginal microbiota, including reductions in Nugent scores; however, they also emphasize substantial heterogeneity in probiotic strains, dosing regimens, outcome definitions, and follow-up durations (de Vrese et al., 2019; Andrews et al., 2025).

Given the high burden of urogenital infections after menopause, the limitations of antibiotic-based prevention, and the growing mechanistic and clinical evidence supporting microbiota restoration, a systematic evaluation of randomized controlled trials investigating probiotic interventions in postmenopausal women is warranted. Therefore, this review aims to synthesize current RCT evidence on the efficacy and safety of probiotics for the prevention and treatment of urogenital infections in this population, with particular emphasis on strain specificity, route of administration, and clinically relevant outcomes.

2. Methods

This systematic review was conducted to identify clinical trials evaluating the use of probiotics for the prevention and treatment of urogenital infections in postmenopausal women. The review was conducted in accordance with the PRISMA 2020 statement (Page et al., 2021), and risk of bias was assessed using the Cochrane RoB 2.0 tool (Sterne et al., 2019). The following databases were searched: PubMed, Scopus and Web of Science from inception to 25 December 2025. The search strategy combined keywords “urogenital infections” AND “postmenopausal women”. Boolean operators were adjusted for each database and filters were applied to include only human studies, publications in English and randomized controlled trials. Eligible article types were restricted to Adaptive Clinical trials, Clinical Studies, Controlled Clinical Trials, Meta-Analyses and Randomized Controlled Trials. Studies were considered eligible if they investigated probiotic interventions, included postmenopausal women with urogenital infections, and reported clinical or microbiological outcomes. Exclusion criteria included non-randomized studies, non-human studies, studies addressing urogenital infections in women before menopause, therapeutic approaches other than probiotics and publications in languages other than English. All records identified through database searches were imported into Rayyan software for screening. The search retrieved a total of 6 records from PubMed, 2 from Web of Science and 4 from Scopus. Records identified through other methods: 1. After removal of 1 duplicate, records underwent title and abstract screening, of which 3 were excluded for reasons such as investigating therapeutic approaches other than probiotics, ineligible study design, wrong population. In total, 9 full text articles were sought for retrieval, of which 3 could not be obtained. 6 articles were assessed for eligibility, and after applying the inclusion and exclusion criteria, 6 studies were included in the final review. The detailed selection process, including reasons for exclusion at each stage, is illustrated in Figure 1. Data collection was performed in duplicate using a standardized extraction sheet. The quality and risk of bias of eligible randomized studies were appraised with the Cochrane Risk of Bias 2.0 tool. Given the heterogeneity of study methodologies, participant groups and outcome assessments, a meta-analysis could not be undertaken, and results are presented narratively.

