

Original Research Article

RECURRENT BACTERIAL VAGINOSIS: CURRENT CHALLENGES IN DIAGNOSIS, TREATMENT, AND RECURRENCE PREVENTION

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ABSTRACT

Introduction. Bacterial vaginosis is the most common cause of abnormal vaginal discharge in women of reproductive age, affecting roughly one in four worldwide. Most relapse within a year of recommended therapy, facing repeated antibiotic courses and sustained risk of sexually transmitted infection and adverse reproductive outcomes. **Method.** We narratively reviewed guidelines, randomised trials, systematic reviews and mechanistic studies on recurrent bacterial vaginosis from PubMed, Scopus and Google Scholar, synthesising findings thematically. **Result & Analysis.** Recurrence reflects interacting mechanisms: a polymicrobial biofilm anchored by *Gardnerella* species, antimicrobial tolerance within it, failure to restore a *Lactobacillus*-dominant microbiome, and reinfection from untreated partners. The community regrowing after metronidazole is typically dominated by *Lactobacillus iners* rather than the protective *Lactobacillus crispatus*, so a *Lactobacillus*-dominant smear does not indicate protection. Positive Amsel result is reliable, whereas a negative one does not exclude disease. Suppressive metronidazole gel controls symptoms without curing the underlying dysbiosis. Live biotherapeutic products reduce recurrence only when antibiotic therapy has first achieved clinical cure, so sequence matters as much as product choice. Male-partner treatment substantially reduced recurrence in a trial stopped early for benefit, and is now endorsed in a practice update. Boric acid, probiotics and microbiota transplantation give variable results, and differing trial definitions of recurrence limit comparison. **Discussion.** Clinicians should reassess the diagnosis before repeating antibiotics, sequence microbiome restoration after antimicrobial cure, and consider partner treatment. Biofilm-targeted agents from antimalarial repurposing remain preclinical. Management is moving from uniform regimens toward microbiome-informed, individualised prevention, though validation in Southeast Asian populations is lacking.

Keywords: *Bacterial Vaginosis, Biofilm, Partner Treatment, Recurrence, Vaginal Microbiome*

INTRODUCTION

Bacterial vaginosis (BV) describes a shift in the vaginal microbiome from *Lactobacillus* dominance toward a polymicrobial community of facultative and strict anaerobes, among them *Gardnerella*, *Prevotella*, *Fannyhessea* (formerly *Atopobium*) and *Megasphaera* species. Lactic acid production falls, vaginal pH rises, and colonisation resistance weakens. BV affects about one in four women globally and accounts for the largest share of abnormal vaginal discharge presenting to primary care, sexual health and dermatovenereology clinics (Bradshaw et al., 2025). In the United States, prevalence reaches 30% among women of reproductive age. (Watkins et al., 2025) Indonesian data remain sparse and single-centre (Sarasmita et al., 2025).

Standard antibiotic treatment often provides only temporary benefit. Between 50% and 80% of women experience at least one recurrence within twelve months (Abbe and Mitchell, 2023), and recurrent BV — three or more episodes in a year — is therefore the common presentation rather than the exception (Workowski et al., 2021). Each relapse brings another antibiotic course, with repeated nitroimidazole exposure causing gastrointestinal intolerance, secondary vulvovaginal candidiasis, and selection pressure on the residual vaginal community. Women report persistent malodour and discharge that disrupt sexual relationships and daily function. Recurrent BV also increases susceptibility to HIV and other sexually transmitted infections and associates with preterm birth, spontaneous abortion and pelvic

inflammatory disease (Bradshaw et al., 2025).

These challenges are closely interconnected. Diagnostic uncertainty allows women with other causes of vaginal symptoms to receive repeated BV treatment. Treatment failure and early recurrence follow because current regimens reduce bacterial load without restoring a stable *Lactobacillus*-dominant ecosystem. Prevention strategies remain few and unevenly supported by evidence, so clinicians return to the course that already failed, and the cycle repeats.

