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Bacterial Vaginosis and Its Association With Incident *Trichomonas vaginalis* Infections: A Systematic Review and Meta-Analysis

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Background: Bacterial vaginosis (BV) has been associated with an increased risk for acquisition of human immunodeficiency virus and sexually transmitted infections. We evaluated the association between BV and incident *Trichomonas vaginalis* (TV) infection in women.

Methods: MEDLINE and ClinicalTrials.gov were searched for articles published between January 1, 1980, and May 7, 2021. Observational studies in women that evaluated the relationship between having/not having BV and the risk for acquiring TV were included.

Results: Fourteen studies were included in the systematic review; 12 studies were included in meta-analyses involving 18,424 participants. Most studies used Nugent scoring to diagnose BV. For TV diagnosis, 12 studies used wet mount microscopy or culture, and 2 used nucleic acid amplification tests. There was diversity in the measures of association used, so an overall effect size could not be calculated. The majority of studies reported odds ratios, which showed an increased risk of incident TV among women with BV versus without BV (adjusted odds ratio, 1.87; 95% confidence interval, 1.45–2.40; $P = 0.007$). However, there were heterogeneity and potential confounding factors (eg, age, sexual partners) reported among studies.

Conclusions: This systematic review and meta-analysis provide evidence for a nearly 2-fold higher risk for acquiring TV among women with BV compared with women without BV.

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Bacterial vaginosis (BV) is the most prevalent type of vaginal infection, affecting 23% to 29% of women globally[1,2] and 27% to 29% of women in the United States.[2,3] Bacterial vaginosis represents a disruption of the vaginal microbiota, characterized by a decrease in lactobacilli and an increase in facultative and strict anaerobic bacteria. Although the majority of patients with BV can be treated effectively with antibiotics,[4] 1-year recurrence rates can be as high as 58%.[5] Systematic reviews and meta-analyses show that women with BV are at increased risk for developing sexually transmitted infections (STIs), including *Chlamydia trachomatis*,[6] human papillomavirus,[7] and human immunodeficiency virus (HIV).[8–11]

There are no published systematic reviews on the association between BV and the risk for incident *Trichomonas vaginalis* (TV) infection in women. TV is the most prevalent, nonviral STI in the US, affecting an estimated 3.7 million individuals.[12,13] Women with TV have a 2- to 3-fold increased risk for other STIs and HIV.[14–16] Trichomoniasis may be associated with vaginitis and cervicitis in women, and nongonococcal urethritis and prostatitis in men.[17,18] TV has been associated with increased risk of adverse birth outcomes,[19] infertility,[20,21] and cervical cancer.[22]

We conducted the first systematic review and meta-analysis of the relationship between BV and the risk for incident TV infection in women. Coinfection rates with BV and TV among women ranges from 60% to 80%,[23] so this review was focused on observational studies in which new TV infections were identified.

MATERIALS AND METHODS

Sources

This systematic review was conducted according to the Meta-analyses of Observational Studies in Epidemiology statement[24] and following a guide for the systematic review and meta-analysis of prognostic factor studies.[25] Because this was a systematic review and meta-analysis, institutional review board approval was not required. We conducted a systematic search of MEDLINE (through PubMed) for English-language studies with publication dates ranging from

January 1, 1980, to May 7, 2021. This start date was selected primarily because Amsel criteria were published in 1983. Before then, there were no standardized approaches to diagnosis for BV, which was often referred to as nonspecific vaginitis. The search strategy is provided in Supplemental Digital Content 1 (http://links.lww.com/OLQ/A737). We also conducted a search of ClinicalTrials.gov, with no date restrictions. The search strategy for this database is provided in Supplemental Digital Content 2 (http://links.lww.com/OLQ/A737). The systematic search was supplemented by manually screening reference lists of the retrieved articles.

