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Beyond Dysbiosis: Multi-Omics, Personalized Interventions, and the Vaginal Microbiome in Female Reproductive Health

Hossein Mokhlesabadi Farahani[1 *] **,Yasin MokhlesabadiFarahani** [1]

[1] **Department of Biology, Faculty of Biological Science, Islamic Azad University, East Tehran Branch, Tehran, Iran.**

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Corresponding author:
Hossein Mokhlesabadi Farahani
Email: hosseinfarahani1382@gmail.com

ABSTRACT

The vaginal microbiome is a dynamic mucosal ecosystem that plays a crucial role in female reproductive health. Unlike the gut microbiome, where high diversity is often considered beneficial, a healthy vaginal microbiome in reproductive-age women is commonly recognized by low microbial diversity and dominance of Lactobacillus species, particularly Lactobacillus crispatus. These communities help maintain an acidic vaginal environment, inhibit pathogen growth, support epithelial barrier integrity, and regulate mucosal immune responses. Growing evidence links vaginal microbial composition and function to fertility, assisted reproductive technology outcomes, pregnancy complications, and gynecological disorders. Lactobacillus-dominant communities are generally associated with favorable reproductive outcomes, whereas high-diversity anaerobe-rich communities have been implicated in bacterial vaginosis, pelvic inflammatory disease, HPV persistence, cervical dysplasia, recurrent infections, preterm birth, and potentially impaired fertility. However, the traditional concept of dysbiosis is insufficient to explain the biological complexity of vaginal microbial ecosystems. Similar taxonomic profiles may differ in microbial gene content, metabolic activity, biofilm formation, inflammatory potential, ecological stability, and clinical impact. Therefore, multi-omics approaches, including metagenomics, metatranscriptomics, metabolomics, proteomics, and host-response profiling, provide a more comprehensive framework for understanding host–microbiome interactions. This review summarizes current evidence on the vaginal microbiome in fertility, pregnancy outcomes, and gynecological disorders, while emphasizing the transition from descriptive dysbiosis models toward functional, ecological, and personalized perspectives. Emerging strategies such as microbiome-based biomarkers, targeted probiotics, live biotherapeutics, vaginal microbiome transplantation, and AI-driven prediction models may support future precision gynecology. Nevertheless, clinical translation requires standardized methods, longitudinal studies, diverse cohorts, validated biomarkers, and careful ethical oversight.

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INTRODUCTION

The human microbiome has emerged as a central determinant of health and disease, reshaping our understanding of host physiology beyond the classical pathogen-centered model. Large-scale initiatives such as the Human Microbiome Project demonstrated that micro-

bial communities vary substantially across body sites and individuals, with the vagina representing one of the most distinctive microbial ecosystems in the human body (1). Unlike the gut microbiome, where high microbial diversity is often interpreted as a marker of ecological resilience, the vaginal microbiome in reproductive-age women is frequently characterized by relatively low bacterial diversity and dominance of *Lactobacillus species* (2). This ecological configuration is considered functionally important because lactobacilli contribute to vaginal acidification, production of antimicrobial metabolites, competitive exclusion of pathogens, and regulation of mucosal immune responses (3, 4).

One of the foundational studies in the field classified vaginal bacterial communities of reproductive-age women into major community state types, or CSTs, including states dominated by *Lactobacillus crispatus*, *Lactobacillus iners*, *Lactobacillus gasseri*, or *Lactobacillus jensenii*, as well as a high-diversity state enriched with anaerobic bacteria (2). This framework has been widely used to interpret vaginal microbial ecology, although subsequent studies have shown that vaginal communities are dynamic rather than fixed. Longitudinal analyses revealed that some vaginal microbiota profiles remain relatively stable over time, whereas others shift rapidly in association with menstruation, sexual activity, hormonal fluctuations, antibiotic exposure, and other host or environmental factors (5). Therefore, vaginal health cannot be understood only by identifying the presence or absence of specific taxa; rather, it requires attention to temporal stability, microbial function, host context, and ecological resilience.

The protective role of *Lactobacillus*-dominant vaginal communities is closely linked to lactic acid production and maintenance of a low vaginal pH. Experimental and clinical studies have shown that vaginal lactobacilli can acidify the vaginal environment to levels that restrict the growth of many reproductive tract pathogens (6). Lactic acid, particularly under acidic conditions, has also been shown to possess microbicidal and immunomodulatory properties, suggesting that its biological relevance extends beyond pH reduction alone (3). Among lactobacilli, L. crispatus is often associated with a more stable and protective vaginal ecosystem, whereas L. iners may represent a more transitional state because it is frequently detected in both healthy and dysbiotic conditions (4, 7). This distinction is important because it challenges the simplified assumption that all *Lactobacillus*-dominant communities have equivalent biological functions.

Vaginal dysbiosis, classically represented by bacterial vaginosis, is characterized by depletion of protective lactobacilli and expansion of diverse anaerobic bacteria such as Gardnerella, Prevotella, Atopobium/Fannyhessea, Sneathia, and other bacterial vaginosis-associated organisms (8). Clinically, bacterial vaginosis is important not only because of symptoms such as discharge, odor, and discomfort, but also because it is associated with increased susceptibility to sexually transmitted infections, pelvic inflammatory disease, and adverse pregnancy outcomes (8, 9). The Centers for Disease Control and Prevention indicate that symptomatic bacterial vaginosis in pregnancy correlates with premature rupture of membranes, preterm delivery, intra-amniotic infection, and postpartum endometritis (9). These associations place the vaginal microbiome at the intersection of gynecology, obstetrics, infectious disease, and reproductive medicine.

Mechanistically, the vaginal microbiome may influence reproductive health through several interconnected pathways, including epithelial barrier integrity, mucosal immune activation, metabolic signaling, and pathogen exclusion. Anahtar et al. showed that cervicovaginal bacterial communities can strongly modulate host inflammatory responses in the female genital tract, with high-diversity communities correlating with elevated pro-inflammatory cytokines and immune activation (10). Such findings provide biological plausibility for the association between vaginal dysbiosis and reproductive tract disorders. Inflammation induced by dysbiotic communities may impair epithelial defense, alter cervical mucus properties, facilitate ascending infection, and disrupt immune tolerance required for implantation and pregnancy maintenance.

The vaginal microbiome is increasingly recognized as a clinically relevant factor in fertility, pregnancy, and gynecological health. In reproductive medicine, observational studies suggest that vaginal and endometrial microbial profiles may be associated with implantation, clinical pregnancy, miscarriage, and live birth outcomes after IVF/ICSI (11-13). Although causality remains uncertain, these findings indicate that the lower female reproductive tract microbiome may serve as a potential biomarker of reproductive success.

During pregnancy, vaginal microbial communities often become more stable and more *Lactobacillus*-dominant, but deviations from this pattern have been associated with adverse outcomes. Multi-omics studies have linked reduced L. crispatus and enrichment of bacterial vaginosis-associated taxa, such as BVAB1 and Sneathia amnii, with preterm birth risk (14, 15). Beyond fertility and pregnancy, vaginal dysbiosis has also been implicated in recurrent bacterial vaginosis, vulvovaginal candidiasis, pelvic inflammatory disease, HPV persistence, cervical disease, endometriosis, and polycystic ovary syndrome, although evidence for some conditions remains largely observational (16-19).