METHOD AND ANALYSIS

This review examines diagnosis, treatment and recurrence prevention in recurrent BV and assesses emerging strategies most likely to change practice. We searched on PubMed, Scopus and Google Scholar for English-language guidelines, randomised trials, systematic reviews and mechanistic studies published between January 2020 and February 2026. Relevant evidence was identified and synthesised thematically according to diagnosis, treatment, and recurrence prevention. Particular attention was given to emerging microbiome-based interventions, sexual partner treatment, and biofilm-targeted therapies. No formal risk-of-bias assessment was undertaken, consistent with the narrative review design.

RESULTS

PATHOGENESIS AND MECHANISMS OF RECURRENCE

1. Vaginal Microbiome Dysbiosis

A healthy vagina hosts a low-diversity community dominated by *Lactobacillus crispatus*, *L. gasseri* or

L. jensenii, which produce lactic acid and hold vaginal pH below 4.5, suppressing anaerobic overgrowth. *L. iners* is the exception: it produces only L-lactic acid and marks an unstable transitional state that *predisposes* to dysbiosis rather than protecting against it (Bloom et al., 2022). In BV this community gives way to a diverse consortium of *Gardnerella* species, *Prevotella bivia*, *Fannyhessea vaginae*, *Megasphaera* and *Sneathia* species (Bradshaw et al., 2025, Abbe and Mitchell, 2023). Vaginal pH rises above 4.5, lactic acid production falls, and sialidase and other mucin-degrading enzymes thin the protective mucus layer (Bradshaw et al., 2025).

2. Biofilm Formation

Gardnerella species adhere to vaginal epithelial cells and form the scaffold of a dense polymicrobial biofilm that later incorporates *F. vaginae* and *Prevotella* (Bradshaw et al., 2025) ; the sequence of these events is now being tested prospectively (Muzny et al., 2024). *Gardnerella* is no longer a single organism: *G. vaginalis*, *G. piotii*, *G. leopoldii* and *G. swidsinskii* are genomically distinct species that differ in virulence and biofilm-forming capacity, which may explain why identical regimens produce different outcomes (Bradshaw et al., 2025),(Vanechoutte et al., 2019). The biofilm matrix limits antibiotic penetration. Among 24 *G. vaginalis* isolates from Northeast China, 87.5% were metronidazole-resistant, and neither metronidazole nor clindamycin eradicated established

biofilms at any concentration tested (Ma et al., 2022).

3. Failure of Microbiome Restoration

Reducing bacterial load does not restore a normal vaginal microbiome. Metronidazole clears anaerobes, but the community that regrows is typically dominated by *L. iners* rather than *L. crispatus* - a *Lactobacillus*-dominant profile on paper, yet one that offers little protection and precedes relapse (Bloom et al., 2022).

4. Antimicrobial Resistance and Microbial Persistence

Resistance, tolerance, and persistence may act together to undermine antimicrobial treatment in BV. Efflux pump activity, single-nucleotide polymorphisms, and biofilm-associated dormancy can enable BV-associated bacteria to withstand antimicrobial concentrations that eliminate their planktonic counterparts (Mohankumar et al., 2022). Repeated antibiotic exposure may further select for these resilient populations, contributing to incomplete eradication and increasing the risk of subsequent treatment failure and recurrence (Mohankumar et al., 2022).

5. Host and Behavioural Factors

Recurrence risk rises with ongoing exposure to a regular or untreated sexual partner and inconsistent condom use, implicating reinfection in recurrence (Bradshaw et al., 2025, Vodstrcil et al., 2021). Vaginal douching and smoking have also been linked to BV, though inconsistently, and douching may reflect cleaning in response to symptoms rather than a cause

(Bradshaw et al., 2025). Contraceptive choice cuts both ways: hormonal contraception is associated with a reduced risk of BV (Bradshaw et al., 2025), (Vodstrcil et al., 2013), (Workowski et al., 2021), whereas copper intrauterine devices are consistently associated with increased BV and recurrence. Host factors including obesity, immunosuppression and differences in host genetics contribute further (Watkins et al., 2025). These factors converge on three routes: introduction of BV-associated bacteria, depletion of resident *Lactobacillus*, and a rise in vaginal pH - so no single behavioural change prevents recurrence alone.