Study Selection

Published studies evaluating the association between the presence of BV and the risk for acquiring TV were included if they met all of these inclusion criteria: (1) study design was observational, (2) participants were women of any age, (3) exposure was the presence of BV, and (4) the outcome was incident TV. Eligible studies must have the following: (1) assessed BV and the absence of TV at the same time point; (2) assessed incident TV at a subsequent time point; and (3) estimated the odds ratio (OR), hazard ratio (HR), or relative risk (RR) for incident TV among women who did or did not have BV at the same time point. For the meta-analysis, a diagnosis of BV was defined by Amsel criteria (presence of 3 or more of the following: vaginal pH >4.5, clue cells on wet mount microscopy, positive whiff test, abnormal homogenous vaginal discharge)[26] or a Nugent score of 7 to 10.[27] Incident TV was defined as a positive result using wet mount microscopy, culture, or nucleic acid amplification testing [NAAT]).

Studies were excluded if they were: (1) cross-sectional; (2) had insufficient data to calculate the OR, HR, and/or RR for incident TV; (3) evaluated BV and TV association only at the same visit; and (4) were ineligible publication types, including non-English language articles, editorials, letters, and commentary; clinical practice guidelines and consensus statements; other narrative or systematic reviews; preclinical studies; and congress abstracts/proceedings.

The literature search was conducted by 1 author (L.A.G.), and results were screened independently by 2 reviewers (L.A.G., E.S.). All titles and available abstracts were reviewed to identify and exclude ineligible articles. For articles that could not be excluded with confidence based on the title and abstract review, full-text publications were reviewed to cull the remaining search results. Inconsistencies in the screening results were resolved through reviewer discussion and/or consensus with other authors.

Relevant data were extracted by 1 author (A.J.P.), including information regarding the data source (study design, locations, number of sites, settings and study dates, number of study visits, observation period, and follow-up duration), participants (recruitment method, eligibility criteria, total number evaluated, age, race/ethnicity, comorbid conditions, contraceptive use, number of sexual partners), BV status at baseline and method used to diagnose BV (Amsel criteria, Nugent score 7–10 by Gram stain), method to diagnose TV (wet mount microscopy, culture, NAAT), and potential confounders in the association (Supplemental Digital Content 3, http://links.lww.com/OLQ/A738).

Because the majority of eligible articles were secondary analyses of large, observational studies, we extracted relevant results and as much of the study design and methods information from the included article. When information was missing or incomplete, we referred to the primary publication(s). If relevant data were not reported in an article or its supplementary material, we contacted the corresponding author to obtain the results for inclusion in the meta-analyses.

All included studies were evaluated for risk of bias using the quality in prognostic factor studies (QUIPS) tool. Quality in prognostic factor studies tool evaluates studies based on 6 domains, and the risk of bias is rated as "high," "moderate," or "low."[25] Quality assessment was independently performed by 1 author (A.J.P.).

Statistical Analysis

Statistical analyses were performed using Stata 16 (StataCorp LLC, College Station, TX) and Excel (Microsoft, 2016). Meta-analysis was performed on log-effect sizes stratified by type of measure (HR, OR, RR) as random-effects models, using τ^2 to estimate the between-study variability with weights inversely related to the total variance. Reported unadjusted and adjusted ratio effect sizes and 95% confidence intervals (CIs) were transformed using the natural logarithm function. The standard error (SE) was estimated as the difference between the low (mean − 1.96 SE) and high (mean + 1.96 SE) log-effect size 95% CI divided by 3.92 (ie, [mean + 1.96] − [mean − 1.96] / 3.92). The stratified meta-analyses of the log effect sizes were performed using Stata's "meta" command; results were converted back to their original ratio metric using the "eform" subcommand. Heterogeneity was assessed based on I^2 and τ^2 statistics. Although I^2 measures the proportion of the variance because of the variation in real effects rather than sampling error (the lower the proportion, the better), τ^2 is an absolute value and measures how the effects are distributed (τ is reported in the same unit as the effect size and is analogous with a standard deviation).

