

Review Article

Vaginal dysbiosis-associated infections: Current and emerging treatment strategies

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ABSTRACT

The vaginal microbiome plays a crucial role in female reproductive health, protecting against pathogens through a *Lactobacillus*-dominated ecosystem. Disruption of this microenvironment, termed vaginal dysbiosis, is implicated in a range of infections, including bacterial vaginosis, vulvovaginal candidiasis, aerobic vaginitis, and mixed vaginitis. Despite their distinct etiologies, these conditions often present with overlapping clinical symptoms, leading to empirical treatment with broad-spectrum antimicrobials. While such interventions may provide brief symptom relief, they frequently fail to eradicate the underlying dysbiosis, resulting in high recurrence rates and the emergence of antimicrobial-resistant strains. This highlights the urgent need for targeted, microbiome-informed therapeutic interventions capable of restoring a stable, health-associated vaginal microbial community and reducing reliance on non-specific antibiotic regimens. This review article gives an overview of the current understanding of this topic, spanning from the heterogeneity of vaginal dysbiosis and its pathogenesis to the current treatment strategies employed and the future therapeutic prospects.

Keywords: Antimicrobial resistance, Emerging treatment strategies, Recurrence, Vaginal dysbiosis, Vaginal microbiome

INTRODUCTION

The vaginal microenvironment is a highly specialized ecosystem designed to protect the female reproductive tract.^[1] Primarily lined by stratified squamous epithelium, overlaid with a mucous layer that is continuously lubricated by cervicovaginal secretions. These secretions, produced by epithelial cells and mucosal plasma cells, are rich in mucins, antimicrobial peptides (AMPs), and immunoglobulins (IgA and IgG), which not only maintain hydration and lubrication but also serve as the primary line of defense against invading pathogens.^[2] This defense is reinforced by a resident microbiome that, in a healthy state, is dominated by *Lactobacillus* species. These bacteria produce bacteriocins, hydrogen peroxide, and lactic acid, which maintain acidic vaginal pH and suppress the growth of opportunistic and pathogenic microorganisms.^[3] Despite the cyclical hormonal and pH changes during the menstrual cycle, the vaginal microbiome remains resilient, often preserving a *Lactobacillus*-rich composition.^[4] However, the composition of the vaginal microbiome is not similar across different populations and varies considerably due to ethnicity, host genetic factors, and geographical regions. Studies using metagenomic and metabolomic profiling have demonstrated that women of African and Hispanic descent often exhibit greater microbial diversity and a higher prevalence of *Gardnerella*, *Atopobium*, and *Prevotella* species^[5] compared to women of European and Asian descent who tend to have *Lactobacillus*-dominant

communities.^[6,7] These differences may manifest in mucosal immune responses, vaginal pH regulation, and hormonal metabolism controlled by host genetic factors. Genes involved in innate immunity, such as toll-like receptors (TLR2, TLR4, TLR9) and NOD2, regulate the recognition of bacterial and fungal components and the downstream inflammatory response. Polymorphisms in these genes can alter immune response to pathogens. Similarly, variants in antimicrobial peptide genes such as β -Defensin 1 and pro-inflammatory cytokines such as interleukin-1 beta, interleukin-6, interleukin-8, and tumor necrosis factor-alpha may lead to impaired defense or exaggerated inflammation.^[8] Beyond soluble immune factors, genes involved in mucosal barrier integrity also have a profound impact. Hormonal regulation genes such as estrogen receptor 1 and CYP19A1 (aromatase) affect epithelial glycogen deposition, which provides essential nutrients for the vaginal microbes. These genetic factors collectively determine the health status of the vaginal environment.^[9]

