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# Bacterial Vaginosis - A Brief Synopsis of the Literature

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## Abstract

Bacterial vaginosis (BV) affects women of reproductive age and can either be symptomatic or asymptomatic. Approximately 50% of women are symptomatic and experience vaginal malodor, discharge, itching and increased vaginal pH. BV can increase the risk of contracting many sexually transmitted infections (STIs) such as human immunodeficiency virus (HIV), *Neisseria gonorrhea* (NG), *Chlamydia trachomatis* (CT), *Trichomonas vaginalis* (TV) and herpes simplex virus-2 (HSV-2). Though effective treatment options do exist, metronidazole or clindamycin, these methods have proven not to be effective long term. The purpose of this review is to summarize current literature on the epidemiology of BV and highlight areas of deficiency in current clinical practice with respect to BV.

BV recurrence rates are high, approximately 80% three months after effective treatment. Furthermore, in some instances treatment is ineffective and BV persists. Literature also documents the relationship between BV and human papillomavirus (HPV). HPV is the most common sexually transmitted infection among young adult women while BV is the most common cause of vaginal symptoms among women of reproductive age. BV is associated with high levels of anaerobic organisms which can damage the vaginal epithelium and increase the risk of HPV infection. Recent research also highlights the role of the vaginal microbiome in BV. The results of this review warrant further exploration into the etiology of BV as well as exploration of more long-term effective treatment and the investigation of prognostic indicators. Additionally, the need for a standard definition of recurrent and persistent BV is recognized.

### Keywords

Bacterial vaginosis; treatment; vaginal microbiome; sexually transmitted infections

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Conflict of interest

The authors declare no conflict of interest.

## Introduction

Bacterial Vaginosis (BV) is a common vaginal dysbiosis among women of reproductive age.(1–4) Gardner and Dukes first described BV in 1955.(2, 5, 6) The syndrome was initially termed *"Haemophilus vaginalis* vaginitis," based on the organism that was previously believed to be the etiologic agent, *H. vaginalis*.(2, 3, 5) It was later discovered that *H. vaginalis* did not belong to the genus *Haemophilus* and the bacteria was renamed *Gardnerella vaginalis*.(2) BV was also called nonspecific vaginitis and *Gardnerella vaginalis* vaginitis.(7–9) Currently, the etiology of BV is unknown.(1, 2, 7, 10–21) However, it has been determined that BV is characterized by overgrowth of opportunistic bacteria and a decrease in the levels of *Lactobacilli*.(4, 7, 9, 13, 14, 16, 17, 20, 22–24) A healthy vaginal flora is dominated by *Lactobacilli*,(2, 7, 14, 15, 17, 21, 22, 25) approximately 90-95% of total bacteria.(2, 26) However, research also indicates that some healthy women do not possess a Lactobacillus-dominated vaginal microbiota.(27–29) In cases of BV, mainly anaerobic microorganisms such as gram-positive cocci and gram-negative bacilli dominate the vaginal flora.(30) Common opportunistic bacteria include *Prevotella* species, *Gardnerella vaginalis* and *Mobiluncus* species.(2, 9, 10, 12, 15, 16, 20, 22, 25, 31)

BV is the most common cause of abnormal vaginal discharge.(2, 7, 13, 20) Symptomatic BV is also characterized by vaginal malodor, increased vaginal pH and vaginal itching.(1, 6, 7, 10, 12, 14, 24) There has been approximately 65 years of research conducted on BV. After over six decades, researchers have still been unable to elucidate the causative agent of BV and issues of adverse BV-associated sequelae are very poorly understood, further emphasizing the clinical conundrum that is BV. This review presents a brief summary of the major research findings with respect to the epidemiology of BV, recurrence and persistence of BV, known correlates of BV and the effect of BV on the vaginal microbiota.