However, the concept of dysbiosis alone is insufficient to explain the complexity of host–microbiome interactions. Taxonomic profiling does not fully cap-

ture microbial function, metabolic activity, host immune responses, or treatment susceptibility. Therefore, multi-omics approaches, including metagenomics, metatranscriptomics, metabolomics, proteomics, and host transcriptomics, provide a more comprehensive framework for understanding vaginal microbial ecology (15, 20, 21). These advances are also supporting the development of personalized interventions, such as targeted probiotics, microbiome-based biomarkers, and experimental approaches including vaginal microbiome transplantation (22-24). Accordingly, this review synthesizes current evidence on the vaginal microbiome in female reproductive health, with a focus on multi-omics, precision diagnostics, and personalized microbiome-targeted strategies.

Composition and Dynamics of the Vaginal Microbiome

The vaginal microbiome is a unique mucosal environment mostly consisting of bacteria, accompanied by lesser quantities of fungus, viruses, archaea, and bacteriophages. In women of reproductive age, this environment is often characterized by diminished bacterial diversity and a predominance of Lactobacillus species, a pattern that distinguishes the vagina from many other human microbial habitats such as the gut, where high diversity is generally considered beneficial (2, 25). The dominance of lactobacilli is biologically important because these organisms contribute to vaginal acidification, competitive exclusion of pathogens, production of antimicrobial compounds, and modulation of local immune responses (26).

A widely used framework for describing vaginal bacterial communities is the classification into community state types, or CSTs. In the landmark study by Ravel et al., vaginal microbial communities from asymptomatic reproductive-age women clustered into five major CSTs: CST I dominated by Lactobacillus crispatus, CST II by Lactobacillus gasseri, CST III by Lactobacillus iners, CST V by Lactobacillus jensenii, and CST IV characterized by reduced lactobacilli and enrichment of diverse anaerobic bacteria (2). Importantly, the distribution of these CSTs varies across populations. Ravel et al. reported that Lactobacillus-dominant communities were more common among Asian and White women than among Hispanic and Black women, who more frequently had higher-diversity communities and higher vaginal pH values (2). These findings indicate that the concept of a “normal” vaginal microbiome should be interpreted cautiously and within demographic, hormonal, and ecological context. The major vaginal community state types and their clinical interpretations are summarized in Table 1.

Among lactobacilli, L. crispatus is often considered one of the most protective species because it is associated with low vaginal pH, high lactic acid production, and relatively stable microbial communities (27). In contrast, L. iners occupies a more ambiguous ecological position. Although it is highly prevalent in the vagina and can dominate apparently healthy communities, it is also frequently detected during transitions between eubiosis and dysbiosis and after treatment for bacterial vaginosis (28). This dual behavior may be partly explained by its smaller genome, limited biosynthetic capacity, and ability to persist in fluctuating vaginal environments (28). Therefore, not all Lactobacillus-dominated states should be considered functionally equivalent.

The safeguarding characteristics of lactobacilli are intimately associated with estrogen-dependent vaginal

Table 1. Major vaginal community state types and their clinical interpretation.

Community state type	Dominant microbial pattern	General ecological interpretation	Potential clinical relevance
CST I	Lactobacillus crispatus	Stable, low-diversity, lactic acid-rich state	Often associated with vaginal health and lower dysbiosis risk
CST II	Lactobacillus gasseri	Lactobacilli-dominant state	Generally considered protective, but less frequently dominant
CST III	Lactobacillus iners	Flexible or transitional lactobacilli-dominant state	May occur in both health and dysbiosis-associated transitions
CST V	Lactobacillus jensenii	Low-diversity lactobacilli-dominant state	Usually associated with low pH and vaginal stability
CST IV	Gardnerella, Prevotella, Fannyhessea/Atopobium, Sneathia, anaerobes	High-diversity, low-lactobacilli state	Associated with BV, inflammation, higher pH, and infection susceptibility

physiology. Estrogen promotes the development of the vaginal epithelium and the buildup of glycogen, which supplies substrates that sustain lactobacilli and lactic acid synthesis (26, 29). The resulting acidic environment, commonly around pH 3.5–4.5 in many reproductive-age women, restricts the growth of numerous opportunistic and sexually transmitted pathogens (25, 29). This relationship can be summarized as:

Estrogen↑→Glycogen↑→Lactobacillus↑→Lactic Acid↑→pH↓→Pathogen Growth↓

However, vaginal microbial composition is not static. Longitudinal studies have shown that some women maintain stable Lactobacillus-dominated communities over time, whereas others experience frequent transitions between CSTs (5). In a 16-week longitudinal study, Gajer et al. demonstrated that vaginal microbial communities may change markedly over short periods, with some CSTs showing greater temporal instability than others (5). These findings emphasize that single time-point sampling may not fully capture vaginal microbial ecology, especially in women with fluctuating or transitional microbiota.

Numerous internal and external variables influence the structure and behavior of the vaginal microbiome. The menstrual cycle is one of the most important physiological drivers. Daily sampling studies have shown that menstruation is often associated with increased microbial diversity, decreased relative abundance of lactobacilli, and higher rates of community change (30). Menstrual blood can transiently increase vaginal pH and introduce substrates such as iron, creating conditions that may favor non-Lactobacillus organisms. After menstruation, many women return to a more lactobacilli-dominant state, although the speed and completeness of recovery vary among individuals (30). Key physiological, behavioral, and environmental factors influencing vaginal microbiome dynamics are presented in Table 2.

Pregnancy represents another major physiological state associated with vaginal microbial remodeling. In normal pregnancy, the vaginal microbiota often becomes more stable and more strongly dominated by Lactobacillus species compared with the non-pregnant state. Romero et al. reported that pregnant women commonly maintained Lactobacillus-dominated CSTs throughout gestation, with higher stability than non-pregnant women (31). This stability may reflect elevated estrogen levels, increased glycogen deposition, and immune adaptations that support reproductive tolerance. Nevertheless, pregnancy-associated microbial patterns vary across individuals and populations, and deviations from stable Lactobacillus dominance have been linked in later sections to adverse obstetric outcomes.

At the other end of the reproductive lifespan, menopause is commonly associated with reduced estrogen, decreased epithelial glycogen, increased vaginal pH, and lower abundance of lactobacilli (32). These changes may contribute to genitourinary syndrome of menopause, recurrent urinary symptoms, vaginal dryness, ir-

Table 2. Major factors influencing vaginal microbiome dynamics.