With regard to the vaginal microbiome composition, based on 16S ribosomal RNA gene sequencing, the five major Community State Types (CSTs) are defined by the dominance or absence of specific *Lactobacillus* species and the degree of microbial diversity. CST I, dominated by *Lactobacillus crispatus*, represents the most stable and protective state, maintaining a consistently low pH. CST II, characterized by *Lactobacillus gasseri*, is similarly protective but may be slightly less stable. CST III, dominated by *Lactobacillus iners*, occupies a transitional state and is found in both healthy and dysbiotic conditions. Genomic and functional characterization reveal that *L. iners* contains a smaller genome, limiting its metabolic capacity. As a consequence, several genes involved in lactic acid and hydrogen peroxide production are absent. Instead, the bacterium produces inerolysin, a pore-forming toxin typically linked to epithelial disruption, and produces insufficient D-lactic acid, which may further explain why *L. iners* are rather the most undesirable *Lactobacilli*.^[10] CST V, with *Lactobacillus jensenii* as the predominant species, shares protective features with CST I and II. In contrast, CST IV is marked by a depletion of *Lactobacillus* species and a rise in anaerobic bacteria such as *Gardnerella*, *Atopobium*, and *Prevotella*, accompanied by elevated vaginal pH. This shift is strongly associated with bacterial vaginosis (BV), which leads to increased susceptibility to sexually transmitted infections and adverse reproductive outcomes.^[11,12]

This delicate balance of a protective *Lactobacillus*-dominated state can be perturbed due to antibiotics, sexual behavior, and poor hygiene.^[13] This disruption compromises the mucosal barrier and immune defenses, creating conditions that are favorable for the overgrowth of opportunistic organisms and facilitating their infection.^[14,15]

In this review, we aim to present the heterogeneity of vaginal dysbiosis, evaluate current treatment strategies, and explore emerging therapeutic approaches with the potential to restore and maintain a healthy vaginal microbiome.

INFECTIONS ASSOCIATED WITH VAGINAL DYSBIOSIS

Vaginal dysbiosis is a consequence of *Lactobacillus* depletion. In its place, opportunistic microbes gain a foothold, creating a complex and imbalanced microbial community enriched with species such as *Candida*, *Gardnerella*, *Atopobium*, *Mobiluncus*, *Sneathia*, and *Prevotella*. This altered microbial landscape disturbs the acidic pH and fuels chronic inflammation and tissue damage. Clinically, such dysbiosis is closely linked to a spectrum of reproductive tract infections, such as BV, vulvovaginal candidiasis (VVC), aerobic vaginitis (AV), and mixed vaginitis [Table 1 and Figure 1].^[16] The consequences can be profound, contributing to recurrent pregnancy loss, infertility, preterm birth, miscarriage, vaginal dryness, and persistent inflammatory conditions of the genital tract.^[17,18]

BV

BV is a polymicrobial infection of the vaginal tract that predominantly affects women of reproductive age and is linked to a range of adverse gynecological and obstetric outcomes. Epidemiological studies estimate that approximately 20–50% of women in this age group experience BV at some point in their lives.^[19] Clinically, BV is characterized by a thin, greyish-white vaginal discharge with a distinctive fishy odor, often accompanied by a vaginal pH >4.5 and the presence of clue cells coated with bacteria on microscopic examination, through Nugent scoring.^[20] The hallmark of BV is the depletion of protective *Lactobacillus* species. This shift fosters the overgrowth of diverse anaerobic and facultative organisms, most notably *Gardnerella vaginalis*, along with *Fannyhessea vaginae*, *Sneathia*, *Mobiluncus*, and others.^[21,22]

While BV is a polymicrobial condition, *G. vaginalis* plays a key role in BV pathogenesis through biofilm formation on the vaginal epithelium, which in turn encourages the adhesion and proliferation of other anaerobic microbes.^[23] *G. vaginalis* causes pathogenesis with adhesins, cytolysins, and sialidases that degrade mucosal barriers, neutralizing their potential for defense.^[24] Recent reports highlight the role of *G. vaginalis*-derived extracellular vesicles (EVs) in BV-associated cellular pathogenesis. These bacterial extracellular vesicles (BEVs) deliver bacterial effectors directly into the vaginal epithelial cells. Literature documents that *G. vaginalis*-derived EVs contain vaginolysin and sialidases, which can degrade epithelial cell junctions, disrupt mucosal integrity, and promote cytolysis.^[25,26] In addition, the synergistic action of

G. vaginalis and other pathogens not only destabilizes the vaginal ecosystem but also contributes to challenges and recurrence associated with BV management^[27] underscoring the need for targeted therapeutic approaches beyond conventional antibiotics.