DIAGNOSTIC CHALLENGES

1. Clinical diagnosis

Amsel criteria require three of four findings: homogeneous thin discharge, vaginal pH above 4.5, clue cells on saline microscopy, and a fishy odour before or after adding 10% potassium hydroxide (Workowski et al., 2021). They require no laboratory and give an answer during the consultation. Against Nugent scoring, Amsel criteria show limited sensitivity (37–70%) but high specificity (94–99%) (Workowski et al., 2021), with false-negative rates ranging from 26% in North America to 40% in Africa (Bradshaw et al., 2025). Thus, a positive Amsel result strongly supports BV, whereas a negative result does not reliably exclude it. Diagnostic performance also depends on microscopy expertise and subjective interpretation of the whiff test.

2. Nugent Scoring

The Nugent score semi-quantitatively assesses *Lactobacillus*, *Gardnerella*/ *Bacteroides*, and curved Gram-negative morphotypes on Gram-stained smears using a 0–10 scale, with scores of 4 to 6 considered intermediate and 7 to 10 indicating BV (Workowski et al., 2021). Although reproducible, the method requires trained microscopy expertise and may delay diagnosis. Misidentification of *L. iners* as *Gardnerella* can further affect scoring (Bradshaw et al., 2025). The intermediate range creates diagnostic uncertainty, particularly after treatment. Moreover, inconsistent definitions of recurrence across studies—using different combinations of Amsel criteria and Nugent scores limit direct comparison of recurrence rates (Bradshaw et al., 2025).

3. Molecular and NAAT diagnosis

Molecular assays quantify BV-associated organisms and *Lactobacillus* species while reducing subjective interpretation and allowing simultaneous detection of other causes of vaginal discharge (Bradshaw et al., 2025). However, specificity remains a concern: 20–21% of asymptomatic women may test positive by Gram stain or NAAT (Danby et al., 2021), while the Affirm VP III probe has a specificity of only 81% against Nugent scoring because *Gardnerella* may be abundant in the absence of clinical BV (Workowski et al., 2021). Thus, positive molecular results in asymptomatic women may represent colonisation rather than disease

(Bradshaw et al., 2025),(Workowski et al., 2021). Laboratory-based molecular testing remains limited by cost in many resource-constrained settings, including Indonesia. Sialidase-based point-of-care cards retain high specificity (>91%) at low cost (Bradshaw et al., 2025), whereas pH- and amine-based cards are cheaper still but considerably less specific (61%) (Workowski et al., 2021).

4. Differential Diagnosis

Persistent symptoms after treatment do not necessarily indicate recurrent BV. In a study of 429 women with vaginitis in northern Taiwan, typical clinical findings were often insufficient for diagnosis, and 55.2% of empirical antifungal and

metronidazole prescriptions were ineffective or unnecessary (Huang et al., 2023). Alternative diagnoses including vulvovaginal candidiasis, trichomoniasis, aerobic vaginitis, cytolytic vaginosis, desquamative inflammatory vaginitis, genitourinary syndrome of menopause, and vulvodynia, should therefore be reconsidered (Mitchell, 2024),(Agoni, 2026). Mixed vaginitis may be more difficult to eradicate and more prone to recurrence than single infections (Qi et al., 2021). Wet mount microscopy can identify several of these conditions in a single, low-cost examination, although molecular testing generally offers greater diagnostic accuracy (Mitchell, 2024), (Agoni, 2026).