Factor	Typical microbial effect	Biological explanation
Estrogen	Increased lactobacilli, lower pH	Promotes epithelial glycogen and lactic acid production
Menstruation	Reduced lactobacilli, increased diversity	Menstrual blood raises pH and alters nutrient availability
Pregnancy	Greater stability and lactobacilli dominance	High estrogen and pregnancy-related immune adaptation
Menopause	Reduced lactobacilli, increased pH	Estrogen decline reduces glycogen availability
Sexual activity	Variable; may increase diversity	Semen and partner-associated microbes may alter pH and composition
Antibiotics	Reduced microbial stability	May deplete lactobacilli and allow recolonization by anaerobes
Hormonal contraception	Often more lactobacilli-dominant	Hormonal effects may reduce BV risk in some populations
Copper IUD	May increase BV-associated diversity in some studies	Possible effects on bleeding patterns and local inflammation
Douching/intimate hygiene products	Increased dysbiosis risk	Disruption of pH, mucus, and resident lactobacilli

ritation, and increased susceptibility to infections (33). Hormone therapy can partially restore lactobacilli and reduce vaginal pH in some postmenopausal women, supporting the role of estrogen in maintaining the vaginal microbial environment (32).

Behavioral and environmental factors also contribute to vaginal microbiome variability. Sexual activity, semen exposure, condom use, douching, smoking, intimate hygiene practices, and antibiotic exposure may alter vaginal pH, introduce new microbes, or disrupt lactobacilli-dominant states. Reviews of behavioral influences suggest that practices such as vaginal douching are associated with dysbiosis and bacterial vaginosis, while condom use may help maintain lactobacilli dominance by reducing exposure to alkaline semen and partner-associated microbes (34). Contraceptive methods may also influence vaginal microbial ecology. Hormonal contraception has often been associated with a lower risk of bacterial vaginosis and more lactobacilli-dominant profiles, whereas copper intrauterine devices have been linked in some studies to increased bacterial vaginosis risk and higher microbial diversity (35, 36). However, contraceptive effects are not uniform and may vary by formulation, route, duration of use, and host factors.

Non-Lactobacillus-dominant communities are typically more diverse and enriched with anaerobic and facultative anaerobic bacteria, including Gardnerella, Prevotella, Fannyhessea/Atopobium, Sneathia, Mobiluncus, Megasphaera, and microorganisms linked to bacterial vaginosis (37). These communities are often grouped under CST IV and are commonly associated with bacterial vaginosis-like states, higher vaginal pH, inflammation, epithelial barrier disruption, and increased susceptibility to reproductive tract infections (4, 37). Nevertheless, high-diversity communities are not always symptomatic, and their clinical meaning may differ across populations. This reinforces the need to distinguish taxonomic composition from microbial function and host response.

From an ecological perspective, the vaginal microbiome can be understood in terms of stability, resilience, and transition. Stability refers to the maintenance of a microbial state over time, resilience refers to the ability to return to a previous state after disturbance, and transition refers to movement from one community configuration to another. For example, a stable L. crispatus-dominant community may resist perturbation after menstruation or sexual exposure, whereas an L. iners-dominant or CST IV community may be more likely to transition toward dysbiosis or recurrence after treatment (5, 28). This ecological interpretation is particularly important for the theme of this review because it moves beyond a simple "healthy versus dysbiotic" model and highlights the dynamic behavior of microbial communities.

Overall, the composition of the vaginal microbiome is determined by the interaction of microbial taxa, host hormones, epithelial metabolism, immune responses, behavior, reproductive stage, and environmental exposures. Although Lactobacillus dominance, particularly L. crispatus, is generally associated with vaginal health, a complete understanding of vaginal microbial ecology requires consideration of temporal dynamics, population diversity, microbial function, and host context. This dynamic framework provides the foundation for multi-omics approaches, personalized diagnostics, and microbiome-targeted interventions discussed in later sections.

Moving Beyond Dysbiosis: Functional and Ecological Perspectives

The term dysbiosis has been widely used to describe vaginal microbial imbalance, particularly the depletion of Lactobacillus species and enrichment of anaerobic bacteria associated with bacterial vaginosis. Although this concept remains clinically useful, it is often too broad to explain the biological complexity of the vaginal ecosystem. A taxonomic shift alone does not reveal whether microbes are metabolically active, whether they induce inflammation, whether they form biofilms, or whether the host can tolerate or recover from that state (4, 5). Recent reviews, therefore, emphasize the need to move from a purely compositional definition of dysbiosis toward a more functional and ecological interpretation of vaginal microbiota. This conceptual transition from a taxonomic dysbiosis model to a functional–ecological framework is illustrated in Figure 1.

A functional perspective asks not only "which bacteria are present?" but also "what are they doing?". For example, two women may both have Lactobacillus-dominant microbiota, but their communities may differ in lactic acid production, antimicrobial activity, epithelial adhesion, immune modulation, and resilience after disturbance. Lactobacillus crispatus is often linked to a more stable, lactic acid-rich, low-pH environment, whereas Lactobacillus iners may occupy a more transitional ecological niche and is frequently observed in both healthy and dysbiotic states (28, 38). This distinction shows that even similar taxonomic profiles may have different biological meanings.

Conversely, anaerobe-rich communities are not merely "imbalanced" versions of healthy microbiota; they may represent functionally distinct ecosystems. In bacterial vaginosis, organisms such as Gardnerella, Prevotella, Sneathia, Fannyhessea/Atopobium, and Megasphaera can contribute to higher pH, production of amines and other metabolites, epithelial disruption, and inflammatory signaling (20, 39). Some Gardnerella-associated communities may also form polymicrobial biofilms that protect bacteria from host defenses and antimicrobial treatment, helping to explain recur-

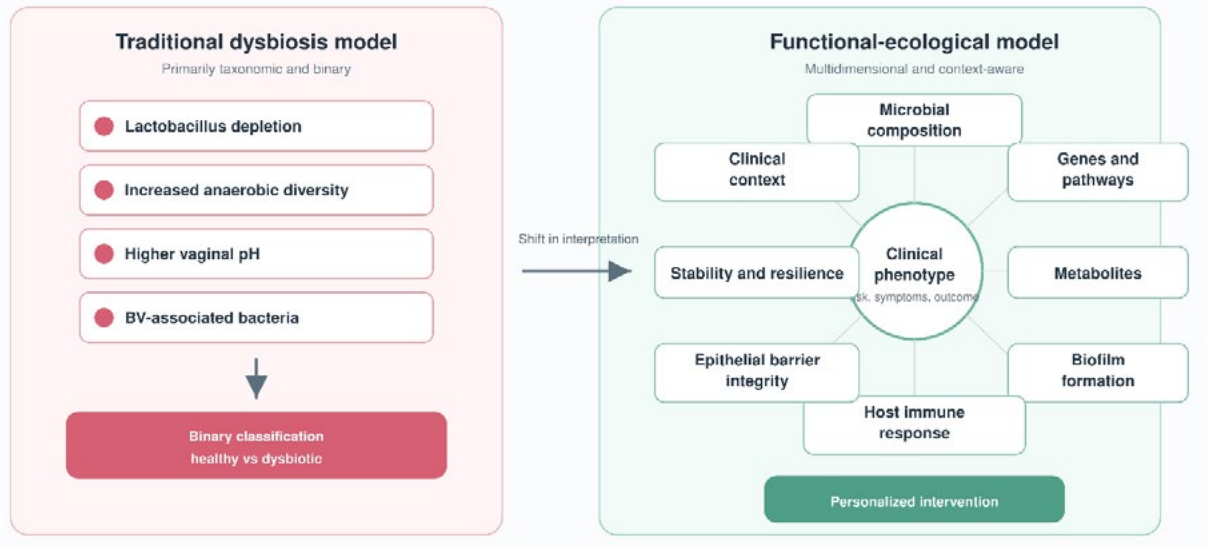

Figure 1. Moving beyond dysbiosis in vaginal microbiome research. Traditional models define vaginal dysbiosis mainly by taxonomic changes, including depletion of Lactobacillus species and enrichment of anaerobic bacteria. A functional–ecological framework integrates microbial composition with gene content, metabolic activity, biofilm formation, host immune responses, epithelial barrier integrity, ecological stability, and clinical context. This multidimensional approach may improve risk stratification, biomarker discovery, and personalized microbiome-targeted interventions.

rence after standard therapy (40).