## Epidemiology of BV

The prevalence of BV varies internationally and intranationally.(2, 11) The prevalence of BV can range from 20-60% from country to country.(2) BV prevalence is highest in Sub-Saharan Africa.(2, 11) The prevalence of BV is higher in South East Africa when compared to West Africa.(2, 11) A study conducted by Myer *et al.* in South Africa reported that the prevalence of BV was 58.3% as of 2002.(11, 32) Additionally, in the year 2000, reported BV prevalence in Zimbabwe was 30.3%.(11, 33) This can be compared to Nigeria, where in 2005 the prevalence of BV was reported to be 14.2%.(11, 34) Prevalence of BV is moderate in regions such as South and Southeast Asia, Latin America and the Caribbean and the US.(11) In these regions the prevalence of BV was determined to be 23.2% in Bangladesh as of 2002,(11, 35) 32% in Chile as of 2006(11, 36) and 29.2% in the US as of 2004.(11, 31, 37) Of note are regions such as Australia and New Zealand and Western Europe where BV prevalence is the lowest.(11) The prevalence of BV in Australia was determined to be 4.7% in 2008.(11, 19) Comparatively low BV prevalence was also reported in Finland for the year 2008 as 8.6%.(8, 11, 38) The aforementioned countries used Nugent Scoring to evaluate the presence of BV.(11)

Literature has not yet explored the predictors of intranational and international differences with respect to the prevalence of BV. Cultural factors may play a role in the in these observed differences. Additionally, there may be differences in surveillance techniques used and BV may not be a reportable disease in every country. Diagnostic techniques vary depending on the availability of resources. Approximately 50% of cases of BV are asymptomatic.(7) Due to variations in clinical guidelines, BV may not be screened for and the true prevalence of BV, within country, and reported prevalence would not be the same. The US Preventive Services Task Force does not currently recommend the screening of asymptomatic pregnant women for BV due to a lack of data supporting the benefits of screening.(39, 40) Furthermore, literature illustrates that there a lack of studies which compare a screened and non-screened population.(39, 41) Similarly Canadian clinical guidelines only recommend BV screening for asymptomatic pregnant women.(42) Our literature search did not highlight the screening practices of other countries. It remains unclear why such a large percentage of cases of BV are asymptomatic.(10) Longitudinal studies are needed to assess the effect of screening for asymptomatic BV among pregnant and non-pregnant women.

## Diagnosis and Treatment of BV

BV is diagnosed using either Amsel's criteria or Nugent score.(6, 7, 10, 22, 25, 31, 43, 44) Amsel's criteria is more commonly used in clinical settings(6, 22, 43–45) since it is faster and more affordable than Nugent scoring.(31) Three of the following Amsel's criteria must be present to be diagnosed with BV; increased homogeneous thin vaginal discharge, pH of the secretion greater than 4.5, amine odor when potassium hydroxide 10% solution is added to a drop of vaginal secretions or presence of clue cells in wet mount preparations.(2, 6, 14, 22, 31, 43, 44) Gram stain techniques are utilized to diagnose BV by Nugent scoring.(2, 44) Scoring is based upon the presence of different bacterial morphotypes where a score ≥ 7 indicates the presence of BV, 4-6 intermediate and 0-3 normal.(2, 6, 22, 37, 44, 46) Due to the methodological differences between these two diagnostic techniques, this results in varying degrees of accuracy when these methods are compared. However, once BV is diagnosed it can be treated.

Treatment is only recommended for symptomatic women, according to the United States (US) Centers for Disease Control and Prevention (CDC) treatment guidelines, due to a lack of sufficient evidence to support treatment of asymptomatic women.(37, 47) The guidelines further indicate that there are limited benefits of treatment in non-pregnant women and that treatment only provides relief of symptoms.(48) Thus women with asymptomatic BV often experience high recurrence rates due to a lack of treatment. The recommended forms of treatment for BV include metronidazole and clindamycin.(7, 12, 13, 24, 30, 49) The aforementioned antibiotics can be administered orally or intravaginally.(12, 50) These recommended regimens have similar efficacy.(7, 24, 50) Though treatment for BV is only recommended for symptomatic cases of the disease,(23) literature suggests that treatment of asymptomatic BV may reduce the risk of BV associated adverse sequelae.(8, 46) Schwebke and Desmond determined that treatment with intravaginal metronidazole gel significantly reduced the risk of *Chlamydia trachomatis* (CT) infection.(23) In light of the studies which suggest that treatment of asymptomatic BV may reduce the risk of acquisition of sexually

transmitted infections (STIs) the current clinical guidelines should be revaluated and modified accordingly. Health care providers should institute screening for BV regularly, similar to screening for STIs, to potentially diagnose asymptomatic cases as well as reduce the risk of incident STIs. However, considering the findings of Ravel and others that indicate that there is a non-Lactobacillus dominant subgroup of healthy women,(27–29) screening practices should implement tools such as molecular testing to discern true cases of BV.

