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# Investigating Microbial Dynamics and Bacterial Vaginosis Susceptibility in Women who have Sex with Women

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## Abstract

Bacterial Vaginosis (BV) remains a prevalent gynecologic health concern, with emerging research indicating a potential association between women who have sex with women (WSW) and an increased susceptibility to BV infections. Recent studies have explored the microbial dynamics within the vaginal microbiota of WSW, revealing distinct patterns that may contribute to a higher incidence of BV in this population. The etiological factors underlying this susceptibility include disruptions in the balance of Lactobacillus species, crucial for maintaining vaginal health. However, the existing literature presents a complex interplay of socio-behavioral and biological factors influencing BV risk among WSW, necessitating further investigation. Future research should strive to gain a more comprehensive understanding of the specific mechanisms influencing microbial communities in the context of same-sex sexual activity among women, exploring potential preventive strategies and tailored interventions to mitigate BV risks in this population. Our review highlights the need for a refined and multidisciplinary approach to address the intricacies of BV susceptibility in women engaging in same-sex relationships.

## Introduction

Bacterial Vaginosis (BV) is a common gynecologic health condition among women. With an estimated global prevalence ranging from 23-29%, BV stands out as the predominant cause of vaginal symptoms among women of reproductive age [1]. It arises from an imbalance in the vaginal microbiota, characterized by an overgrowth of bacteria such as *Gardnerella species (spp.) and Prevotella spp.,* which overgrow the beneficial *Lactobacilli* found in healthy vaginal flora [1]. While not classified as a Sexually Transmitted Infection (STI), BV can be triggered by sexual activity and is associated with various risk factors, including multiple partners, a new partner, vaginal cleansing products, and seropositivity to Herpes Simplex Virus (HSV-2) [1,2]. This imbalance often occurs due to alterations in genital chemistry caused by sexual activity of the use of harsh products near the vaginal area, resulting in bacterial overgrowth. Moreover, BV increases the risk of acquiring other STIs, such as Human Immunodeficiency Virus (HIV) [3].

Symptoms commonly associated with BV include vaginal discharge, odor from the vagina, and irritation around the vagina; however, many women will not experience any symptoms [1]. While BV typically does not present with any serious complications, untreated BV can lead to Pelvic Inflammatory Disease (PID) and adverse pregnancy outcomes such as preterm delivery or spontaneous abortion [1,3,4]. Treatment of BV usually involves antibiotics, most commonly metronidazole and clinda-

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mycin, administered orally or intravaginally. Notably, BV is easily treatable, with various options available, and during treatment, sexual activity should be avoided or condoms used [3].

Diagnosis of BV in women varies, with common methods including the Gram stain test using microscopy, which reveals an increase in gram-positive and gram-negative cocci and a decrease in gram-positive *Lactobacilli* species indicative of BV [1]. Another widely utilized criterion is the Ansel criteria, encompassing parameters like a white homogenous vaginal discharge, elevated vaginal pH (>4.5), positive amine odor (the "Whiff test"), and the presence of clue cells on wet mount microscopy, all aiding in BV diagnosis [1].

Emerging research suggests a potential association between Bacterial Vaginosis (BV) and women who have sex with women (WSW). Studies indicate that sexual behaviors among WSW, coupled with specific BV-associated bacteria (*Prevotella bivia, Gardnerella vaginalis,* and *Atopobium vaginae*) and the exchange of vaginal and microbiota could play a crucial role in the pathogenesis of BV in WSW [5].

## Discussion

### Microbial dynamics in vaginal microbiota of WSW

The vaginal microbiota represents a sophisticated ecosystem influenced by genetics, physiological, and behavioral factors. It plays a pivotal role in our immune system, functioning as the primary defense mechanism within the female genital tract [6]. This symbiotic relationship allows the immune system to recognize beneficial bacteria, *particularly Lactobacillus spp.*, as self rather than foreign. While every woman has a unique vaginal microbiota, these environments can be broadly classified by the dominant bacteria, usually *Lactobacillus spp.* [7]. However, it has been questioned whether a *Lactobacillus* dominated microbiota truly defines vaginal microbial health. Several studies have shown that *Lactobacillus* species were more commonly found in abundance in White and Asian women, while Black and Hispanic women more often had vaginal microbiota not dominated by *Lactobacillus* [8,9]. Therefore, it can be harmful to draw associations between "optimal" reproductive health and race given that race acts as a surrogate for multifaceted life experiences that can impact both biological and behavioral traits [6].