Host response is another key reason why dysbiosis should not be interpreted only as a microbial pattern. Anahtar et al. showed that cervicovaginal bacterial communities can strongly modulate local inflammatory responses, with high-diversity communities associated with increased genital inflammation (10). This suggests that clinical risk may depend on the interaction between microbial composition and host immunity rather than microbial composition alone. Therefore, a vaginal microbiome profile should ideally be interpreted together with inflammatory markers, epithelial barrier status, hormonal state, and clinical phenotype.

Metabolomic studies further support this functional view. Srinivasan et al. demonstrated that bacterial vaginosis is associated with strong metabolic signatures involving amino acid, carbohydrate, and lipid metabolism (20). Similarly, multi-platform metabolomics studies identified metabolites associated with bacterial diversity and clinical BV, suggesting that metabolic biomarkers may improve diagnosis and risk stratification beyond conventional microscopy or 16S rRNA profiling (41). These findings indicate that vaginal health is shaped by microbial activity and biochemical output, not simply by the presence or absence of specific taxa.

From an ecological perspective, the vaginal microbiome should be understood in terms of stability, resilience, resistance, and transition. Stability refers to the persistence of a microbial state over time; resistance refers to the ability to withstand disturbance; resilience refers to recovery after disturbance; and transition refers to movement between community states. Longitudinal studies have shown that vaginal communities can shift rapidly over short periods and that these shifts may be influenced by menstruation, sexual activity, bacterial composition, and other host factors (42). Thus, a single cross-sectional sample may not fully represent a woman's vaginal microbial ecology.

The development of gene-centered and multi-omics resources has accelerated this transition from descriptive microbiome research to functional ecology. The VIRGO catalog provided a vaginal microbiome-specific gene reference containing approximately 0.95 million non-redundant genes, enabling more detailed metagenomic and metatranscriptomic analyses (43). More recently, VIRGO2 expanded this framework to more than 1.7 million annotated genes, aiming to improve understanding of vaginal microbial function, ecology, and strain-level variation (44). Such tools allow researchers to investigate microbial pathways, virulence potential, metabolic capacity, and host–microbe interactions with greater precision.

Overall, moving beyond dysbiosis means shifting from a binary model of "healthy versus abnormal" microbiota toward a multidimensional model that integrates microbial composition, functional capacity, metabolic activity, host immunity, ecological stability, and clinical context. This approach is particularly important for precision gynecology, where the same taxonomic community may have different implications depending on reproductive stage, symptoms, immune response, recurrence risk, and fertility goals.

Multi-Omics Approaches in Vaginal Microbiome Research

Traditional vaginal microbiome studies have largely relied on culture-based methods, microscopy, Nugent

scoring, Amsel criteria, and later 16S rRNA gene sequencing. Although these approaches have been essential for defining microbial composition and community state types, they provide limited information about microbial function, gene expression, metabolite production, host response, and strain-level variation. Multi-omics approaches address these limitations by integrating complementary molecular layers, including metagenomics, metatranscriptomics, metabolomics, metaproteomics, and host immune or transcriptomic profiling. This shift is central to understanding the vaginal microbiome beyond dysbiosis, because similar taxonomic profiles may differ substantially in biological activity and clinical impact (15, 43, 44).

16S rRNA Sequencing and Shotgun Metagenomics

16S rRNA gene sequencing remains widely used because it is relatively cost-effective and suitable for profiling bacterial community composition. It can identify dominant taxa and classify samples into CSTs, but it often has limited species- or strain-level resolution and provides only indirect functional inference. In contrast, shotgun metagenomics sequences total microbial DNA, allowing more detailed assessment of microbial genes, functional pathways, virulence potential, antimicrobial resistance genes, and strain-level diversity (45, 46). A major advance in this field was the development of VIRGO, a vaginal microbiome-specific non-redundant gene catalog containing approximately 0.95 million genes (43). More recently, VIRGO2 expanded this resource to more than 1.7 million annotated genes and improved representation of bacteria, fungi, viruses, and phages from vaginal samples (44). These gene-centered resources enable more precise functional profiling of vaginal metagenomic and metatranscriptomic datasets.

Metatranscriptomics

Metatranscriptomics analyzes microbial RNA and therefore identifies which genes are actively expressed in vivo. This is particularly valuable because microbial abundance does not always reflect microbial activity. For example, integrative metagenomic and metatranscriptomic analyses have shown that the transcriptional activity of Lactobacillus iners, Lactobacillus crispatus, and Gardnerella vaginalis can vary depending on the surrounding microbial community (47, 48).

Metatranscriptomic studies have also revealed functional differences between health-associated and bacterial vaginosis-associated communities. A recent meta-analysis of vaginal metatranscriptomes identified functional BV subgroups characterized by pathways related to motility, chemotaxis, biofilm formation, epithelial barrier disruption, and resistance to host antimicrobial peptides (49). These findings suggest that transcriptomic states may provide more clinically meaningful information than taxonomy alone.

Metabolomics

Metabolomics measures small molecules produced by microbes, host cells, or their interactions. This layer is especially relevant in the vagina because metabolites such as lactic acid, amines, short-chain fatty acids, amino acid catabolites, and lipid mediators can influence pH, inflammation, odor, epithelial integrity, and pathogen growth (50). Srinivasan et al. demonstrated that bacterial vaginosis correlates with pronounced metabolic signatures in amino acid, carbohydrate, and lipid metabolism, with distinct metabolite profiles seen between women with and without BV (20). In a similar vein, McMillan et al. used a multi-platform metabolomics strategy and discovered a robust correlation between the vaginal metabolome and bacterial diversity; metabolites including 2-hydroxyisovalerate and γ-hydroxybutyrate were associated with high-diversity BV-related conditions (51). These studies demonstrate that metabolomics can identify functional biomarkers that may improve diagnosis and risk stratification beyond compositional profiling.

Metaproteomics and Host-Response Profiling

Metaproteomics provides information about proteins expressed by both microbes and host cells. Although technically more challenging than DNA-based approaches, it can help identify active microbial pathways, host inflammatory proteins, antimicrobial peptides, and epithelial response markers. Studies using cervicovaginal or residual Pap test samples suggest that metaproteomics can complement sequencing by linking microbial composition to expressed proteins and functional activity (52).