Table 1 Comparison of Diagnostic Methods for Bacterial Vaginosis in Routine Practice

Method	Basis	Sensitivity	Specificity	Practice notes
Amsel criteria	≥3 of 4: homogeneous discharge, pH >4.5, clue cells, positive whiff test	37–70% vs Nugent (Workowski et al., 2021); false negative 26% North America, 32% India/Nepal, 40% Africa (Bradshaw et al., 2025); 98.7% against composite clinical criteria in one US study (Danby et al., 2021).	94–99% vs Nugent (Workowski et al., 2021).	Immediate, no laboratory, low cost; a positive result is reliable, a negative is not; whiff test subjective
Nugent score	Gram stain morphotype scoring 0–10; 4–6 intermediate, 7–10 BV	82.7% against composite clinical criteria (Danby et al., 2021); false negative 8–19% vs Amsel (Bradshaw et al., 2025).	Reference standard	Reproducible, permanent slide; trained microscopist needed; intermediate band unhelpful; <i>L. iners</i> misread as <i>Gardnerella</i> (Bradshaw et al., 2025).
Hay–Ison criteria	Gram stain assigned to five categories (0, I–IV)	>96% against Amsel (Bradshaw et al., 2025).	73–90% (Bradshaw et al., 2025).	Simpler than Nugent; used in UK/European guidelines; assignment subjective

Method	Basis	Sensitivity	Specificity	Practice notes
Wet mount microscopy	Saline microscopy of vaginal fluid	Operator-dependent; 48.5% for VVC, 75% for <i>T. vaginalis</i> (Danby et al., 2021).	High for positive findings (Agoni, 2026).	Screens BV, candidiasis, trichomoniasis, aerobic and cytolytic vaginosis in one examination (Agoni, 2026); microscope cost and declining training (Agoni, 2026).
Sialidase point-of-care assay	Chromogenic detection of bacterial sialidase	Variable — not all BV-associated bacteria produce sialidase (Bradshaw et al., 2025).	>91% (Bradshaw et al., 2025).	Inexpensive, rapid, low-complexity; specificity comparable to Amsel criteria, making it the most feasible objective test where laboratory NAAT is unaffordable (Workowski et al., 2021).
pH/amine card (FemExam)	Vaginal pH, trimethylamine, proline aminopeptidase	91% vs Nugent (Workowski et al., 2021).	61% (Workowski et al., 2021).	Studied primarily in resource-poor settings; low specificity precludes stand-alone use (Workowski et al., 2021).
DNA probe (Affirm VP III)	Probe for high-concentration <i>G. vaginalis</i> ($>5 \times 10^5$ CFU/mL)	97% in symptomatic women, with pH and amine odour (Workowski et al., 2021).	81% vs Nugent (Workowski et al., 2021).	Illustrates why a positive molecular result is not equivalent to disease
Laboratory NAAT	Quantification of BV-associated bacteria and <i>Lactobacillus</i> (BD Max Vaginal Panel, Aptima BV, Xpert Xpress MVP)	78.7% against composite clinical criteria (Danby et al., 2021); high vs molecular standards (Bradshaw et al., 2025).	High (Bradshaw et al., 2025); 20–21% of asymptomatic women positive (Danby et al., 2021).	Objective, valid on self-collected swabs, identifies other causes of discharge; cost and laboratory requirement; laboratory-developed tests lack published performance data (Bradshaw et al., 2025).
Point-of-care multiplex NAAT	Cartridge-based PCR (Xpert Xpress MVP)	High (Bradshaw et al., 2025).	High (Bradshaw et al., 2025).	Same-visit decision; performance consistent across operator job function and education level, including untrained staff (Van Der Pol et al., 2025); instrument and cartridge cost

Note. BV = bacterial vaginosis; CFU = colony-forming units; KOH = potassium hydroxide; NAAT = nucleic acid amplification test; VVC = vulvovaginal candidiasis. Regional false-negative rates are pooled estimates from (Bradshaw et al., 2025). Sensitivity figures from (Danby et al., 2021) were measured against composite clinical criteria rather than Nugent scoring and are not directly comparable with guideline estimates.