VVC

VVC is the most common fungal infection characterized by inflammation of the vulvovaginal region. Clinical manifestations include intense pruritus, erythema, edema, and a thick curdy white vaginal discharge. Epidemiological data indicate that approximately 75% of women experience at least one episode of VVC during their lifetime, and 40–50% of these women have a second episode. A subset of these women, estimated at 5–8% develop recurrent VVC, defined as three or more symptomatic episodes within 12 months.^[28-30]

Approximately 85–90% are caused by *Candida albicans*, whose virulence is linked to host cell adherence, biofilm formation, proteolytic enzymes, and yeast-to-hyphae morphogenesis features that enhance tissue invasion and immune evasion. The remaining 10–15% of infections are attributed to non-*albicans* species, primarily *C. glabrata*, *C. krusei*, *C. tropicalis*, and *C. parapsilosis*.^[30,31] While less frequent, non-*albicans* species are gaining clinical prominence due to their reduced susceptibility or intrinsic resistance to azole antifungals, complicating treatment and increasing recurrence rates.^[32,33]

In recent years, there has been a noticeable epidemiological shift toward a higher proportion of non-*albicans* infections, particularly in immunocompromised women and those with poorly controlled glycemic status. This is largely attributed to immune suppression, altered mucosal defense, and selective antifungal pressure that together create a permissive environment for opportunistic yeasts. The inflammatory pathology of VVC arises from the interplay between fungal virulence determinants and host immune responses, notably the activation of pattern recognition receptors (e.g., Dectin-1, TLRs) on epithelial and immune cells, which trigger pro-inflammatory cytokine release and neutrophil recruitment.^[34,35] While these immune mechanisms are essential for fungal clearance, they also amplify tissue inflammation, thereby intensifying clinical symptoms.^[36]

AV

AV is a distinct form of vaginal dysbiosis characterized by the predominance of aerobic microorganisms, most commonly *Escherichia coli* and *Staphylococcus aureus*, along with other facultative pathogens such as *Enterococcus faecalis* and group B *Streptococcus*.^[37,38] Unlike BV, which is typically associated with anaerobic overgrowth, AV presents with more severe local inflammation, epithelial atrophy, and a

marked shift in the vaginal immune profile. Epidemiological studies report AV prevalence rates ranging from 4% to 12% in the general female population, with higher rates in women presenting with recurrent vaginal symptoms or during pregnancy.^[39] A significant proportion of AV cases are associated with concurrent or preceding urinary tract infections, as many causative organisms, particularly uropathogenic *E. coli* and *S. aureus* are capable of colonizing both the urogenital tract and vaginal mucosa.^[40,41]

The pathogenesis of AV reflects the virulence strategies of its causative agents. Uropathogenic *E. coli* employs adhesins such as type 1 and P fimbriae to bind vaginal epithelial cells, followed by biofilm formation and the release of toxins such as hemolysin, which contribute to epithelial damage and neutrophil recruitment.^[42] Similarly, *S. aureus* produces an array of virulence factors, including surface adhesins,^[43] hemolysins, and superantigen toxins, which can induce intense inflammatory responses and compromise epithelial barrier integrity. The heightened inflammation in AV not only drives symptom severity, manifesting as erythema, burning, and yellowish discharge, but may also predispose affected women to secondary infections and adverse reproductive outcomes.^[44] Given its distinct etiology and inflammatory profile, AV requires targeted diagnostic approaches and antimicrobials to avoid misclassification as BV and to decrease the risk of recurrence.^[45]