Data Integration and Clinical Translation

The major strength of multi-omics is its ability to connect multiple biological layers:

Taxa→Genes→Transcripts→Proteins→Metabolites→Host Response→Clinical Phenotype

This integrated framework can help identify microbial biomarkers for bacterial vaginosis recurrence, preterm birth risk, IVF outcomes, HPV persistence, and response to microbiome-targeted interventions. Nonetheless, the clinical translation is constrained by restricted sample numbers, varied research designs, disparate sequencing technologies, contamination hazards, batch effects, high-dimensional data, and the need for standardized bioinformatic workflows. Future studies should prioritize longitudinal sampling, diverse populations, harmonized metadata, and validation of multi-omics biomarkers in independent cohorts. A multi-omics framework can link microbial composition, functional activity, host response, and clinical phenotype to support mechanism-based interpretation

of vaginal microbial states (Figure 2).

Overall, multi-omics approaches provide a functional and mechanistic framework for vaginal microbiome research. Rather than asking only which microbes are present, they allow researchers to determine what microbial communities can do, what they are actively expressing, what metabolites they produce, how the host responds, and how these interactions influence reproductive health.

Host–Microbiome Interactions and Mechanistic Pathways

The vaginal microbiome influences female reproductive health through continuous interactions with the mucosal epithelium, local immune system, hormones, metabolites, and reproductive tract physiology. These interactions help determine whether a microbial community remains protective, becomes inflammatory, or contributes to disease susceptibility. Therefore, vaginal microbial states should be interpreted not only by taxonomic composition but also by their functional effects on the host environment (3, 4, 53).

A central protective mechanism of Lactobacillus-dominant communities is the maintenance of an acidic vaginal environment. Vaginal lactobacilli metabolize glycogen-derived substrates and produce lactic acid, which lowers vaginal pH and restricts the growth of many opportunistic and sexually transmitted pathogens. Lactic acid also has direct antimicrobial and immune-modulatory effects, suggesting that its role extends beyond simple acidification (54). In particular, Lactobacillus crispatus is often associated with strong lactic acid production, lower pH, and greater ecological stability, whereas Lactobacillus iners may be more permissive to transition toward dysbiosis (4).

The epithelial barrier is another key site of host–microbiome interaction. A healthy vaginal epithelium provides a physical and biochemical barrier through tight junctions, mucus, antimicrobial peptides, and immune mediators. Experimental studies indicate that physiological concentrations of lactic acid can enhance cervicovaginal epithelial barrier integrity and increase the expression of junction-associated molecules (55). In contrast, dysbiotic communities enriched with anaerobes may compromise barrier function through inflammatory metabolites, mucin degradation, and enzymes such as sialidases and mucinases (39, 56). These processes may facilitate pathogen adherence, epithelial exfoliation, and ascending infection.

Local immune modulation is a major pathway linking the vaginal microbiome to reproductive outcomes. Anahtar et al. demonstrated that cervicovaginal bacterial communities are strong modulators of genital tract inflammation, with high-diversity communities associated with increased pro-inflammatory cytokines and immune activation (10). Such inflammation may increase vulnerability to sexually transmitted diseases, impair mucosal tolerance, and contribute to adverse reproductive outcomes. Conversely, lactobacilli-dominant communities are generally associated with lower inflammatory tone and a more protective mucosal environment (53, 55).

Microbial metabolites provide an important biochemical bridge between vaginal microbes and host tissues. In eubiotic states, lactic acid predominates and supports antimicrobial defense, epithelial protection, and immune regulation. In bacterial vaginosis-associated states, lactic acid is often depleted, while short-chain fatty acids, amines, succinate, and other metabolites increase (57). These metabolic shifts can affect

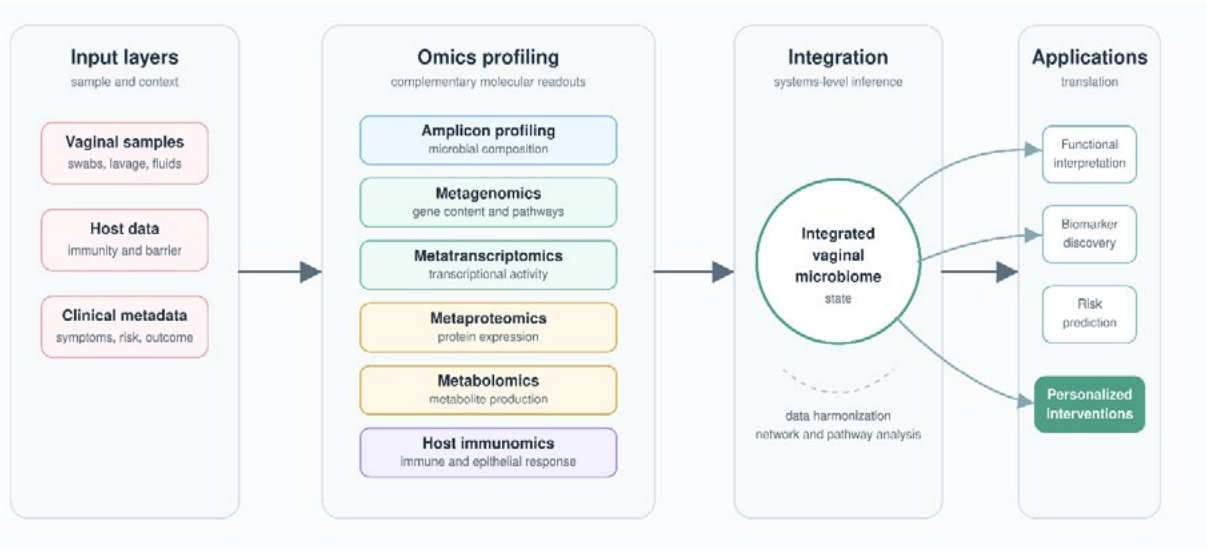

Figure 2. Multi-omics approaches in vaginal microbiome research. Multi-omics integration connects microbial composition with gene content, transcriptional activity, protein expression, metabolite production, host immune responses, and clinical phenotypes. This framework enables a more functional interpretation of vaginal microbial states and supports biomarker discovery, risk prediction, and personalized interventions.

vaginal odor, pH, epithelial integrity, cytokine production, and pathogen growth. Therefore, metabolite profiles may be more directly linked to biological activity than microbial composition alone (57).

Biofilm formation represents another important mechanism, especially in recurrent bacterial vaginosis. Gardnerella species and other BV-associated bacteria can adhere to vaginal epithelial cells and form polymicrobial biofilms, which may protect bacteria from host defenses and reduce antibiotic penetration (58, 59). This helps explain why bacterial vaginosis frequently recurs after standard antimicrobial therapy. However, Gardnerella is not uniformly pathogenic; recent work shows species- and strain-level heterogeneity in virulence potential, suggesting that clinical risk depends on microbial function, community context, and host response (60).