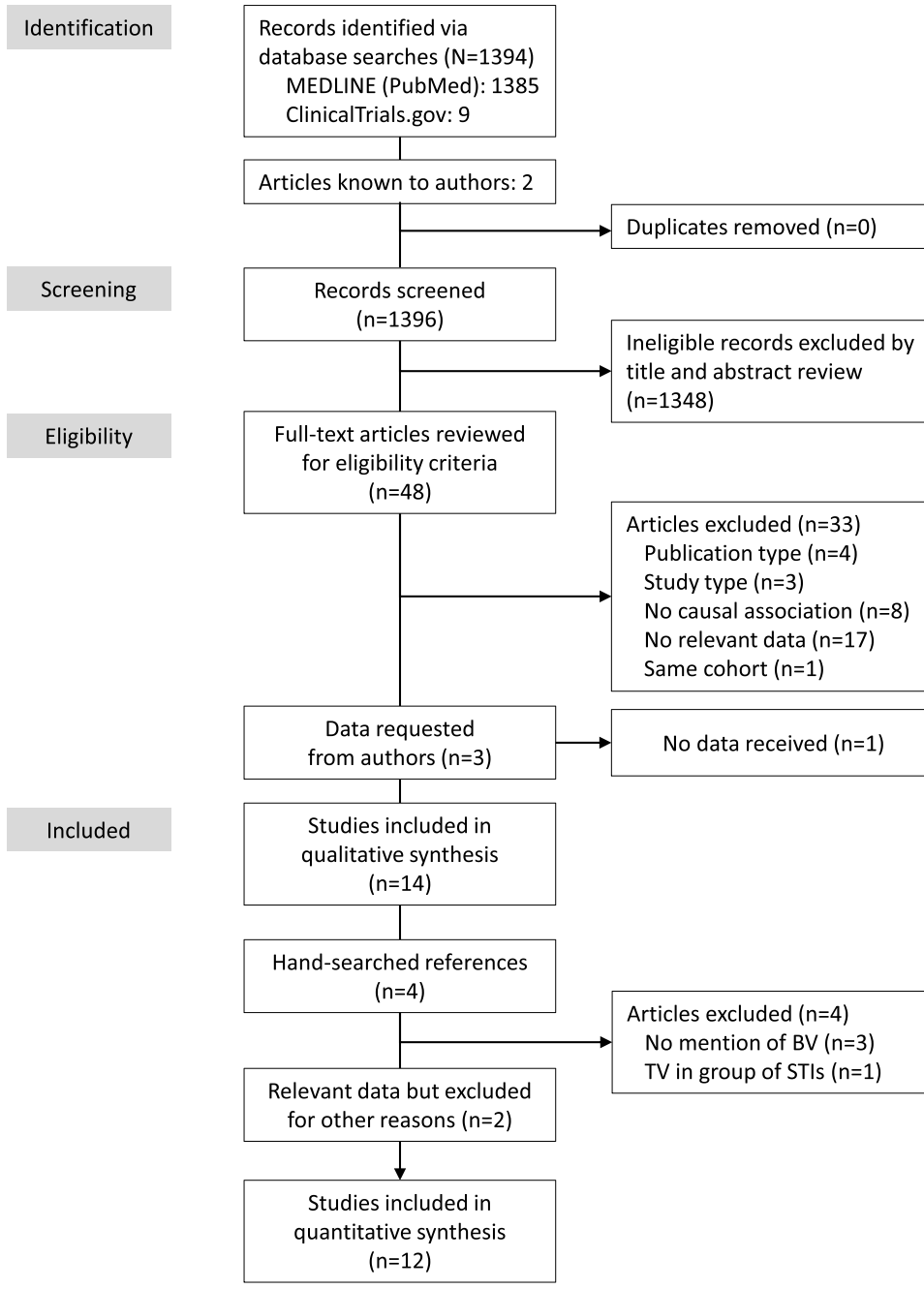
To determine whether there were significant between-study differences based on geography, we performed a post hoc subgroup meta-analysis comparing the results from studies conducted exclusively in Africa[28–32] versus those conducted exclusively in the US.[33–36] We used the "meta forestplot subgroup" command for unadjusted and adjusted effect sizes.