Mixed vaginitis

Mixed vaginitis refers to a polymicrobial infection of the vaginal ecosystem in which two or more pathogens coexist and contribute to disease pathology. It represents a complex interplay of bacterial, fungal, and sometimes aerobic organisms that simultaneously disrupt the mucosal barrier and alter local immunity. Clinically, the most frequently documented co-infection is BV-VVC^[46], and a co-occurrence is approximated at 20–30% of women diagnosed with BV.^[47] This overlap likely reflects the antibiotic-induced depletion of protective *Lactobacillus* species during BV treatment, creating a niche that favors *Candida* overgrowth.^[48] Other reported combinations include BV with *E. coli* colonization^[49], *Candida* with *E. coli*^[50], and more complex microbial assemblages involving anaerobes such as *G. vaginalis*, *Atopobium vaginae*, and aerobic species like *E. faecalis*.^[51] These mixed infections often present with more severe symptoms, longer disease duration, and a higher likelihood of recurrence compared to single-pathogen infections, highlighting the clinical importance of accurate diagnosis and tailored, multi-targeted treatment strategies.

The overlapping clinical features of these infections present diagnostic and therapeutic complexities; the latter is further elaborated in the subsequent discussion on current treatment strategies.

CURRENT TREATMENT

Clinically, antimicrobial agents are the first line of therapy for the management of vaginal infections and are generally administered either orally or intravaginally. BV treatment typically includes oral metronidazole or intravaginal clindamycin, which restricts the growth of anaerobes.^[21] In case of VVC, antifungals that target ergosterol synthesis are mainly employed.^[29] AV, characterized by the predominance of aerobic bacteria, is managed using broad-spectrum antibiotics, including kanamycin or quinolones.^[38] In mixed vaginitis, where multiple pathogens coexist, dual antimicrobial therapy is suggested with broad-spectrum antibiotics and antifungal agents.^[48]

Despite the availability of antimicrobial agents, treatment failures and recurrent infections are increasingly reported on account of antimicrobial resistance (AMR). Biofilm forms of *G. vaginalis*, *Candida albicans*, and other opportunistic pathogens create a protective matrix that reduces drug penetration and facilitates microbial persistence. Within these biofilms, pathogens exhibit altered metabolic states and horizontal gene transfer, further contributing to reduced antimicrobial susceptibility. The emergence of azole-resistant strains of *Candida* spp. and metronidazole or clindamycin-resistant bacterial strains poses a growing challenge of AMR in vaginal infections.^[52] In India, the National AIDS Control Organization recommends the syndromic management approach for the diagnosis and treatment of these infections. Under this approach, treatment is based on identifiable symptoms such as vaginal discharge, lower abdominal pain, and fever. The vaginal discharge is managed using a combination therapy that empirically targets the most common causative agents, such as *Candida* species, anaerobic, and aerobic bacteria. While this strategy ensures rapid, broad treatment in resource-limited settings, its limitation of only addressing clinical symptoms without identifying the underlying microbiological cause can lead to altered vaginal microbiota, incomplete resolution, recurrence, and potential antimicrobial overuse, eventually giving rise to the development of AMR.^[53]

The antimicrobial pressure, combined with incomplete eradication of causative agents, sets the stage for recurrent infections, often with one form of dysbiosis following another in a frustrating clinical cycle. A woman treated for BV may soon develop candidiasis due to fungal overgrowth facilitated by the antibiotics.^[54] In these cases, bacterial and fungal species, or multiple bacterial taxa, coexist and contribute to pathogenesis, creating a synergistic disruption that is more resistant to conventional monotherapy. Mixed vaginitis not only complicates diagnosis but also challenges current treatment measures, as the use of a single antimicrobial agent or insufficient dosage may leave one pathogen unchecked, perpetuating inflammation and increasing the risk of

chronic, recurrent disease.^[55] This highlights the need to develop non-antibiotic-based alternative strategies to ensure not just the reduction of recurrence but also as an essential component of global AMR stewardship through promoting optimal and judicious use of antimicrobials.

This interplay between microbial diversity, host immunity, and therapeutic interventions underscores the urgent need for precision-based diagnostics and targeted therapies to break the cycle of dysbiosis.

EMERGING PROSPECTIVES

Owing to its highly heterogeneous microbial composition and multifactorial pathogenesis, the management of vaginal dysbiosis associated with infections necessitates the need for precision-based therapeutic approaches tailored to the individual's microbiome profile. Conventional empirical treatments, such as broad-spectrum antibiotics, often result in incomplete resolution due to biofilm and the evolution of resistant strains. This highlights the need for suitable alternatives, some of which are discussed below.