TREATMENT OF RECURRENT BV

1. Initial Treatment

Recommended regimens are oral metronidazole 500 mg twice daily for seven days, 0.75% metronidazole gel 5 g intravaginally once daily for five days, and 2% clindamycin cream 5 g intravaginally at bedtime for seven days. Alternatives include oral clindamycin 300 mg twice daily for seven days, clindamycin ovules 100 mg intravaginally at bedtime for three days, single-dose secnidazole 2 g oral granules, and tinidazole 2 g daily for two days or 1 g daily for five days (Workowski et al., 2021). Four-week cure rates of 70–80% are similar across the recommended regimens (Bradshaw et al., 2025), yet none alters the recurrence trajectory (Abbe and Mitchell, 2023). Table 2 sets out the regimens for first-episode and recurrent disease.

2. First Recurrence

Confirm the diagnosis before repeating therapy, since symptoms alone misdirect treatment in more than half of empirical prescriptions (Huang et al., 2023). Ask about adherence and about premature discontinuation once discharge settles. Patients previously advised to avoid alcohol during nitroimidazole therapy can be reassured that this restriction is no longer considered necessary (Workowski et al., 2021). Then either repeat the original regimen or switch class: after a first recurrence, retreatment with the same recommended regimen and use of a different one are both acceptable (Workowski et al., 2021).

3. Multiple Recurrences

For women with three or more episodes in twelve months, suppression with 0.75% metronidazole gel or a 750 mg metronidazole vaginal suppository twice weekly for more than three months reduces recurrence, although the benefit does not persist once suppression stops (Workowski et al., 2021). A second option sequences an oral nitroimidazole for seven days, then intravaginal boric acid 600 mg daily for 21 days, then suppressive metronidazole gel twice weekly for four to six months (Workowski et al., 2021). Months of nitroimidazole exposure raise rates of vulvovaginal candidiasis (Mitchell, 2024); monthly oral metronidazole 2 g given with fluconazole 150 mg has been evaluated as an alternative suppressive regimen that reduced BV incidence while promoting colonisation with normal vaginal microbiota (Workowski et al., 2021).

4. Partner Treatment

Trials conducted before 2020 treated male partners with oral nitroimidazole monotherapy and found no benefit, which shaped the guideline position that routine treatment of sex partners is not recommended (Workowski et al., 2021). Those trials were underpowered, omitted topical penile treatment, and suffered poor partner adherence (Vodstrcil et al., 2021). Molecular studies since then have shown concordance between penile and vaginal microbiota within couples, supporting reinfection as a driver of relapse (Vodstrcil et al., 2021).

The StepUp trial tested combined therapy. Women received first-line

treatment while male partners took oral metronidazole 400 mg twice daily and applied 2% clindamycin cream to penile skin twice daily for seven days. Recurrence within twelve weeks occurred in 24 of 69 women (35%) in the partner-treatment group against 43 of 68 (63%) under standard care, and the data and safety monitoring board stopped the trial early because treating the woman alone proved inferior (Vodstrcil et al., 2025). The trial was open-label and enrolled only monogamous couples, so its applicability to women with concurrent partners is untested. The American College of Obstetricians and Gynecologists issued a Clinical Practice Update in 2025 providing new guidance on concurrent sexual partner therapy for recurrent BV (ACOG, 2025). Couples should be informed that this is recent guidance and has not yet been incorporated into all national guidelines.

5. Probiotics and Microbiome Restoration

Evidence remains heterogeneous. A systematic review of 16 randomised

trials found benefit varying by species, strain, dose and duration, with no consensus regimen and limited long-term safety data, although *Lactobacillus rhamnosus* TOM 22.8 at 10×10^9 CFU daily for ten days emerged as the best-supported single regimen (Udjianto et al., 2025). Among 716 Chinese women with asymptomatic BV, vaginal probiotics produced lower cumulative recurrence than metronidazole at two, three and four months (Zhang et al., 2025). A double-blind trial in 55 women found no difference between oral and vaginal routes, although unequal group sizes leave it underpowered to establish equivalence (Rezazadeh et al., 2024). A phase IV trial in 80 women living with HIV showed no benefit from lactobacilli vaginal tablets added to oral metronidazole (Bangar et al., 2023). Population, strain and baseline microbiome all shape the result. Products designed to engraft a defined *Lactobacillus* strain are considered separately.