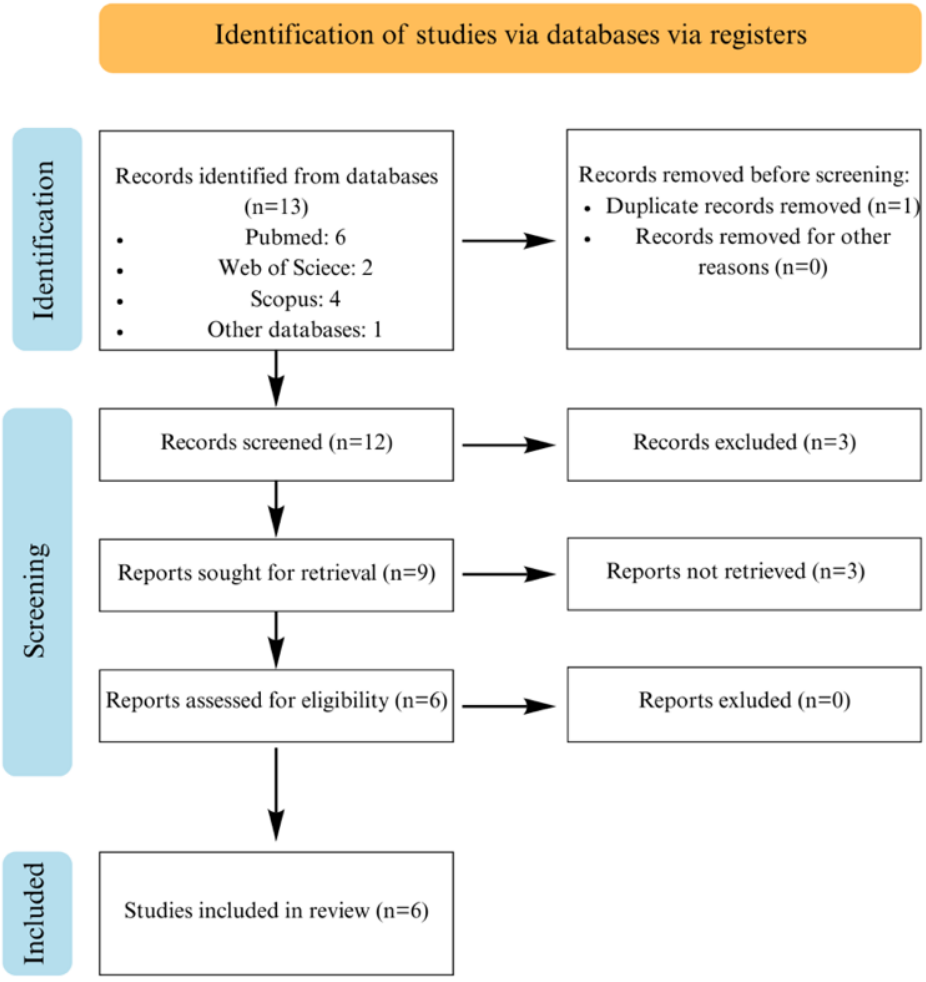

Fig. 1. *PRISMA 2020 flow diagram*

3. Results

Six randomized controlled trials met the inclusion criteria and were analyzed in this review. These studies investigated the use of probiotics for the prevention or treatment of urogenital infections or vaginal dysbiosis in postmenopausal women. Although the studies varied in probiotic strains, administration routes, and outcome measures, all shared the common goal of assessing the clinical or microbiological impact of probiotic therapy in this population.

Bisanz et al. conducted a double-blind, placebo-controlled, crossover trial in 14 postmenopausal women. Participants received a three-day course of vaginal probiotics containing Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14. No significant changes were observed in Nugent scores or vaginal pH. However, microbiome sequencing revealed temporary increases in Lactobacillus abundance and decreases in Atopobium in some participants. Additionally, transcriptomic analysis indicated upregulation of immune-related genes, including toll-like receptor 2 (TLR2), suggesting local immunomodulatory effects (Bisanz et al., 2014).

In a study by Colodner et al., 42 healthy postmenopausal women received orally administered Lactobacillus rhamnosus GG (LGG) for four weeks. Although gastrointestinal colonization occurred in 78.6% of participants, only 9.5% showed vaginal colonization, and the bacterial load was minimal. No differences were observed between once- and twice-daily dosing groups. The authors concluded that LGG was not suitable for vaginal colonization and was therefore unlikely to be effective in preventing urogenital infections in this population (Colodner et al., 2003).

A systematic review and meta-analysis by de Vrese et al. included three RCTs, one of which focused on postmenopausal breast cancer patients. Participants received a mixture of four oral probiotic strains: L. crispatus, L. gasseri, L. jensenii and L. rhamnosus. Pooled analysis revealed a significant reduction in Nugent scores in the intervention group compared to placebo (standardized mean difference [SMD] = -0.561; 95%

CI: -0.935 to -0.186; p = 0.004). The odds of improvement were nearly four times higher in the probiotic group (OR = 3.9; 95% CI: 1.7-9.1; p = 0.001). No heterogeneity was detected among the studies (I^2 = 0%) (de Vrese et al., 2019).

The study by Petricevic et al. included 72 postmenopausal women with intermediate Nugent scores (4-6). Participants received oral capsules containing L. rhamnosus GR-1 and L. reuteri RC-14 for 14 days. A Nugent score reduction of at least two grades was observed in 60% of participants in the probiotic group, compared to 16% in the placebo group (p = 0.0001). The median reduction in the intervention group was three points, while no change occurred in the control group (Petricevic et al., 2008).