BV treatment is usually effective. Studies have reported initial cure rates varying between 80-90% after one month.(12, 13) However, there are high rates of recurrence of BV.(3, 15, 18, 24, 45, 51) Bradshaw *et al.* reported the recurrence rate of BV could be as high as 58% in the first year after treatment.(13, 50) Cook *et al.* determined that after the completion of treatment with metronidazole that 30-40% of women would experience another episode of BV within three months.(30) Comparatively, Wilson *et al*, reported recurrence rates between 15-30% after treatment.(16) Additionally, BV recurrence rates of up to 60% have been reported within twelve months,(25) whereas Hillier and Holmes reported recurrence rates up to 80% within 9 months.(30) It may be necessary for the scientific community to explore alternative methods of treatment for BV since the current treatment methods are highly ineffective.

## Recurrent and Persistent BV

Recurrent BV, though recognized as a common problem associated with the treatment of BV,(7) has no universally accepted definition and therefore no means of definitive diagnosis.(14, 25) However, it is accepted that the presence of repeated cases of BV after treatment is indicative of recurrent BV.(14) In literature, recurrent BV is diagnosed in multiple ways. Klatt *et al.* defined recurrent BV as *"at least three clinic visits within the previous two years that results in an I CD-9 diagnosis code for BV"*.(14) Cook *et at.* defined recurrent BV as *three or more episodes of BV in the previous year*.(30) Chen *et al.* defined recurrent BV as *"filling a vaginal or oral prescription for BV therapy 4-28 weeks post index date"*.(50) Marshall also defines recurrent BV as BV cases that *"recur one or more times after the completion of an episodic regimen"*.(25) A standard definition of recurrent BV is required for effective and efficient diagnosis, treatment and surveillance of this irregular dysbiosis. Nocturnal application of topical metronidazole twice a week for six months is the only approved treatment for recurrent BV.(25) Currently, the treatment of the partners of women with recurrent BV is not recommended.(25) The etiology of recurrent BV is not known, however there are many theories as to why it may occur.

Available research suggests that recurrent BV may be caused by reinfection or relapse of infection.(16, 30) BV reinfection may occur by two mechanisms, either endogenously or via infection by a partner who has been colonized by BV associated microorganisms.(30) Literature supports the hypothesis that recurrent BV occurs by reinfection through studies which indicate that recurrence rates are lower among women who abstain from sex or use condoms consistently after sex compared to women who have unprotected sex.(52) Conversely, Wilson suggests that the lack of evidence to support partner therapy as a means to reduce recurrent BV indicates that reinfection may not be the cause of recurrent BV.(16) Fethers *et al.* also determined that partner therapy failed to reduce recurrent BV rates in

women.(19) For example, Hay determined, after reviewing four double blind placebo-controlled clinical trials that after treatment of male partners there was no difference in the rate of recurrence of BV.(7)

In 2012, Mehta reviewed six randomized clinical trials (RCTs) which assessed the treatment of male sexual partners for improved bacterial vaginosis outcomes.(53) It was determined that though the RCTs concluded that male partner treatment did not provide beneficial effect on BV recurrence in women, that these RCTs were inherently flawed.(53) For example, Vejtorp *et al.* determined that there was no significant difference in symptom improvement or cure between the intervention and control groups [RR=1.03, 95% CI:0.83-1.29],(54) but their methods were subpar.(53) Recruitment and screening methods were not reproducible; eligibility criteria for both men and women were not reproducible; sample size calculations were not appropriately addressed; blinding methods were not reported; adherence was not reported for both men or women; and harms of treatment were not reported in women or women.(53) Furthermore it should be noted that many studies do not assess the treatment of male partners.

The theory of relapse versus reinfection may be more plausible.(30) Relapse may occur due the inability to reestablish a *Lactobacillus* dominant vaginal flora or ineffective treatment.(30) Clinical guidelines do not recommend routine test of cure after treatment of an initial BV infection.(25) Relapse of BV infection could indicate persistent BV where positive BV diagnosis remains unchanged after treatment.(30) Thus it is important to consider prognostic indicators of BV. There is a lack of diagnostic tests which predict BV recurrence after treatment.(55) Sobel *et al.* present novel findings where they illustrate the use of a quantitative PCR-based test in combination with Lactobacillus Relative Composition and Nugent scores to predict the likelihood of BV recurrence.(55) They determined that the microbial composition of women with BV within seven days of completing standard metronidazole treatment determined the likelihood of BV recurrence.(55) It is important to consider whether BV is an STI versus a sexually enhanced infection in order to further understand the etiology of BV and its risk factors and develop enhanced diagnostic and prognostic tests.