Table 2 Guideline-Based Regimens for Bacterial Vaginosis and Recurrent Bacterial Vaginosis

Indication	Agent	Dose and duration	Practice notes
First episode, recommended	Metronidazole, oral	500 mg twice daily for 7 days	Alcohol avoidance is no longer considered necessary (Workowski et al., 2021).
	Metronidazole gel 0.75%	5 g intravaginally once daily for 5 days	Lower systemic exposure; better tolerated
	Clindamycin cream 2%	5 g intravaginally at bedtime for 7 days	Oil-based; may weaken latex condoms and diaphragms for 5 days after use (Workowski et al., 2021).
First episode, alternative	Clindamycin, oral	300 mg twice daily for 7 days	Reserve where topical therapy is declined

Indication	Agent	Dose and duration	Practice notes
Recurrent BV (≥ 3 episodes in 12 months)	Clindamycin ovules	100 mg intravaginally at bedtime for 3 days	Shorter course aids adherence; oleaginous base — avoid latex products for 72 h after treatment (Workowski et al., 2021).
	Secnidazole	2 g oral granules, single dose	Single dose aids adherence; cost and availability limit use in many settings (Bradshaw et al., 2025).
	Tinidazole	2 g once daily for 2 days, or 1 g once daily for 5 days	No alcohol restriction required (Workowski et al., 2021).
	Suppressive metronidazole gel 0.75%	5 g intravaginally twice weekly for >3 months after induction	Suppresses without curing; relapse common after withdrawal
	Metronidazole vaginal suppository	750 mg intravaginally twice weekly for >3 months	Guideline-listed alternative to the gel (Workowski et al., 2021).
	Sequential combination	Oral nitroimidazole 7 days $\rightarrow$ boric acid 600 mg intravaginally daily for 21 days $\rightarrow$ metronidazole gel twice weekly for 4–6 months	Boric acid is toxic if swallowed and contraindicated in pregnancy
	Monthly metronidazole plus fluconazole	Oral metronidazole 2 g with fluconazole 150 mg, monthly	Reduced BV incidence and promoted normal microbiota; addresses nitroimidazole-associated candidiasis (Workowski et al., 2021).
	Concurrent male-partner therapy	Metronidazole 400 mg orally twice daily plus clindamycin 2% cream to penile skin twice daily, 7 days	Recurrence 35% vs 63%; (Vodstrcil et al., 2025) open-label trial in monogamous couples; endorsed by ACOG (ACOG, 2025).

Note. Regimens for first-episode and recurrent disease follow the 2021 CDC sexually transmitted infections treatment guidelines unless stated otherwise. (Workowski et al., 2021) Women should be advised to refrain from sexual activity or to use condoms consistently and correctly during treatment. (Workowski et al., 2021) ACOG = American College of Obstetricians and Gynecologists; BV = bacterial vaginosis.

RECURRENCE PREVENTION

1. Behavioural Interventions

Women should be advised to avoid vaginal douching and intravaginal cleansing products, which are associated with Lactobacillus-depleted microbiota (OR 2.24) (Abbe and Mitchell, 2023). Consistent condom use may reduce BV risk (pooled RR 0.8), while smoking is associated with approximately threefold higher odds of

BV, supporting smoking cessation counselling (Abbe and Mitchell, 2023). Patients can be reassured that alcohol avoidance is not required during metronidazole therapy (Workowski et al., 2021).

