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Risk Factors and Emerging Therapies for Vulvovaginal Candidiasis and Bacterial Vaginosis: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 October 2026 and was last updated on 22 October 2026.

INTRODUCTION

Review question / Objective Among women of reproductive age and adults with or at risk for vulvovaginal candidiasis, recurrent vulvovaginal candidiasis, or bacterial vaginosis, how are receptive orogenital sexual activity, contraceptive type, and emerging antifungal therapies, compared with their respective comparison groups, associated with the risk of vulvovaginal candidiasis/recurrent vulvovaginal candidiasis or bacterial vaginosis and clinical treatment outcomes?

Rationale Vulvovaginal candidiasis (VVC) and bacterial vaginosis (BV) are among the most common causes of vaginitis and represent a substantial burden on women's reproductive and overall health. Recurrent VVC (RVVC) is particularly problematic because recurrence and treatment failure can significantly affect quality of life. Despite the prevalence of these conditions, important

questions remain regarding modifiable risk factors and optimal treatment strategies.

This study was undertaken to synthesize available evidence regarding selected risk factors for VVC, RVVC, and BV, as well as emerging treatment options for VVC. Specifically, the study evaluates the association between receptive orogenital sexual activity and VVC/RVVC, the relationship between contraceptive type and BV risk, and the efficacy of the newer antifungal agents oteseconazole and ibrexafungerp compared with fluconazole.

A systematic review and meta-analysis provides an opportunity to quantitatively synthesize findings across individual studies and assess the consistency and magnitude of these associations. The findings may help clarify potentially modifiable behavioral and contraceptive-related risk factors and provide comparative evidence regarding newer therapeutic options for VVC. This information may ultimately support more informed prevention, counseling, and treatment approaches for patients with VVC, RVVC, and BV.

Condition being studied The conditions being studied are vulvovaginal candidiasis and bacterial vaginosis which are two of the most common causes of vaginitis.

METHODS

Participant or population Women ages 15-65.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Study designs to be included are as follows: case-control studies, cross-sectional studies, prospective cohort studies, observational studies, randomized control trials, clinical trials.

Eligibility criteria Studies were eligible if they met the predefined inclusion criteria for at least one of the three analyses. For the vulvovaginal candidiasis (VVC) risk-factor analysis, peer-reviewed observational studies published between 2000 and 2024, including case-control, cross-sectional, prospective cohort, and other observational studies using self-reported survey data, were included. Studies investigated receptive orogenital sexual activity as a risk factor for VVC or recurrent VVC (RVVC) among women aged 15–49 years. Studies involving pregnant women, women with HIV or diabetes, and women engaged in sex work were excluded.

For the bacterial vaginosis (BV) analysis, English-language studies published between 2004 and 2024 were eligible, including clinical trials, cross-sectional studies, case-control studies, and prospective or retrospective cohort studies. Eligible studies investigated injectable hormonal contraception, specifically depot medroxyprogesterone acetate (DMPA), or non-hormonal contraceptive methods in relation to BV occurrence. Studies were required to provide baseline BV measurements, assess BV occurrence, specify the contraceptive method, and establish BV status using Nugent scoring, Amsel criteria, or Ison-Hay criteria. Studies were excluded if they assessed BV recurrence, lacked a clear BV diagnosis or baseline measurements, did not specify the contraceptive method, lacked relevant outcome data, were non-peer-reviewed or non-human studies, or evaluated non-contraceptive devices or contraceptive methods outside the specified scope.

For the VVC treatment analysis, peer-reviewed clinical trials or randomized controlled trials

published between 2014 and 2024 were eligible if they compared oteseconazole or ibrexafungerp with fluconazole for VVC treatment. Studies involving other publication types or treatment comparisons that were not comparable with the selected interventions and outcomes were excluded.

Information sources Information sources used were electronic databases such as PubMed, Embase, Medline (Ovid), Web of Science, Ebsco, and CINAHL.

Main outcome(s) Among participants who engaged in receptive orogenital sexual activity, there was approximately a two-fold increased likelihood for the development of vulvovaginal candidiasis (VVC) or a recurring vulvovaginal candida infection (RVVC) when compared to those who did not. Meta analysis revealed an OR of 2.0415 (95% CI [1.539;2.7076], $p < 0.0001$). No statistically significant association between injectable hormonal contraceptives and risk of bacterial vaginosis (BV) infection was found when compared to non-hormonal contraceptive options. Meta-analysis revealed an OR of 1.0663 (95%CI [0.6087-1.8680], $p = 0.8224$). Two novel drugs, oteseconazole and ibrexafungerp, demonstrated a statistically significant reduction in risk of clinical failure as compared to the standard treatment for VVC, fluconazole. Analysis of oteseconazole revealed an OR of 0.0755 (95% CI [0.0512; 0.1113], $p < 0.0001$) while analysis of ibrexafungerp revealed an OR of 0.4629 (95% CI [0.3476; 0.6163], $p < 0.0001$). Meta-regression analysis was used to compare risk of clinical failure between oteseconazole and ibrexafungerp. A Q test was performed to evaluate subgroup differences. The meta-regression showed a significant difference between the two drugs with $p < 0.0001$ indicating that oteseconazole may have a significantly lower risk of clinical failure than ibrexafungerp. Additionally, oteseconazole showed a smaller odds ratio than ibrexafungerp revealing a significantly lower risk of clinical failure than ibrexafungerp.

Quality assessment / Risk of bias analysis The certainty of evidence was assessed for the primary outcomes using an established evidence-grading framework, where appropriate. For human clinical evidence, the GRADE approach was utilized to evaluate certainty based on factors including risk of bias, inconsistency, indirectness, imprecision, and publication/reporting bias.

Strategy of data synthesis The strategy of data synthesis was assessed for the primary outcomes using an established evidence-grading framework,

where appropriate. All studies followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). All statistical analyses were performed using “RStudio version 4.2”. A fixed and random effects model was used to conduct all meta-analyses.

Subgroup analysis Subgroup analyses were conducted according to the clinical outcomes and exposures investigated. For receptive orogenital sexual activity, separate analyses evaluated its association with vulvovaginal candidiasis (VVC) and recurrent vulvovaginal candidiasis (RVVC), along with a combined analysis of VVC and RVVC. For bacterial vaginosis (BV), analyses separately evaluated depot medroxyprogesterone acetate (DMPA), an injectable hormonal contraceptive, and non-hormonal contraceptive use in relation to BV risk. For VVC treatment efficacy, separate meta-analyses compared oteseconazole and ibrexafungerp with fluconazole, followed by a meta-regression comparing the two antifungal agents. A Q test was used to evaluate differences between treatment subgroups. Random-effects models were used for the primary meta-analyses, with fixed-effect models used for sensitivity analyses.

Sensitivity analysis Sensitivity analyses were performed using fixed-effect models to assess the robustness of the primary meta-analysis findings obtained using random-effects models. This approach was applied to all three analyses: receptive orogenital sexual activity as a risk factor for vulvovaginal candidiasis (VVC) and recurrent VVC (RVVC), hormonal and non-hormonal contraceptive use in relation to bacterial vaginosis (BV), and the efficacy of oteseconazole and ibrexafungerp compared with fluconazole for VVC. The sensitivity analyses were intended to assess whether the findings were consistent across alternative statistical models.

Country(ies) involved United States of America.

Keywords vulvovaginal candidiasis; recurrent vulvovaginal candidiasis; bacterial vaginosis; orogenital sexual infections; antifungal resistant candida; contraceptive methods.

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