## Predisposing Factors associated with BV

Numerous risk factors are associated with BV, such as sexual history, intravaginal practices, contraceptive use, antibiotic use, race, education, age and menstrual cycle.(4, 17, 18) However data with respect to risk factors of recurrent BV are lacking.(18) It is uncertain whether or not BV is an STI.(3, 9, 18, 37) The lack of a known etiologic agent makes it difficult to classify BV as an STI.(2, 19) However, current literature suggests that BV is related to sexual activity.(3, 19) Factors such as number of lifetime sex partners, women who have sex with women (WSW), use of a sex toy, early coitarche, frequency of vaginal intercourse, recent partner change, oral sex, anal sex and history of bacterial STIs, have been proven in the literature to increase the risk of BV.(2–4, 6, 18–20, 37, 45, 52) Fethers and colleagues reported that BV did not occur in women without a history of sexual experience.(19) Further to this, they also determined that there was a strong association between BV and penile-vaginal sex with multiple sex partners.(19)

Additionally, Morris *et al.* determined that the diagnosis of BV was positively associated with a recent sex partner change, increasing number of lifetime sex partners, WSW and a history of bacterial STIs.(3) Furthermore, Madhivanan *et at.* presented findings that indicated that *Trichomonas vaginalis* (TV) was positively associated with BV.(56) Few studies have reported the prevalence of BV among women who report never having sex.(19) Flowever, Koumans *et at.* determined that the prevalence of BV among women who never reported having had sex was 18.8.%.(37) Papanikolaou *et al.*, assessed a serious case of recurrent BV in a 17 year old female adolescent.(57) Physical examination revealed an intact hymen and Amsel's criteria confirmed the presence of BV.(57) This may indicate that other factors are necessary for BV infection,(2, 37) and BV may be a sexually enhanced rather than sexually transmitted infection.(2)

The association between BV and methods of birth control varies depending on which methods are used. Studies have shown that combined oral contraceptives, progestin only contraceptives and condom use,(45) are protective against BV.(2, 4, 6, 20, 22) Ranjit *et al.* reported that the risk of BV increased among women that used contraceptives on anatomical sites compared to women that did not.(4) They postulated that the observed difference among women that used oral contraceptives compared to those that did not could have been attributed to the effect of increased levels of estrogen that could potentially support the growth of specific bacteria responsible for lowering the risk of BV.(4) Of note, Ranjit *et al.* reported that the risk of BV was higher among individuals who used condoms daily compared to those that used condoms sometimes, however this difference was not statistically significant. They also determined that oral contraceptives reduced the risk of BV. (4) Conversely, consistent condom use has been reported in other studies to significantly lower the risk of recurrent BV.(2, 18, 52) The relationship between BV and intrauterine devices (IUDs) is unclear.(22) Some studies have determined that IUDs increase the risk of BV,(11) while others determined that there is a decreased risk.(22) Madden and colleagues did not find a statistically significant association between IUDs and BV.(22) However, they determined that intravaginal bleeding during the first six months among IUD users resulted in a twofold increased risk of BV.(22) They further postulated that irregular bleeding may be on the causal pathway between IUD use and BV.(22) Conversely, Joesoef determined that BV was significantly associated with IUDs.(58) It is important to consider that there may be differences in the type of IUDs used in each study (hormone loaded versus copper IUDs). The aforementioned studies did not differentiate between the types of IUDs used.

Intravaginal practices such as douching, also known as vaginal cleansing or vaginal washing, have been determined to be associated with BV.(3, 4, 6, 9, 11, 18, 20, 45, 59–61) Mixed conclusions about this relationship have been posed in current literature.(18, 62) Some studies have determined that douching increased the risk of BV infection.(2–4, 18, 20, 37) Ranjit and colleagues reported a statistically significant difference between women that douched daily compared to women that douched occasionally and BV.(4) Women who douched daily were more likely to have BV.(4) Additionally, Schwebke *et al.*, determined that women who refrained from douching were more likely to be cured of BV.(63) Conversely, Jespers *et al.*, Demba *et al.* and Fethers *et al.* determined that douching was not associated with BV.(19, 62, 64) Few studies present findings related to douching as a risk factor of recurrent BV. However, Guedou *et al.* determined that recent douching was