2. Suppressive Antimicrobial Therapy

Twice-weekly metronidazole gel for more than three months can suppress BV symptoms during treatment, but recurrence is common after discontinuation (Workowski et

al., 2021). Prolonged nitroimidazole exposure may also increase the risk of vulvovaginal candidiasis and select for tolerant organisms (Mohankumar et al., 2022). For women in whom recurrent candidiasis limits suppressive therapy, monthly oral metronidazole 2 g combined with fluconazole 150 mg is a guideline-supported alternative (Workowski et al., 2021).

3. Boric Acid

Intravaginal boric acid 600 mg daily may be used as an adjunct between oral nitroimidazole therapy and suppressive treatment in guideline-supported combination regimens (Workowski et al., 2021). Although it has been proposed to disrupt BV-associated biofilms, in vitro data suggest that it inhibits biofilm formation without reducing viability within established biofilms (Abbe and Mitchell, 2023). The 600-mg dose is extrapolated from vulvovaginal candidiasis rather than established in BV-specific trials (Bradshaw et al., 2025). In one study of 105 women, adding boric acid to antibiotic therapy was associated with a 69% six-month cure rate (Abbe and Mitchell, 2023). Its low cost and availability may make it an accessible option after first-line treatment failure, but it should not be swallowed and is contraindicated during pregnancy (Bradshaw et al., 2025), (Mitchell, 2024).

4. Probiotics and *Lactobacillus* Restoration

As discussed in Section 3.5, vaginal probiotics reduced cumulative recurrence compared with

metronidazole in one multicentre trial (Zhang et al., 2025), whereas adding *Lactobacillus* to metronidazole showed no benefit among women living with HIV (Bangar et al., 2023). Route of administration may be less important than strain selection; one double-blind trial found no significant difference between oral and vaginal administration (Rezazadeh et al., 2024). Sustained vaginal colonisation may be a determinant of efficacy; one regimen achieved strain colonisation in 82% of participants (Udjianto et al., 2025).

5. Microbiome Restoration

LACTIN-V, a live biotherapeutic containing *L. crispatus* CTV-05, reduced 12-week recurrence to 30% compared with 45% with placebo following vaginal metronidazole gel (RR 0.66, 95% CI 0.44–0.87) (Cohen et al., 2020). A post hoc analysis suggested that this benefit was limited to women who achieved clinical cure with preceding antibiotic therapy (RR 0.56, 95% CI 0.35–0.77) and was not observed among the 26 women without prior clinical cure (Hemmerling et al., 2024). These findings highlight the importance of treatment sequence, with microbiome restoration appearing most effective after successful antibiotic therapy. Vaginal microbiota transplantation has also restored *Lactobacillus* dominance in small human case series, but evidence remains limited to 36 treated women, with donor screening and regulatory pathways yet to be standardised (Luo et al., 2024).

Table 3 Evidence for Recurrence-Prevention Strategies in Bacterial Vaginosis

Strategy	Study design	Participants	Principal finding	Source
Male-partner treatment	Open-label RCT, stopped early	164 couples randomised; 137 women in mITT analysis	Recurrence at 12 weeks 35% (24/69) vs 63% (43/68) with standard care	(Vodstrcil et al., 2025)
LACTIN-V (<i>L. crispatus</i> CTV-05)	Phase 2b RCT	228 women	Recurrence at 12 weeks 30% vs 45% on placebo (RR 0.66, 95% CI 0.44–0.87)	(Cohen et al., 2020)
LACTIN-V, post hoc analysis	Secondary analysis	227 women (201 cured, 26 not cured by preceding antibiotic)	Benefit confined to women cured by the preceding antibiotic (RR 0.56, 95% CI 0.35–0.77)	(Hemmerling et al., 2024)
Vaginal probiotics	Multicentre RCT	716 women with asymptomatic BV	Lower cumulative recurrence than metronidazole at 2, 3 and 4 months	(Zhang et al., 2025)
Probiotics, pooled	Systematic review	16 RCTs	Strain- and dose-dependent benefit; no consensus regimen	(Udjianto et al., 2025)
Oral versus vaginal probiotics	Double-blind trial	55 women (20 vaginal, 35 oral)	No difference between routes; underpowered to establish equivalence	(Rezazadeh et al., 2024)
Lactobacilli tablets in women with HIV	Phase IV RCT	80 women	No benefit added to oral metronidazole	(Bangar et al., 2023)
Vaginal microbiota transplantation	Scoping review	36 women treated; 5 registered trials enrolling 556 women	<i>Lactobacillus</i> dominance restored; donor screening unresolved	(Luo et al., 2024)
Pyrimethamine	In vitro	Not applicable	MIC 0.125–4 mg/L vs 2–128 mg/L for metronidazole; outperformed metronidazole against biofilms in 3 of 4 strains; spares <i>Lactobacillus</i>	(Rosca et al., 2025)
MMV1582487	In vitro drug screen	Not applicable	>4 log ₁₀ CFU/mL reduction in a preformed biofilm of one high biofilm-forming isolate; synergy with antibiotics; non-cytotoxic	(Johnston et al., 2026)