Nevertheless, it is widely acknowledged that a low-diversity microbiota dominated by *Lactobacillus* is linked to lower levels of proinflammatory cytokines, thus maintaining a state of low inflammation. Conversely, high diversity microbiota are associated with elevated concentrations of inflammatory cytokines, particularly in cases of BV, where heightened levels of interleukin (IL)-1, IL-8, and IL-12 have been observed [6,10]. It has been well established that BV microbiota are linked to high concentrations of these proinflammatory cytokines. Consequently, some classify BV not as an infection, but as dysbiosis, signifying a microbial imbalance in the vaginal flora [11].

### Microbial patterns

Using hierarchical clustering techniques, dominant bacterial taxa can be identified in the vaginal microbiome. These are known as Community State Types (CSTs). In a comprehensive study exploring the diverse Community State Types (CSTs) of vaginal bacteria in women who have sex with women (WSW), researchers identified eight distinct CSTs, each delineating a unique microbial community pattern [12]. Among these, five were characterized by the predominance of *Lactobacillus spp.* (including *L. crispatus, L. iners, L. gasseri, L. jensenii/L. fornicalis*), while the remaining three exhibited the presence of *Gardnerella vaginalis (G. vaginalis)*, anaerobic bacteria, and *Bifidobacterium longum*. Significantly, the majority of BV cases in WSW were associated with the latter three CSTs [12]. Previous studies have shown that *A. vaginae, U. urealyticum, Prevotella, Staphylococci,* and gram-negative rods have been associated with BV in WSW [13,14]. This underscores the heightened risk of BV in WSW populations [5].

## Biological factors influencing BV susceptibility

### Lactobacillus species in maintaining vaginal health

The etiology of BV is multifaceted, with disruptions in the balance of *Lactobacillus* species playing an important role. Recent studies have shed light on the intricate microbial dynamics within the vaginal microbiota of WSW. For example, a longitudinal study comparing Nugent scores among women who have sex with women (WSW) and women who have sex with women and men (WSWM) with women who have sex with men (WSM) found that WSW and WSWM were significantly more likely to have BV than WSM ($P<0.01$ for both groups, WSW and WSWM) [15]. Another cross-sectional study aimed to assess BV prevalence among WSW and WSM within the community reported that WSW have a 2.5-fold increased likelihood in developing BV compared to WSM [16].

These investigations have revealed distinct patterns contributing to a higher incidence of BV in this population. Understanding the interplay between biological and behavioral factors is crucial in elucidating the increased susceptibility to BV among WSW. The role of *Lactobacillus* species in maintaining vaginal health is well-documented. Research on asymptomatic North American women from diverse ethnic backgrounds demonstrates that a significant portion of vaginal microbiomes are predominantly composed of one or more *Lactobacillus* species [17]. These bacteria play a crucial role in protecting the vaginal environment against pathogenic organisms, mainly through the production of lactic acid, which contributes to an acidic pH hostile to many pathogens [17-19]. However, in WSW, this critical balance of *Lactobacillus* species is often disrupted, leading to an overgrowth of anaerobic bacteria typical of BV [20,21].

### Host genetics and immune system

The examination of biological factors contributing to BV susceptibility reveals a complex interplay between the vaginal microbiota composition, host genetics, and immune responses. While evidence on the relationship between genetics and vaginal microbiota is limited, recent studies have uncovered specific genetic variations associated with innate immune pathways, such as Toll-Like Receptors (TLRs) and cytokine signaling molecules, which play critical roles in orchestrating host defense mechanisms against microbial colonization [6]. Polymorphisms in genes encoding TLRs, responsible for recognizing microbial ligands and initiating immune responses, have been linked to altered susceptibility to BV in pregnant women and Black women, however no study has yet to explore host genetics and polymorphisms in modulating BV risk in WSW [22].