positively associated with recurrent BV,(18) whereas Klatt *et al.* determined that douching was not associated with recurrent BV.(14) Discrepancies observed in the literature may be due to the varying cultural differences that influence vaginal practices and a lack of understanding of the causal relationship between BV and douching.(18, 60) Hutchinson and colleagues determined that existing abnormal flora influenced the association between BV and douching.(60) They determined that douching was associated with incident cases of BV among women with intermediate vaginal flora but not among women with normal vaginal flora.(60) Literature further suggests that women douche following the development of BV to reduce the effect of the associated symptoms.(60) Studies which assess the relationship between BV and douching using longitudinal versus cross sectional methods should be further explored.

The risk of BV also varies by race and ethnicity.(3, 4, 6, 9, 20, 37, 65–67) African American (AA) race is a risk factor for BV,(11, 68) however, the cause of this relationship remains unclear.(9, 20) AA women are more likely to have BV compared to non-Hispanic white women.(59, 67) Fettweis and colleagues further suggest that AA women are more than twice as likely to develop BV compared to women of European ancestry (non-Hispanic Caucasians) and more than twice as likely to have a preterm delivery.(66) AA race is also positively associated with recurrent BV.(14) It is also important to consider the difference between AA women and women from continental Africa in terms of the prevalence and recurrence of BV. Torrone *et al.* determined that the prevalence of BV was 42.1%, 35.2% and 49.5% among 15-24 year olds in the Southern African, Sothern/Eastern African and Eastern African regions of continental Africa respectively.(69) BV occurs in approximately 29% of US women and approximately 50% of these cases occur among AA women.(70) Rates of BV infection are higher among women from continental Africa compared to AA women.(70) Statistically significant differences are also observed among the vaginal microbiomes of women of different ethnic backgrounds.(45) Education level is also associated with BV.(4, 9) Holzman *et al.* determined that lower education level was a significant predictor of BV.(9) Ranjit *et al.* also came to a similar conclusion in their study where data indicated that BV was most prevalent among illiterate women.(4)

Current literature suggests that menstrual cycle is associated with BV.(2, 7, 9, 11) Holzman *et al.* concluded that BV was more common during the first week of the menstrual cycle.(9) Bautista and colleagues have also reported a positive association between BV and the menstrual cycle as well as vaginal hygiene.(2) For example, the use of cloth or cotton for menstrual hygiene compared to sanitary pads was found to be a risk factor for BV.(61, 71) A history of pregnancy also increases the risk of BV.(2) Broad spectrum antibiotic use is also a risk factor for BV.(4, 71) Baeten and colleagues determined that recent antibiotic use was a risk factor for loss of *Lactobacilli* which is associated with BV.(72)

## The Vaginal Microbiota and BV

The vaginal microbiota is instrumental in female reproductive health.(45) Advancements in bioinformatics allow for the characterization of the changes in vaginal microbiota during BV through 16S RNA sequencing.(73) Current literature indicates that there is a correlation between vaginal microbiota and BV.(45, 73) A healthy vaginal microbiota typically presents

with a low pH and low levels of species diversity.(74) Community state types (CSTs) can be used to describe the variation in the vaginal microbiota by classifying them into dominant groups.(29, 74) CSTs are dominated by *Lactobacillus* such as *L. crispatus, L. iners, L. gasseri, L. jensenii* or a diverse community.(29, 74) Vitali and colleagues determined that *L. iners* was more common among women infected with BV compared to *L. crispatus* which is more common among women with a healthy vaginal microbiota.(73) They further conclude that *Atopobium, Prevotella* and *M. hominis* were more prevalent among women with BV. (73) Deng *et al.* determined that G. vaginalis was the most abundant active species in BV. (74)