These pathways are particularly relevant to fertility and pregnancy. Dysbiosis-associated inflammation, impaired epithelial barrier integrity, altered metabolites, and ascending infection may influence sperm survival, embryo implantation, cervical remodeling, membrane integrity, and preterm birth risk. Recent pregnancy-focused studies and reviews suggest that vaginal microbiota can influence pregnancy outcomes through immune modulation, epithelial integrity, and inflammatory pathways, although the strength of these associations varies across populations and study designs (14, 61).

Overall, host–microbiome interactions in the vagina operate through interconnected mechanisms: acidification, antimicrobial activity, epithelial barrier maintenance, immune regulation, metabolic signaling, biofilm formation, and ecological stability. These mechanisms explain why similar taxonomic profiles may lead to different clinical outcomes and why functional biomarkers are increasingly important for precision gynecology and reproductive medicine.

Vaginal Microbiome and Fertility

The vaginal microbiome may influence fertility through its effects on the cervicovaginal environment, sperm survival, mucosal inflammation, ascending microbial exposure, endometrial receptivity, and implantation. In general, Lactobacillus-dominant communities, particularly those enriched with Lactobacillus crispatus, are considered more favorable for reproductive health, whereas high-diversity anaerobe-rich communities and bacterial vaginosis-associated dysbiosis have been linked to poorer reproductive outcomes (62-64).

Evidence from both natural conception and assisted reproduction suggests a potential relationship between vaginal microbial composition and fertility. In a prospective study of pregnancy attempts, persistent bacterial vaginosis was associated with reduced fecundability, indicating that vaginal dysbiosis may negatively affect the probability of conception in some populations (63). In infertility and IVF cohorts, abnormal vaginal microbiota has been associated with lower clinical pregnancy rates and higher risk of early pregnancy loss, although findings are not fully consistent across studies (11, 65, 66).

In assisted reproductive technology, the vaginal microbiome has gained attention as a possible predictor of IVF/ICSI outcomes. Koedooder et al. reported that vaginal microbiome profiling before IVF or IVF-ICSI could stratify the probability of pregnancy, supporting its potential use as a reproductive biomarker (11). Similarly, a meta-analysis by Singer et al. found that abnormal vaginal microbiota was associated with lower rates of early pregnancy development after IVF, although methodological heterogeneity remained a major limitation (65). Additional ART research has shown that Lactobacillus-dominant vaginal microbiome could correlate with enhanced implantation and pregnancy outcomes (67).

The endometrial microbiome may also be relevant because embryo implantation occurs in the uterine cavity. Moreno et al. proposed that a non-Lactobacillus-dominant endometrial microbiota may be associated with implantation failure and poorer reproductive outcomes (12). However, the existence, composition, and clinical relevance of the low-biomass endometrial microbiome remain debated because of contamination risk, sampling differences, and methodological variability (68, 69). Therefore, vaginal microbiome findings should not be directly extrapolated to the endometrium without careful interpretation.

Several mechanisms may explain the association between vaginal dysbiosis and reduced fertility. Dysbiotic communities may increase vaginal pH, reduce lactic acid, promote local inflammation, alter cervical mucus, facilitate pathogen ascension, and impair immune tolerance required for implantation. In contrast, Lactobacillus-dominant communities may support a low-inflammatory, acidic, and pathogen-resistant environment that is more compatible with conception and embryo implantation (70, 71).

Despite growing interest, vaginal microbiome testing is not yet a routine standard in fertility care. Most available studies are observational; sample sizes are often small, and definitions of “favorable” or “unfavorable” microbiota vary across studies. Future research should prioritize longitudinal sampling before and during fertility treatment, standardized sequencing and diagnostic methods, integration with endometrial and immune markers, and interventional trials testing whether microbiome modulation can improve live birth outcomes (72).

Overall, current evidence suggests that the vaginal microbiome may act as both a biomarker and a pos-

sible modifiable factor in fertility. However, stronger causal evidence is needed before microbiome-based diagnostics or interventions can be routinely integrated into reproductive medicine.

Vaginal Microbiome and Pregnancy Outcomes

Pregnancy is associated with marked hormonal, immunological, and epithelial changes that influence the vaginal microbiome. In uncomplicated pregnancies, vaginal microbial communities often become more stable and more strongly dominated by Lactobacillus species compared with the non-pregnant state (31). This stability is thought to support maternal–fetal health by maintaining low vaginal pH, limiting pathogen overgrowth, and reducing the risk of ascending infection.

The most compelling evidence connects changes in the vaginal microbiota with premature delivery. Numerous longitudinal investigations have shown that diminished Lactobacillus prevalence and heightened concentrations of anaerobic or bacterial vaginosis-related taxa could correlate with spontaneous premature delivery (14, 31, 73). In a significant multi-omics investigation, Fettweis et al. found that women who had preterm delivery exhibited reduced vaginal concentrations of Lactobacillus crispatus and elevated levels of BVAB1, Sneathia amnii, TM7-H1, and other Prevotella species (14). Kindinger et al. similarly discovered that the prevalence of Lactobacillus iners at 16 weeks of gestation correlated with a shortened cervix and premature delivery, whereas dominance of L. crispatus was indicative of full-term birth (73).

Vaginal dysbiosis may contribute to adverse pregnancy outcomes through multiple mechanisms, including increased vaginal pH, reduced lactic acid, epithelial barrier disruption, local inflammation, biofilm formation, and ascending infection. These pathways may promote cervical remodeling, weakening of fetal membranes, intra-amniotic inflammation, and premature rupture of membranes (9, 74, 75). The CDC further observes that symptomatic bacterial vaginosis in pregnancy is linked to premature rupture of membranes, preterm delivery, intra-amniotic infection, and postpartum endometritis (9).

Beyond preterm birth, altered vaginal microbiota has been investigated in relation to PPROM, chorioamnionitis, miscarriage, low birth weight, and neonatal outcomes. However, the evidence is less consistent for these outcomes than for preterm birth, partly because studies differ in sampling time, sequencing methods, population characteristics, diagnostic criteria, and adjustment for confounders. Importantly, microbiome-associated pregnancy risk may also vary by ancestry, geography, socioeconomic context, prior obstetric history, and host immune response (76).

Overall, a stable Lactobacillus-dominant vaginal microbiome, particularly one enriched with L. crispatus, appears to be associated with more favorable pregnancy outcomes, whereas high-diversity anaerobe-rich communities may indicate increased obstetric risk. Nevertheless, vaginal microbiome profiling is not yet a routine clinical tool for predicting pregnancy complications. Future studies should combine longitudinal microbiome sampling with metagenomics, metabolomics, cytokine profiling, cervical length measurement, and clinical risk factors to improve prediction and prevention of adverse pregnancy outcomes.

Table 3. Key gynecological disorders associated with vaginal microbiome alterations.