Prebiotic interventions

Prebiotic interventions targeting the vaginal microbiome aim to selectively trigger the growth and metabolic activity of beneficial microbes, thereby promoting restoration of a healthy vaginal environment. Prebiotics typically contain non-digestible oligosaccharides, polysaccharides, or other bioactive substrates that serve as preferential fermentable carbon sources for *Lactobacillus* species, which suppress opportunistic and pathogenic microorganisms. Recently, topical gel-based prebiotic formulations have garnered interest as an adjunct or standalone therapy for vaginal dysbiosis. These formulations offer localized delivery, prolonged mucosal contact time, and targeted modulation of the vaginal microbiota while minimizing systemic absorption and off-target effects. Hakimi *et al.* reported that the cure rate was 86.2% in the group receiving the prebiotic vaginal gel plus oral metronidazole, compared to 62.1% in the metronidazole-only group.^[56] The recurrence rate after 3 months was significantly lower in the combination group (10.3% vs. 34.5%).^[56]

Nonetheless, further randomized controlled trials are required to determine optimal dosing regimens, formulation stability, synergistic potential with probiotics or vaginal microbiota transplantation (VMT), and long-term safety. In addition, a key limitation of prebiotic therapy is its strain specificity, as prebiotics stimulate only certain bacteria capable of metabolizing the substrate, leading to variable and sometimes inconsistent microbiota responses across individuals.^[57,58]