The vaginal metabolome also highlights characteristics of BV; however, few studies explore this relationship.(75) Significant differences have been demonstrated between the metabolic profiles of women with and without BV.(75) In cases of BV there is a general increase in amines such as tyramine, trimethylamine and cadaverine.(73, 75) In addition to assessing the vaginal metabolome, the frequency and length of time of sampling needs to be explored. The vaginal microbiome is dynamic and findings from cross sectional versus longitudinal studies can vary. Literature suggests that there are high levels of species turnover in the vaginal microbiota.(76) Lambert and colleagues determined from their longitudinal analysis of the vaginal microbiome of women with recurrent BV, levels of *Lactobacilli* decrease long before symptomatic BV presents.(15) Ravel and colleagues determined through daily assessment of the vaginal microbiota that prior to symptomatic BV the vaginal microbiota mainly comprised of strict anaerobes like *Atopobium, Prevotella, Megasphera*, BV-associated bacterium 2 and *G. vaginalis.*

## BV and Adverse Sequalae

The epidemiological profile of BV is similar to many common bacterial STIs.(2) BV also increases the risk of acquiring many STIs such as human immunodeficiency virus (HIV),(2, 20, 21, 51, 59, 61, 68) *Neisseria gonorrhoeae* (NG),(2, 21, 51, 59, 68) CT,(2, 21, 51, 59, 68) TV and herpes simplex virus-2 (HSV-2)(21, 51, 59, 61, 68).(11, 37, 43) Wiesenfeld *et al.* determined that the likelihood of positive NG/CT increased as the abnormality of vaginal flora increased and that BV was associated with a 4 and 3.4 times increased risk of testing positive for NG and CT respectively.(77) Similarly, Baustista *et al* determined that there was a 1.5 and 2.4 times increased risk of CT and NG diagnosis respectively among women diagnosed with BV.(21, 59) Furthermore, *Lactobacillus* bacteria produce $H_2O_2$ which inhibits the growth of NG.(68) In cases of BV where Lactobacillus decrease and the levels of $H_2O_2$ also decrease, there is increased risk of NG.(68) Though research supports that BV increases the risk of STIs through biological mechanisms, BV can also be a consequence of STIs.(68)

Studies have shown mixed results about the treatment of BV to prevent acquisition of STIs. Schwebke *et al* determined that treatment of BV resulted in significantly lower number of CT cases.(23) BV has been associated with concurrent infections of NG/CT, as well as longitudinal studies have shown that BV is associated with NG/CT bidirectionally.(3, 21, 78) In addition to BV increasing the risk of HIV,(32) BV also increases HIV viral shedding.(37, 61) Among women HIV seropositive women, BV increases the risk of transmission of HIV

to male partners.(51) There is a twofold increased risk of HSV-2 among women with BV.(37) Additionally, BV increases the risk of human papillomavirus (HPV).(21, 59, 79) Brotman et al. determined that women with a *L. gasseri* dominant vaginal microbiota were more likely to clear detectable HPV from the vaginal microbiota.(79) Additionally, they concluded that BV associated vaginal microbiota, low levels of *Lactobacillus* spp or *L. iners* dominant, had the greatest relative proportion of HPV positive samples.(79) BV is also associated with adverse reproductive outcomes, such as preterm delivery, intrauterine infection and pelvic inflammatory disease.(3, 61, 67)

## Conclusions and Implications for the Future

Conflicts in the literature further highlight what little is known about the etiology and pathogenesis of BV, recurrent BV and persistent BV. Though we have presented many known risk factors of BV in this narrative review no true causative agent has been identified. Further investigation is needed to determine potential predictors that may differentiate whether or not BV is a sexually transmitted or sexually enhanced disease. Enhanced analytical techniques such as structural equation modelling or multi-state Markov models should be implemented to better understand the relationship between sexual correlates and BV.

In addition to the current literature which examines the serious associated medical comorbidities, lack of known etiology and poor long-term treatment, future research should investigate the predictors and prognostic indicators of recurrent and persistent BV, differences in the vaginal microbiota of women with recurrent and persistent BV, the effect of recurrent and persistent BV on incident NG/CT and the effect of treatment of the aforementioned factors. Emphasis should be places on the novel findings of Sobel et al with respect to prognostic indicators and further explored. There is a noted lack of standard definitions of recurrent and persistent BV. This hinders the scientific community in making definitive conclusions with respect to treatment options of these very common conditions associated with BV cases. Additionally, the current screening and treatment guidelines should be reviewed.

Furthermore, the designs of studies to investigate BV need to be addressed. Many studies measure BV at long intervals or cross sectional. More emphasis should be placed on the daily assessment of BV. Additionally, studies which examine the vaginal microbiome of women with BV should place more emphasis on metabolomic assessments in order to assess the effects of metabolites on the vaginal microbiome.

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