Furthermore, investigations into the vaginal microbiota's composition have highlighted the significance of dysbiosis in BV pathogenesis. Reduced diversity and abundance of *Lactobacillus* species, coupled with overgrowth of anaerobic bacteria like

*Gardnerella vaginalis* and *Atopobium vaginae,* are characteristic features of BV. This dysbiosis-induced inflammation, mediated by cytokine responses and TLR signaling, is essential for mounting an effective immune defense against pathogens but can lead to epithelial barrier damage and long-term gynecological complications when sustained. Notably, the female genital tract microbiota, characterized by a high abundance of *Lactobacilli* and low bacterial diversity, is associated with lower levels of inflammation, and is often considered indicative of genital microbial health. Conversely, a more diverse microbiota, marked by reduced *Lactobacilli* abundance and increased presence of taxa such as *Gardnerella spp., Prevotella spp.,* and *Atopobium spp.,* correlates with heightened mucosal inflammation levels and elevated risk of conditions like BV and STIs [6].

**Hormonal influences**

Hormonal influences play a crucial role in shaping the composition and stability of the vaginal microbiota. Fluctuations in hormonal levels, particularly estrogen, throughout the menstrual cycle influence the abundance and diversity of microbial species within the vagina. During periods of high estrogen levels, such as the follicular phase, estrogen stimulates glycogen accumulation in vaginal epithelial cells, maintaining a substrate for *Lactobacillus* fermentation and lactic acid production. This helps to maintain an acidic pH and suppress growth of the pathogenic bacteria associated with BV [6]. Thus, in high estrogen states, the vaginal microbiota tends to be more diverse and dominated by *Lactobacillus spp.,* contributing to a healthier vaginal environment [6]. Conversely, during low estrogen phases, such as menstruation or menopause, there is reduced glycogen availability, predisposing individuals to vaginal dysbiosis, inflammatory microbiomes, and increased susceptibility to BV [23,24]. Overall, hormonal influences play a nuanced yet significant role in maintaining the balance of the vaginal microbiota and modulating susceptibility to BV.

**Behavioral factors influencing BV susceptibility**

The heightened bacterial diversity observed in the vaginal microbiota of WSW, contributes to the increased incidence of BV, influenced by various factors. These include engaging in sexual activities with new female partners, receptive oral sex from female partners, frequent sexual activity, and douching [12,13,25-29]. Furthermore, the sharing of sex toys has been identified as a potential vector for the transmission of BV [27,28,30,31]. This practice can introduce and exchange bacteria between partners, disrupting the individual vaginal microbiota. Previous research has highlighted diminished concentrations of *Lactobacillus* and increased colonization of *G. vaginalis* among WSW, with oral sex and the shared use of sex toys implicated as potential contributors to BV susceptibility in this population [6,12]. Notably, women reporting recent sexual activity with new partners were more prone to harboring a microbiota dominated by *G. vaginalis* or anaerobic bacteria CSTs [12]. Moreover, the sharing of sex toys was linked to microbiota dominance by *G. vaginalis*, while douching correlated with an abundance of anaerobic bacteria [12].

The increased susceptibility of WSW to BV is a multifactorial issue, rooted in both biological and behavioral elements. The disruption of *Lactobacillus* in the vaginal microbiome, influenced by sexual practices and hormonal factors, plays a significant role in this context. Addressing these risk factors requires a holistic approach, combining medical understanding with behavioral interventional tailored to the unique needs of WSW.

**Socio-cultural factors influencing BV susceptibility**

The prevalence and management of BV in WSW are influenced not only by biological factors but also by a range of socio-cultural factors. Stigma, particularly prevalent in societal attitudes towards sexual minorities, is an important factor. WSW often face societal stigmatization, leading to hesitancy in seeking medical care or reluctance in discussing sexual behaviors with healthcare providers. This hesitance not only affects the diagnosis and treatment of BV but also contributes to a broader lack of awareness regarding WSW-specific health issues, both among healthcare professionals and within the WSW community itself [32-34].