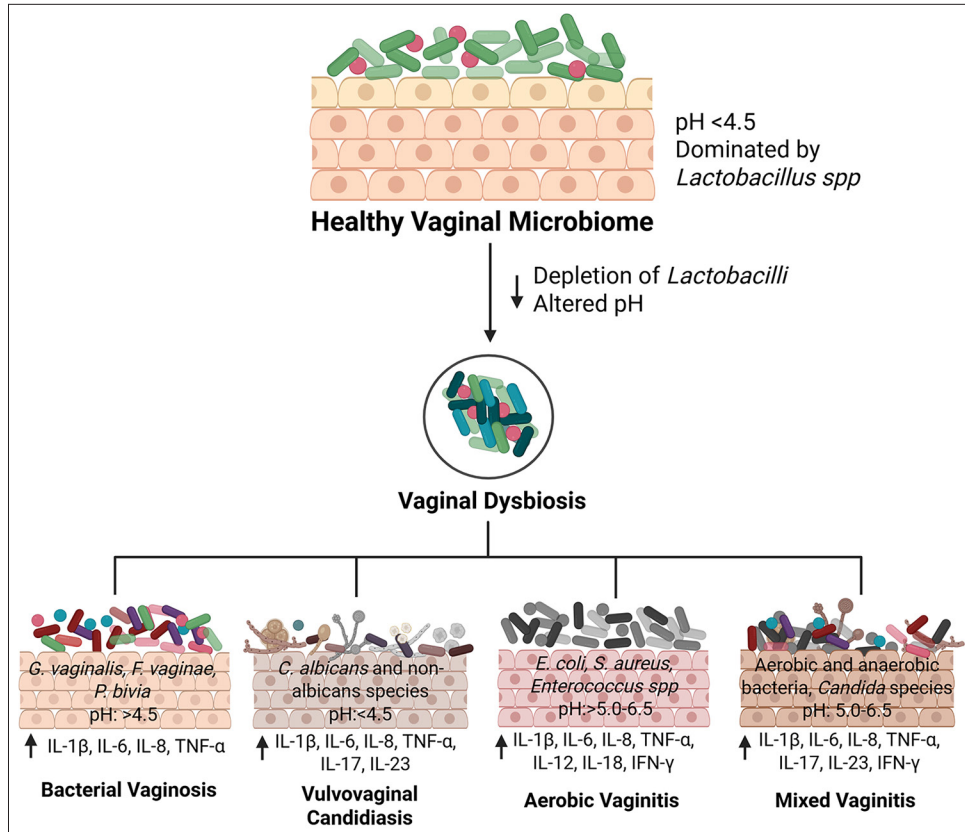


Figure 1: Overview of the shift from a healthy *Lactobacillus*-dominated vaginal microbiome to dysbiotic states: Bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), aerobic vaginitis (AV), and mixed vaginitis. Loss of *Lactobacillus* leads to anaerobic overgrowth and elevated pH in BV, *Candida* proliferation with inflammation in VVC, aerobic colonization with epithelial damage in AV, and combined microbial overgrowth with heightened inflammation in mixed vaginitis. IL: Interleukin

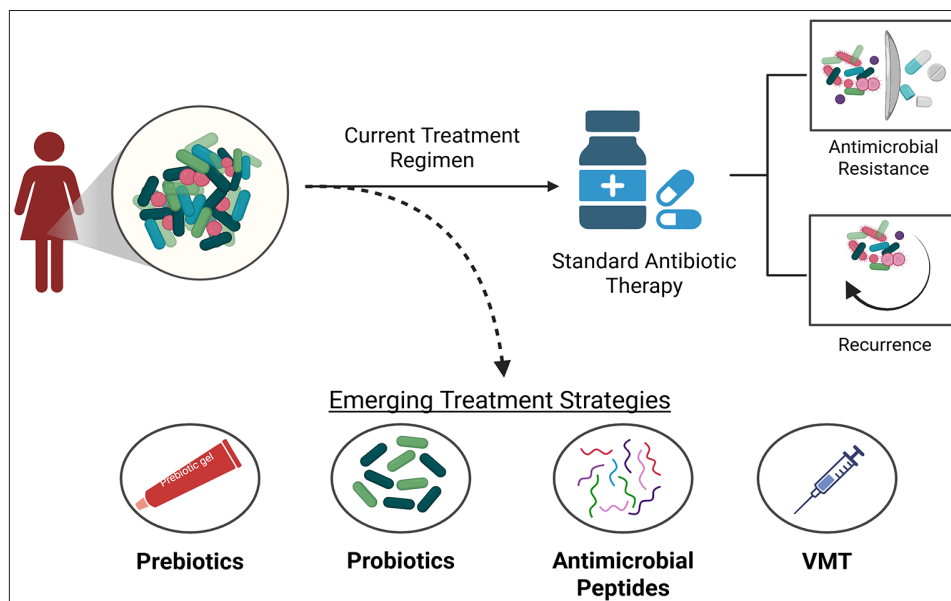


Figure 2: Schematic depicting the contribution of current broad-spectrum treatments to recurrence and antimicrobial resistance through non-targeted or incomplete regimens, highlighting the need for targeted and sustainable therapeutic interventions. VMT: Vaginal microbiome transplantation

Table 1: Comparative summary of vaginal pathologies (BV, VVC, AV, and mixed vaginitis) outlining key differences in pathogens, symptoms, diagnosis, prevalence, risk factors, treatment, and associated clinical challenges.