Disorder	Common microbiome-associated pattern	Possible mechanism	Strength of evidence
Bacterial vaginosis	Low Lactobacillus, high anaerobic diversity	Higher pH, biofilm, amines, inflammation	Strong
Vulvovaginal candidiasis	Variable bacterial profile; fungal overgrowth	Host immune response, fungal adhesion, microbial interactions	Moderate
Pelvic inflammatory disease	BV-like anaerobic communities	Ascending infection, epithelial disruption, inflammation	Moderate
HPV persistence / cervical dysplasia	High diversity, L. iners or non-Lactobacillus dominance	Inflammation, impaired antiviral immunity, barrier disruption	Moderate to strong
Endometriosis	Altered vaginal/gut/reproductive tract microbiota	Inflammation, immune dysregulation, estrogen-related pathways	Emerging
PCOS	Possible vaginal and gut dysbiosis	Metabolic inflammation, endocrine–immune interactions	Emerging

Vaginal Microbiome and Gynecological Disorders

The vaginal microbiome is closely linked to several gynecological disorders, particularly conditions involving infection, inflammation, epithelial barrier disruption, and altered mucosal immunity. Although not all associations are causal, a recurring pattern across many disorders is the depletion of protective Lactobacillus species and enrichment of anaerobic or pathobiont-dominated communities (8).

Bacterial vaginosis (BV) is the most established example of vaginal dysbiosis. It is characterized by reduced Lactobacillus abundance and expansion of anaerobic bacteria such as Gardnerella, Prevotella, Fannyhessea/Atopobium, Mobiluncus, Sneathia, and BV-associated bacteria (9). BV is clinically significant due to its correlation with vaginal symptoms, recurrence post-treatment, heightened vulnerability to sexually transmitted infections, pelvic inflammatory disease, and negative reproductive consequences. Mechanistically, BV-associated communities may increase vaginal pH, produce amines and short-chain fatty acids, form biofilms, degrade mucus, and promote local inflammation (8).

Vulvovaginal candidiasis (VVC) is another common vaginal disorder, but its relationship with the bacterial microbiome is more complex than BV. VVC is mainly caused by Candida species, especially Candida albicans, and may occur even in the presence of lactobacilli-dominant bacterial communities (77, 78). Therefore, VVC should not be interpreted simply as a bacterial dysbiosis. Instead, disease expression depends on fungal overgrowth, epithelial adhesion, host immune response, estrogen status, antibiotic exposure, and local microbial interactions. Recurrent VVC may involve altered bacterial–fungal interactions and metabolic changes, but stronger longitudinal and mechanistic studies are still needed (77).

The vaginal microbiome is also relevant to pelvic inflammatory disease (PID) and sexually transmitted infection susceptibility. BV-like communities may facilitate ascending infection by weakening epithelial and mucosal barriers, increasing inflammation, and reducing colonization resistance against pathogens (79, 80). Although classic PID pathogens include Chlamydia trachomatis and Neisseria gonorrhoeae, anaerobic bacteria and BV-associated taxa are increasingly recognized as contributors to polymicrobial upper genital tract infection (80).

A growing body of evidence links vaginal microbiota composition with human papillomavirus (HPV) infection, HPV persistence, cervical intraepithelial neoplasia, and cervical cancer risk. Systematic reviews and meta-analyses suggest that Lactobacillus crispatus-dominant communities are generally associated with lower HPV-related risk, whereas Lactobacillus iners-dominant, non-Lactobacillus-dominant, and high-diversity anaerobic communities are more often associated with HPV infection and cervical dysplasia (81-83). Possible mechanisms include altered vaginal pH, epithelial barrier disruption, inflammation, and impaired local antiviral immunity. However, causality remains uncertain, and vaginal microbiota should be considered a potential cofactor rather than a direct cause of cervical disease.

Emerging evidence also suggests possible associations between vaginal or reproductive tract microbiota and inflammatory or endocrine gynecological conditions such as endometriosis and polycystic ovary syndrome (PCOS). In endometriosis, microbiome alterations may interact with chronic inflammation, immune dysregulation, estrogen metabolism, and pelvic pain pathways (18, 84). In PCOS, studies suggest possible links between dysbiosis, hyperandrogenism, insulin resistance, and chronic low-grade inflammation, although most evidence currently comes from gut microbiome studies and limited vaginal microbiome data (19, 85). Therefore, these conditions should be discussed as promising but still developing areas of research.

Overall, vaginal microbiome alterations are most strongly established in BV and increasingly supported in HPV-related cervical disease, PID susceptibility, and recurrent vaginal infections. For endometriosis and PCOS, evidence remains preliminary and heterogeneous. Future research should distinguish correlation from causation, integrate bacterial, fungal, viral, metabolic, and immune data, and determine whether microbiome-targeted interventions can improve gynecological outcomes.

Personalized Microbiome-Based Interventions

Personalized interventions targeting the vaginal microbiome aim to move beyond uniform treatment strategies toward approaches guided by microbial composition, recurrence risk, symptoms, reproductive goals, and host factors. Current clinical management of bacterial vaginosis still relies mainly on antibiotics such as metronidazole or clindamycin, but recurrence remains common and optimal strategies for persistent or recurrent BV are still limited (8, 9). This has encouraged interest in microbiome-restorative approaches that not only suppress anaerobic bacteria but also promote durable recolonization by protective lactobacilli, particularly Lactobacillus crispatus.

Probiotics and live biotherapeutic products are among the most studied strategies. A randomized trial showed that L. crispatus CTV-05, known as Lactin-V, significantly reduced BV recurrence after vaginal metronidazole treatment compared with placebo, supporting the concept of strain-specific microbiome restoration (22). Meta-analytic evidence also suggests that probiotics may reduce BV recurrence, although effects

vary by strain, dose, route of administration, and study design (86). Therefore, probiotic therapy should not be treated as a single uniform intervention; its efficacy likely depends on selecting appropriate strains and matching them to the patient's baseline microbiome and clinical context.

More experimental strategies include vaginal microbiome transplantation and partner-based treatment. Vaginal microbiome transplantation has been reported in an exploratory study of women with intractable recurrent BV, showing potential benefit but requiring larger controlled trials, strict donor screening, and long-term safety evaluation before clinical adoption (23). More recently, a randomized trial found that treating male partners with combined oral and topical antimicrobial therapy reduced BV recurrence in women in monogamous heterosexual couples, highlighting the role of partner-associated microbial exchange (24). Overall, the future of vaginal microbiome intervention will likely involve stratified approaches that combine antibiotics, targeted live biotherapeutics, behavioral or partner-based strategies, and multi-omics biomarkers to predict treatment response and recurrence risk (87).

Microbiome-Based Biomarkers and AI-Driven Prediction

Microbiome-based biomarkers are increasingly being explored for risk stratification in reproductive and gynecological health. These biomarkers may include taxonomic markers such as community state types, Lactobacillus crispatus dominance, Lactobacillus iners dominance, or enrichment of BV-associated anaerobes, as well as functional markers such as microbial genes, metabolites, cytokines, and host-response profiles. In reproductive medicine, vaginal microbiome profiling before IVF/ICSI has been proposed as a potential predictor of pregnancy outcome (11). In bacterial vaginosis, metabolomic studies have identified distinct biochemical signatures involving amino acid, carbohydrate, lipid, and amine metabolism, suggesting that functional biomarkers may improve diagnosis beyond taxonomy alone (20, 51). Similarly, vaginal microbial patterns have been associated with HPV persistence and cervical dysplasia risk, supporting their potential value as adjunctive biomarkers in cervical disease research (81).