Disparities in healthcare access further compound these challenges. Research indicates that WSW are less likely to engage in routine healthcare compared to their heterosexual counterparts [32,35,36]. Charlton et al. observed notably lower odds of WSW undergoing pap smears both in their lifetime and within the past year [36]. Furthermore, experiencing sexual orientation stigma has been linked to lower engagement in care [35]. Liu et al. also found that WSW had higher odds of not having a regular source of care, not consulting a healthcare professional in the past year, and forgoing or delaying medical care due to cost concerns [37].

LGBT individuals have reported discomfort and safety concerns within the healthcare system, citing discriminatory practices and attitudes [38-40]. This environment leads to the avoidance of seeking healthcare due to fears of receiving substandard care. Such disparities not only contribute to delayed diagnosis and treatment of BV and STIs but also correlate with poorer overall health outcomes.

**Complexity and necessity for further investigation**

The examination of BV risk among WSW necessitates an understanding of the intricate interplay between socio-behavioral and biological factors. While sexual practices among WSW, such as the sharing of sex toys and receptive oral sex from female partners, contribute to disruptions in the vaginal microbiota, biological factors also play a crucial role in susceptibility to BV. Hormonal influences, particularly fluctuations in estrogen levels throughout the menstrual cycle, impact the composition and stability of the vaginal microbiota, thereby influencing susceptibility to BV. Moreover, genetic variations associated with the innate immune pathways, such as TLRs and cytokine signaling molecules, have been linked to altered susceptibility in other populations, though this area remains under studied in WSW.

Despite the comprehensive literature supporting the association between increased BV prevalence in WSW, there is a critical need for further investigation into the complexities of the vaginal microbial ecosystem and the interplay between socio-behavioral and biological factors. While traditionally, a *Lactobacillus*-dominated microbiota has been equated with vaginal health and absence of dysbiosis, recent research challenges this notion. Racial disparities in microbiota composition emphasize the need for a more nuanced understanding of the underlying factors influencing microbiota diversity. Moreover, while this review focuses on the impact of bacterial components of the vaginal microbiota, investigating the interactions between bacterial and nonbacterial components (fungi, viruses) could provide a more comprehensive insight into female genital tract health and disease. Addressing these gaps necessitates further research into the interplay among genetics, physiology, be-

havior, and socio-cultural experiences, ultimately enabling the development of more accurate frameworks for assessing and promoting vaginal microbial health across diverse populations. Furthermore, there is a need to explore how host genetics and polymorphisms influence susceptibility to BV in WSW. The lack of research in this area underscores a significant gap in understanding BV pathogenesis, particularly in underrepresented communities like WSW.

## Future research directions

As mentioned above, there are several known factors that shape the microbial communities common among women who have sex with women. The research that has been done pertaining to biological aspects such as host genetics and immune response is an area of opportunity for continued research on this subject. The hormonal changes that happen specifically throughout the menstrual cycle also have been shown to contribute to the vaginal microbiome and its susceptibility to pathogenic bacteria. While data supports higher estrogen states contributing to a healthier vaginal environment, the association between BV for example and the vaginal microbiome during menses is unclear and welcomes further research [6]. Research regarding the microbial communities among men who have sex with men as well as other sexual activities is a growing area of opportunity to understand how various practices impact the microbiome in these populations.

A more complete understanding of the mechanisms that influence BV susceptibility in WSW is an opportunity for further research. An observational study of WSW reported that women who had BV had increased likelihood to report their sexual partner having BV, sharing sex toys inserted vaginally, as well as using vaginal lubricant. This same study found that among women who had one lifetime partner of the same sex BV was more prevalent. These findings suggested that sexual activity with a regular female partner carries the highest risk of BV among this population [41]. The mechanism would potentially include the lifetime female partner having BV already known or unknown. Further research into this mechanism and various factors surrounding why having one lifetime female partner would increase BV susceptibility can be further investigated.

### Preventive strategies and tailored interventions

There is a myriad of potential preventive strategies for BV documented in the literature, and these interventions for treatment and prevention of BV can be applied specifically to WSW. For example, pH modulation to make the vaginal pH more acidic may be beneficial in providing an environment where BV-associated bacteria is less likely to thrive. This is often accomplished with a lactic acid-based gel or vitamin C, however there is a gap in the literature regarding quality evidence to support this intended effect. Another example includes the disruption of biofilms that exist on BV-associated bacteria. This is typically accomplished with boric acid or an astodrimer vaginal gel, and shows moderate quality evidence for benefit, by which it enhances the bacteria's susceptibility to antibacterial mechanisms.