RESULTS

Description of Studies

A total of 1396 articles were screened; 1348 were excluded after title and abstract review. For 48 articles, the full text was reviewed, and 33 were excluded because they did not contain relevant data (n = 17), did not evaluate associations between BV and TV (n = 8), met exclusion criteria for study and publication type (n = 4), and represented older data from an included study (n = 1) (Fig. 1). We contacted the corresponding authors of 3 articles to obtain relevant data[37–39]; we received the requested data from 2 authors.[38,39] Thus, 14 studies (consisting of 19,547 participants; range, 68–3620) were included in the systematic review (Table 1),[28–36,38–42] and 12 studies (18,424 participants) were included in the meta-analyses (Fig. 1).[28–36,39,40] Two of the studies included in the systematic review were not included in the meta-analyses.[41,42] Martin et al[42] used a Nugent score of 7 to 10 to define the presence of BV; however, the results for the association between BV and incident TV was reported for "abnormal vaginal flora," which was defined as a Nugent score of 4 or greater. Kaul et al[41] was excluded because the investigators' definition of risk exposure ("ever" having BV at enrollment or during clinical follow-up, or as "never" having had BV) was different from those defined in other included studies.

All studies were conducted between 1990 and 2014. Among the 14 studies included in the systematic review, 8 were secondary analyses of data collected during prospective cohort studies.[28,30,34–36,38–40] Two were secondary analyses of case-control studies,[31,33] and 1 was a secondary analysis of data collected during a randomized controlled trial.[41] The remaining 3 were prospective cohort studies.[29,32,42] Eight studies were conducted exclusively in African countries,[28–32,38,41,42] 4 were conducted exclusively in the United States,[33–36] 1 included sites in Africa and the United States,[40]



BV, bacterial vaginosis; MOOSE, Meta-analyses of Observational Studies in Epidemiology; STI, sexually transmitted infection; TV, *Trichomonas vaginalis*.

Figure 1. MOOSE flowchart. MOOSE, Meta-analyses of Observational Studies in Epidemiology.

and 1 was conducted in India.[39] When reported, participant age criteria ranged from 11 to 18 years[33] to 15 to 55 years.[28–31,34,36,38–40] Follow-up durations ranged from 21 days[42] to 7 years.[36] To diagnose BV, 12 studies used Nugent scores of 7–10[29–33,35,36,38–42]; 2 studies used Amsel criteria.[28,34] To diagnose TV, 7 studies used wet mount microscopy,[29,32,33,36,38,40,42] 3 used wet mount microscopy or TV cultures,[34,35,39] and 2 used TV cultures only.[30,41] Two of the more recent studies used a NAAT (polymerase chain reaction testing, transcription-mediated amplification) for TV detection.[28,31] No study included in the systematic review or meta-analysis used Pap smear to diagnose TV. Of the 12 studies included in the meta-analysis, 7 did not report whether baseline BV was treated. Among the 5 remaining studies, treatment was reported for symptomatic BV (n = 2) or any BV detected (n = 3).

Risk of Bias and Heterogeneity

Using the QUIPS tool, 1 author (A.J.P.) rated the risk for bias across 6 domains for each study (Table 2). All but 1 article, which was rated as having a High risk for bias,[33] adequately reported the study's recruitment methods, dates and settings, and patient

TABLE 1. Characteristics of Included Studies in the Systematic Review and Meta-Analysis