Artificial intelligence and machine learning can help integrate high-dimensional microbiome data with clinical, hormonal, immunological, and reproductive variables. Early machine-learning studies showed that vaginal microbial profiles could classify bacterial vaginosis-associated communities with high accuracy (88). In pregnancy research, models combining vaginal microbiota with clinical markers such as cervical length and white blood cell count have been used to predict preterm birth risk (89). The Microbiome Preterm Birth DREAM Challenge further demonstrated the potential of harmonized multi-cohort microbiome datasets for machine-learning prediction of preterm and early preterm birth (90). More recent deep-learning and IVF-focused models have begun integrating vaginal microbiome composition with inflammatory markers to improve the prediction of preterm birth or IVF success (91, 92).

Despite these advances, microbiome-based prediction is not yet ready for routine clinical use. Many models are limited by small cohorts, population heterogeneity, batch effects, differences in sequencing methods, inconsistent outcome definitions, and insufficient external validation. In addition, AI models must be interpretable and clinically actionable, not merely statistically accurate. Future biomarker studies should prioritize longitudinal sampling, multi-omics integration, standardized metadata, diverse populations, explainable AI, and prospective validation. Ultimately, microbiome-based biomarkers and AI-driven models may support precision gynecology by identifying women at higher risk of BV recurrence, IVF failure, preterm birth, or HPV persistence and by guiding personalized prevention or treatment strategies.

Challenges, Limitations, and Ethical Considerations

Despite rapid progress, vaginal microbiome research faces several methodological challenges. Differences in sampling site, menstrual or pregnancy timing, DNA extraction, sequencing platform, reference database, bioinformatic pipeline, and clinical definitions of dysbiosis or bacterial vaginosis can limit comparability across studies (93). Standardized reporting frameworks such as the STORMS checklist are therefore important for improving transparency, reproducibility, and cross-study interpretation (93). Another major issue is contamination, especially in low-biomass reproductive tract samples such as endometrial, placental, or upper genital tract specimens. Without appropriate negative controls, contamination-aware analysis, and biologically plausible interpretation, microbial signals in low-biomass samples may be overinterpreted (94, 95).

A second limitation is the difficulty of establishing causality. Many studies are cross-sectional or observational, making it unclear whether vaginal dysbiosis causes reproductive or gynecological disorders, results from them, or acts as a biomarker of another underlying process. Longitudinal sampling, mechanistic experiments, and interventional trials are needed to determine whether modifying the vaginal microbiome can improve outcomes such as IVF success, bacterial vaginosis recurrence, HPV persistence, or preterm birth. Multi-omics and AI-based models also face analytical challenges, including small sample sizes,

high-dimensional data, compositionality, sparsity, batch effects, overfitting, and limited external validation (96-98). Therefore, prediction models should be tested in independent and diverse cohorts before being translated into clinical practice.

Ethical considerations are equally important. Vaginal microbiome data are highly sensitive because they may reveal information related to sexual health, reproductive status, infection risk, pregnancy outcomes, partner-associated microbial exchange, and ethnicity-linked microbial variation. Human microbiome research raises concerns about informed consent, privacy, data sharing, identifiability of samples, return of results, incidental findings, commercialization, and potential stigmatization (99-101). These concerns are especially relevant for direct-to-consumer microbiome tests and AI-based reproductive risk prediction, where premature clinical claims may create anxiety or inappropriate treatment decisions. Future research should therefore combine methodological rigor with ethical safeguards, including transparent consent, privacy protection, equitable cohort representation, careful communication of uncertainty, and avoidance of deterministic interpretations of microbiome profiles.

Future Directions

Future vaginal microbiome research should move from descriptive taxonomy toward functional, longitudinal, and clinically validated frameworks. Large, diverse, and well-characterized cohorts are needed to clarify how vaginal microbial communities change across the menstrual cycle, pregnancy, menopause, fertility treatment, and gynecological disease states. Standardized methods for sampling, sequencing, metadata collection, and reporting will be essential to improve reproducibility and cross-study comparison (93). Resources such as vaginal microbiome-specific gene catalogs, including VIRGO and VIRGO2, can further support functional interpretation by enabling more precise analysis of microbial genes, pathways, and strain-level diversity (44).

Another priority is the integration of multi-omics and host-response data. Future studies should combine metagenomics, metatranscriptomics, metabolomics, proteomics, cytokine profiling, hormone measurements, and clinical metadata to determine not only which microbes are present, but also what they are doing and how the host responds. This approach may help identify clinically useful biomarkers for BV recurrence, IVF outcomes, HPV persistence, and preterm birth risk. However, these biomarkers must be validated prospectively in independent and ethnically diverse populations before clinical implementation.

Interventional research is also needed to determine whether modifying the vaginal microbiome can improve reproductive and gynecological outcomes. Promising approaches include targeted live biotherapeutics, strain-specific probiotics such as Lactobacillus crispatus CTV-05, optimized antibiotic–probiotic combinations, partner-based treatment strategies, and carefully regulated vaginal microbiome transplantation (22-24). At the same time, AI-driven prediction models may help personalize these interventions by integrating microbiome profiles with clinical, hormonal, immune, and behavioral data. Future translation should therefore emphasize explainable AI, patient privacy, equity, safety, and avoidance of premature commercialization. Ultimately, the field should aim to develop precision gynecology strategies in which microbiome-based diagnostics and interventions are evidence-based, individualized, and clinically actionable (102).

CONCLUSION

The vaginal microbiome is an ever-evolving and functionally important ecosystem that provides an essential role in female reproductive health, with growing evidence linking its composition and activity to fertility, assisted reproductive outcomes, pregnancy complications, and major gynecological disorders. While Lactobacillus-dominant communities, particularly those enriched with Lactobacillus crispatus, are generally associated with low vaginal pH, epithelial protection, reduced inflammation, and favorable reproductive outcomes, high-diversity anaerobe-rich communities are often linked to bacterial vaginosis, HPV persistence, pelvic inflammatory disease, adverse pregnancy outcomes, and recurrent dysbiosis. However, the traditional concept of dysbiosis alone is insufficient to explain the biological complexity of vaginal microbial ecosystems, as similar taxonomic profiles may differ in microbial gene content, metabolic activity, biofilm formation, immune stimulation, ecological stability, and clinical impact. Multi-omics approaches therefore provide a more comprehensive framework by integrating microbial composition with functional pathways, metabolites, host immune responses, and clinical phenotypes. In the future, targeted probiotics, live biotherapeutics, optimized antimicrobial strategies, partner-based treatment, vaginal microbiome transplantation, and AI-driven prediction models may support personalized approaches in precision gynecology and reproductive medicine. Nevertheless, clinical translation will require standardized methods, longitudinal and interventional studies, diverse cohorts, validated biomarkers, ethical oversight, and careful avoidance of premature commercialization.

Conflict of Interest

The authors declare that they have no conflicts of interest related to this manuscript.

Consent for Publication

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