Note. BV = bacterial vaginosis; CFU = colony-forming units; CI = confidence interval; MIC = minimum inhibitory concentration; mITT = modified intention-to-treat; RCT = randomised controlled trial; RR = risk ratio. The final two entries are preclinical and are included as prospective rather than current options.

DISCUSSION

Microbiome-based approaches are led by live biotherapeutic products such as LACTIN-V, whereas vaginal microbiota transplantation remains investigational. A scoping review identified only three

published human studies, although five registered trials involving 556 women are currently underway and may provide the first substantial efficacy data (Luo et al., 2024).

Biofilm-targeted therapy is advancing through antimalarial drug

repurposing. Screening of 640 Medicines for Malaria Venture compounds identified MMV1582487, which reduced viable counts in a preformed biofilm by $>4 \log_{10}$ CFU/mL at 10 μ M, while sparing *L. crispatus*, showing no cytotoxicity to vaginal epithelial cells, and acting synergistically with antibiotics (Johnston et al., 2026). Pyrimethamine inhibited all tested *Gardnerella* strains at lower MICs than metronidazole (0.125–4 vs. 2–128 mg/L) and showed superior biofilm activity in three of four strains while sparing *Lactobacillus* (Rosca et al., 2025). Both agents remain under preclinical investigation.

Other non-antibiotic strategies include agents targeting *Gardnerella* adhesion, enzymes that disrupt the biofilm matrix, antimicrobial peptides, and nanoformulations designed to penetrate biofilm-embedded organisms (Mohankumar et al., 2022).

Precision medicine may offer a path beyond one-size-fits-all treatment. Community state typing, sialidase activity, and post-treatment *Lactobacillus* recovery could help stratify women by recurrence risk and guide individualized therapy. However, as most trial data derive from North American cohorts, regional validation is needed before these approaches can be routinely applied in Indonesia.

CONCLUSION

Recurrent BV persists because *Gardnerella*-anchored biofilm survives antibiotic exposure, tolerant organisms repopulate the mucosa, and the flora that regrows is often *L. iners* rather than the protective *L. crispatus*. Inadequate

antibiotic therapy explains only part of the pattern. Persistent symptoms warrant diagnostic reassessment rather than another prescription. A positive Amsel result is reliable but a negative one does not exclude BV, and candidiasis, trichomoniasis, aerobic vaginitis, desquamative inflammatory vaginitis and mixed presentations all mimic recurrence.

Management is shifting from repeated antibiotic courses toward a sequenced model: antimicrobial cure first, then microbiome restoration with a colonising *Lactobacillus* strain, with partner treatment in recurrent cases and prevention matched to relapse risk. Biofilm-targeted agents remain preclinical. Dermatovenereologists are well placed to deliver this combination, which draws on sexual health and partner management as much as on gynaecological care. Trials in Southeast Asian populations remain the missing piece.

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