In a multicenter, double-blind RCT, 252 postmenopausal women with recurrent UTIs received either trimethoprim-sulfamethoxazole or oral L. rhamnosus GR-1 plus L. reuteri RC-14 for 12 months. The mean number of UTIs was similar between groups (2.9 vs. 3.3/year), and the probiotic regimen did not meet noninferiority criteria. Median time to first UTI was shorter with probiotics (3 vs. 6 months). However, while antibiotic use rapidly increased E. coli resistance (~80–95%), no resistance emerged in the probiotic group (Beerepoot et al., 2012)

Additionally, a 2017 narrative review synthesized non-antibiotic prophylactic strategies for postmenopausal women with recurrent UTIs. The authors reported that intravaginal estrogens normalize vaginal flora and substantially reduce UTI risk, and noted that other approaches - including probiotics, cranberry products, and D-mannose - have been studied. The review also highlighted emerging options such as oral immunostimulants, vaginal vaccines, and bladder instillations with hyaluronic acid and chondroitin sulfate aimed at improving urinary symptoms and quality of life. While not an RCT, this evidence map situates probiotics among several non-antibiotic strategies considered for this population. (Caretto et al., 2017)

None of the included studies reported serious adverse events. All probiotic interventions were well tolerated.

4. Discussion

The findings of this review suggest that certain probiotic strains may contribute to the restoration of a healthy vaginal microbiota in postmenopausal women. However, the efficacy of probiotics appears to depend on strain selection, route of administration and treatment duration.

Short courses of vaginal probiotics were generally insufficient to induce sustained clinical improvements. Nevertheless, changes in microbial composition and host gene expression indicate that even brief probiotic exposure may influence the vaginal ecosystem at the molecular level (Bisanz 2014). Oral administration produced more consistent benefits, particularly when strains with vaginal tropism such as L. rhamnosus GR-1 and L. reuteri RC-14 were used. In contrast, strains optimized for gastrointestinal colonization, such as L. rhamnosus GG, showed limited clinical effect. This finding highlights the importance of selecting strains with specific adherence properties and vaginal tropism when designing interventions targeting urogenital health (Colodner 2003).

Pooled analyses support the role of multi-strain probiotic formulations. The combination of vaginally derived strains administered orally resulted in consistent reductions in Nugent scores across diverse populations, including women undergoing chemotherapy. The absence of heterogeneity among trials supports the robustness and generalizability of the findings (Vrese 2019).

Oral administration of L. rhamnosus GR-1 and L. reuteri RC-14 has shown the most promising results. In women with intermediate Nugent scores, supplementation produced both statistically and clinically significant improvements in vaginal microbiota, even after a relatively short intervention period. These strains are known for their ability to adhere to urogenital epithelial cells and inhibit pathogen growth (Petricevic 2008).

Large-scale trials show that probiotics are less effective than antibiotics in preventing recurrent UTIs, yet they avoid the rapid emergence of antimicrobial resistance. Thus, while not a replacement for antibiotics, they may serve as a safer adjunct or alternative for selected patients (Beerepoot 2012). Within non-antibiotic strategies, probiotics complement vaginal estrogens - still the most effective option - and other approaches such as cranberry, D-mannose, or immunomodulatory therapies. This highlights their role in personalized, multifaceted management of urogenital health in postmenopausal women (Caretto 2017).

Overall, these findings suggest that well-selected probiotic strains, particularly when administered orally, may offer a safe and effective non-hormonal approach to managing vaginal dysbiosis in postmenopausal women.

5. Conclusions

Evidence from randomized controlled trials supports the use of specific probiotic strains - L. rhamnosus GR-1, L. reuteri RC-14, L. crispatus, L. gasseri and L. jensenii - to improve vaginal microbiota in postmenopausal women. Oral administration of these strains has been associated with reductions in Nugent scores and the restoration of a lactobacilli-dominant vaginal environment.

The effectiveness of probiotic interventions is strain-dependent. Strains not adapted to the vaginal niche, such as L. rhamnosus GG, may be ineffective for genitourinary applications. In contrast, vaginally derived strains with strong adherence capacity and antimicrobial activity have demonstrated more consistent benefits.

Probiotic use in this population appears to be safe and well tolerated. However, further research is needed to establish optimal dosing strategies, assess long-term outcomes, and explore individual variability in treatment response. Future studies should also incorporate microbiome and immunological markers to better understand the underlying mechanisms of probiotic action.

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Data Availability Statement: All data supporting this review are contained within the article. No new data were generated.

Conflicts of Interest: The authors declare no conflict of interest.

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