	Bacterial vaginosis	Vulvovaginal candidiasis	Aerobic vaginitis	Mixed vaginitis	References
Pathogens	<i>Gardnerella vaginalis</i> , <i>Fannyhessea vaginae</i> , <i>Prevotella bivia</i> , etc	<i>Candida albicans</i> and Non-albicans species	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Enterococcus</i> spp.	Anaerobic and aerobic bacteria, <i>Candida</i> species.	Centers for Disease Control and Prevention, ^[21] Gandhi <i>et al.</i> , ^[28] Donders <i>et al.</i> , ^[37] and Benyas and Sobel ^[46]
Symptoms	Vaginal discharge, fishy odor, dysuria, dyspareunia.	Curdy white discharge, dysuria, dyspareunia	Yellow or green vaginal discharge with rotten odor, fishy odor, dysuria, dyspareunia.	Overlapping symptoms of BV, VVC, and AV	Jahic <i>et al.</i> ^[16]
Diagnosis	Nugent scoring/ amsel criteria	Vaginal culture	Wet mount microscopy	Microscopy and vaginal culture	Jahic <i>et al.</i> ^[16]
Prevalence	23–40%	75%	7–12%	4.44–59.1%	Kenyon <i>et al.</i> , ^[19] Centers for Disease Control and Prevention, ^[29] Zarmakoupi <i>et al.</i> , ^[39] and Shawaky <i>et al.</i> ^[47]
Risk factors	Sexual behavior, vaginal douching, genetic predisposition.	Diabetes mellitus, sexual behavior, genetic predisposition	Sexual behavior, vaginal douching	Risk factors of BV, VVC, AV	Valeriano <i>et al.</i> ^[13]
Treatment	Metronidazole, secnidazole, clindamycin	Fluconazole, clotrimazole, miconazole	Topical corticosteroids and antibiotics	Antibiotic and antifungal agents (Syndromic management)	Centers for Disease Control and Prevention, ^[21] Centers for Disease Control and Prevention, ^[29] Achdiat <i>et al.</i> , ^[38] and Sobel and Vempati ^[48]
Challenges	AMR, Recurrence, asymptomatic nature	AMR, recurrence	Asymptomatic, misdiagnosis	Misdiagnosis, AMR, recurrence	Bradshaw and Sobel ^[52]

AMR: Antimicrobial resistance, BV: Bacterial vaginosis, VVC: Vulvovaginal candidiasis, AV: Aerobic vaginitis

Probiotic therapy

Probiotics aid in symptom relief, recurrence prevention, and vaginal health by producing antimicrobials, regulating pH, and boosting immunity. Current research backs their usage as an alternate or complementary therapy, despite considerable drawbacks. While probiotics are widely regarded as a promising alternative to antibiotics, evidence on their sustained clinical effectiveness is still evolving.

The overuse of antibiotics has accelerated AMR among vaginal pathogens, further strengthening the case for developing safe, sustainable alternatives. In this context, probiotics offer significant advantages in terms of suitability, accessibility, and ease of administration. Clinical evidence suggests that oral supplementation with encapsulated strains such as *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14, taken once or twice daily, can promote restoration of the vaginal microbiome toward a *Lactobacillus*-dominant state. These strains exhibit strong adhesion to vaginal and cervical epithelial cells, allowing them to

compete with the pathogens. In addition, they release high amounts of lactic acid, hydrogen peroxide, and bacteriocin, inhibiting the growth of harmful vaginal pathogens.^[59] Lagenaur *et al.* conducted a phase 2b clinical trial in which the microbiome-based biologic drug, LACTIN-V (containing *L. crispatus* strain), was administered after metronidazole treatment.^[60] At 12 weeks post-treatment, the incidence of recurrent BV was significantly lower in the LACTIN-V group (30%) as compared to the placebo group (45%). This represents a relative risk reduction of approximately 34% indicating the adjunct probiotic therapy decreased the risk of BV recurrence.^[60]

However, not all studies have reported robust or durable effects. In a longitudinal metagenomic study, Hertz *et al.* investigated whether probiotic supplementation with *Lactobacillus* strains could effectively modulate the vaginal microbiome.^[61] Using shotgun metagenomics, they observed only minor shifts in microbial composition during the intervention, suggesting that probiotic efficacy may vary depending on host and microbial context.^[61,62]

AMPs and small-molecules

AMPs and small molecules represent promising alternatives for the treatment of vaginal dysbiosis, particularly in light of rising AMR and the limitations of conventional antibiotic therapies. The vaginal innate immune system naturally produces a repertoire of AMPs, including defensins, secretory leukocyte protease inhibitors, calprotectin, lysozyme, lactoferrin, and elafin, that play multifaceted roles in maintaining mucosal homeostasis. Beyond their direct antimicrobial activity, these peptides are integral to host defense against sexually transmitted infections, modulation of local immune responses, and even the exertion of anticancer effects. Harnessing or augmenting the activity of these endogenous AMPs could therefore offer a targeted strategy for restoring a healthy vaginal microenvironment.^[63]