An analysis by Abbe et al. shows that other preventive strategies such as the use of probiotics to recolonize the vagina with health promoting Lactobacillus species (administered orally or vaginally), or diet such as avoiding sugar and fat intake and increasing the intake of vitamins A, C, D, and E have shown up to moderate quality evidence for benefit in mitigating the risk of BV. Other potential preventive strategies include barrier contraception to prevent the introduction of bacteria into the vaginal environment, and the cessation of smoking [42].

### Development of tailored interventions based on identified risk factors

A qualitative study on women's management of recurring bacterial vaginosis and experiences of clinical care delved into lifestyle modifications that women adopted to prevent recurrence of BV. Some of these tailored interventions include changes in sexual practices and hygiene (no longer sharing toys, washing hands more frequently), more informed purchases of personal products and clothing (loose clothing, cotton underwear, hypoallergenic toilet paper, no fabric softeners or harsh soaps) and general improvements to health and wellbeing (low-sugar diets and increased consumption of probiotics) [43].

Of the patients surveyed in the qualitative study conducted by Bilardi et al. many reported having female sexual partners who had been treated for BV and noted no further episodes of BV since implementing the aforementioned lifestyle changes. Nevertheless, it is important to consider the limitations associated with qualitative studies. As a result, further quantitative studies are warranted to investigate the impact of specific lifestyle changes on BV incidence and recurrence in large sample sizes to better demonstrate correlation [43].

### Refined and multidisciplinary approach

Further understanding surrounding BV in WSW is needed due to the importance in diagnosing and treating this condition medically as well as in light of its social and emotional implications. As commonly stated in the literature BV increases risk of PID, spontaneous abortions, and other adverse outcomes of pregnancy. Promptly and accurately diagnosing BV then is crucial in providing excellent medical care to WSW. Socially, stigmas and beliefs surrounding WSW contribute to gaps in care as well as hesitancy in patients belonging to this population to in seeking treatment. The collaboration of specialties increases patient satisfaction as well as positive patient outcomes which is important in all populations but crucial in sexual minorities and their comfortability in bringing complaints and concerns to a medical provider. Collaboration among gynecologists, microbiologists, behavioral scientists, and public health professionals is not only an area for advocacy but also an avenue by which understanding of BV in WSW but microbial communities in sexual minorities and other patient populations can grow and improve.

## Conclusion

Highlighted throughout this review is a discussion of microbial dynamics in the vaginal microbiota of women who have sex with women (WSW), in addition to the various etiological factors, such as the disruptions in *Lactobacillus* species, socio-behavioral practices and biological factors such as hormonal influences on the increased susceptibility of BV in WSW. Despite the comprehensive amount of literature supporting the association between the increase in BV prevalence in WSW, there is a need for further investigation to assess the complex interplay of socio-behavioral and biological factors in BV risk among WSW demographics, and an imperative to identify gaps in current understanding of BV transmission.

The critical need for continued research and a comprehensive approach to mitigate Bacterial Vaginosis (BV) risks among women in same-sex relationships cannot be overstated. Despite

BV being a prevalent issue affecting women's health and over 21 million women a year nationally, there remains a significant gap and need for continued research in the mitigation of BV risks among WSW [5]. Comprehensive research is imperative to unravel the nuanced factors contributing to BV among women in same-sex relationships, including behavioral, biological, and socio-cultural determinants, much like Evans et al. have done in their qualitative study to assess behaviors among WSW within the community [16]. Furthermore, a tailored approach to prevention and treatment strategies is essential to address the unique needs and challenges faced by this population. This would include updating guidelines and best practices for healthcare providers, particularly gynecologists and primary care providers who are often on the frontline of prescribing treatment for BV. By prioritizing research and adopting a holistic approach, we can better safeguard the reproductive health and well-being of women in same-sex relationships, fostering both inclusivity and equity in healthcare.

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