In parallel, small molecules of microbial origin are emerging as novel therapeutic candidates. Of particular interest are nanoscale molecules and metabolites derived from *Lactobacilli* species, which have been shown to disrupt pathogenic biofilms, which happens to be a major barrier to successful treatment of vaginal dysbiosis [Figure 2]. For instance, Khan *et al.*^[45] evaluated EVs derived from *L. gasseri* and demonstrated their efficacy in disrupting pathogenic biofilms *in vitro*. These findings highlight the potential of probiotic-derived small molecules as biofilm-targeting agents that could complement or replace traditional antimicrobials.^[45]

While these early observations are promising, thorough *in vivo* studies and clinical trials are required to establish their safety, efficacy, and long-term impact on vaginal microbial ecology. Advancing this line of research holds significant potential not only for developing precision therapies for vaginal dysbiosis but also for contributing to global antimicrobial stewardship efforts.^[64,65]

VMT

VMT involves the transfer of a healthy donor's vaginal microbial community to restore a balanced, *Lactobacillus*-dominated ecosystem in the recipient's vaginal environment. The rationale behind this approach stems from the pivotal role of *Lactobacillus* spp., particularly *L. crispatus*, which provides colonization resistance against pathogenic microorganisms. Recent studies and clinical trials have reported encouraging outcomes, demonstrating the potential of VMT in managing recurrent BV and other gynecological disorders linked to persistent vaginal dysbiosis. A pilot study led by Lev-Sagie and group investigated the use of VMT from healthy donors as a therapeutic alternative for patients with intractable and recurrent BV, where 4 of 5 recruited BV individuals showed restoration of a healthy vaginal state.^[66] In 2023, a study by Wrønding *et al.* explored the use of VMT without antibiotics

for a woman with a history of complicated pregnancy. After the administration of VMT, the woman successfully conceived a healthy child after a series of late pregnancy losses/stillbirths.^[67] The study emphasizes the potential of VMT for vaginal dysbiosis-related pregnancy complications.^[67] Given the substantial heterogeneity in the etiology, microbial profiles, and host immune responses associated with vaginal dysbiosis, VMT offers a targeted, microbiome-based intervention that could surpass the limitations of conventional antimicrobial and probiotic therapies.^[68-70]

However, for the clinical translation of VMT, major challenges related to safety, standardization, and regulatory approval need to be addressed before it can be adopted as a mainstream therapeutic intervention. The development of robust donor screening protocols, optimal sample storage methods, microbiome composition evaluation standards, and clinical consistency cutoffs is the need of the hour.

CONCLUSION

Vaginal dysbiosis-associated infections may lead to serious gynecological problems such as preterm labor, recurrent pregnancy loss, and vaginal inflammation, all of which can have profound repercussions on women's health. Current therapeutic approaches predominantly target symptom management, often relying on broad-spectrum antibiotics. While these agents may provide temporary relief, they frequently fail to restore a healthy microbiome, leading to high recurrence rates, suggesting the need for new alternatives. In this regard, current emerging treatment strategies may prove to be useful. Probiotics and prebiotics are generally more accessible and affordable, with over-the-counter formulations available in many regions, but their efficacy can be strain-specific and inconsistent, complicating standardized clinical use. Although AMPs and small molecules have shown promise in various *in vitro* studies, clinical studies need to be initiated for greater insights into this therapy. Likewise, although VMT holds promise as a high-impact solution for recurrent and refractory BV, its clinical translation remains constrained by resource-intensive procedures, the need for standardized donor screening protocols, limited regulatory approval, and small-scale trials conducted in only a few ethnic populations. Future research should prioritize the execution of these trials across diverse geographical regions, the development of rapid microbiome-based diagnostic tools, standardized VMT protocols, and large-scale randomized clinical trials for prebiotics, probiotics, and VMT. Furthermore, integrating microbiome profiling, transcriptomics, metabolomics, and host-response biomarkers into clinical frameworks will enable personalized treatment strategies aimed at improving therapeutic efficacy and reducing recurrence. Advancements in these areas through well-coordinated, multidisciplinary research will

contribute to the development of sustainable alternatives to conventional treatment strategies.

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