Reference	Study Design (Dates)	Location(s)	Follow-Up Period	n	Key Inclusion Criteria	Age, y Mean (SD)/Median (Range)	BV+ at Baseline	BV Diagnosis Method	TV Diagnosis Method
Abbai et al[28]	Cohort, retrospective (2003–2005)	Durban, South Africa	24 mo	435	18–49 y, CT−, HIV−, NG−, abnormal physical examination	25 (21–35)	31.0%	Amsel criteria	Urine PCR (NAAT)
Balkus et al[29]	Cohort, prospective (1993–2005)	Mombasa, Kenya	Unclear	570	≥16 y, sex workers	35 (5)	44.4%	Nugent score 7–10	Wet mount microscopy
Balkus et al[40]	Cohort, retrospective (2005–2008)	Malawi; South Africa; USA; Zambia; Zimbabwe	12–30 mo	2920	≥18 y, HIV−, not pregnant, sexually active	91.6% ≤34 y	37.1%	Nugent score 7–10	Wet mount microscopy
Brahmbhatt et al[30]	Cohort, retrospective (2011–2012)	Rakai, Uganda	12 mo	2374	15–49 y, TV−, sexually active	86.6% <40 y	39.7%	Nugent score 7–10	TV culture
Brotman et al[33]	Case-control, retrospective (1990–2002)	Baltimore, MD	Unclear	762	11–18 y, ≥3 visits to STD clinic	15.6 (14.4–16.8)	26.0%	Nugent score 7–10	Wet mount microscopy
Brotman et al[34]	Cohort, retrospective (1999–2002)	Birmingham, AL	1 y	3620	15–44 y, not pregnant	24.5 (17.4–31.5)	39.6%	Amsel's criteria	Wet mount microscopy or TV culture
Fichorova et al[38]	Cohort, retrospective (1999–2004)	Uganda; Zimbabwe	2 y	934	18–25 y, HIV−, not pregnant, sexually active	NR	NR	Nugent score 7–10	Wet mount microscopy
Jarrett et al[31]	Case-control, retrospective (2012–2014)	Mombasa, Kenya	Unclear	68	Not pregnant, HIV−	36.2 (9.2)	25.0%	Nugent score 7–10	TMA (NAAT)
Kapiga et al[32]	Cohort, prospective (2003–2004)	Durban, South Africa; Moshi, Tanzania; Lusaka, Zambia	1 y	958	NR	28.6 (16–62)	NR	Nugent score (no scale)	Wet mount microscopy
Kaul et al[41]	RCT, retrospective (1998–2002)	Nairobi, Kenya	≤4.4 y	466	Sex workers, HIV−	28.6 (18–52)	50.6%	Nugent score 7–10	TV culture
Kenyon et al[35]	Retrospective (1999–2003)	Birmingham, AL	1 y	3620	Healthy, not pregnant	25.3 (7.0)	NR	Nugent score 7–10	Wet mount microscopy or TV culture
Martin et al[42]	Cohort, prospective (1993–1997)	Mombasa, Kenya	21–1603 d	657	Sex workers, HIV−	NR	40.0%	Nugent score 7–10	Wet mount microscopy
Nijhawan et al[36]	Cohort, retrospective (1993–1995)	Bronx, NY; Detroit, MI; Providence, RI; Baltimore, MD	≤7 y	1310	16–55 y, high-risk sex behaviors	16–55	50.0%	Nugent score 7–10	Wet mount microscopy
Rathod et al[39]	Cohort, retrospective (2005–2006)	Mysore, India	6 mo	853	15–30 y, not pregnant, sexually active	15–30	15.3%	Nugent score 7–10	Wet mount microscopy or TV culture

CT, *C. trachomatis*; NG, *Neisseria gonorrhea*; NR, not reported; PCR, polymerase chain reaction; SD, standard deviation; TMA, transcription-mediated amplification.

TABLE 2. QUIPS Tool, Subjective Grading for Bias (High*, Moderate†, Low‡)

Reference	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Adjustment for Other Prognostic Factors	Statistical Analysis and Reporting
Abbai et al[28]	Moderate	Moderate	Low	Low	Moderate	Low
Balkus et al[29]	Moderate	High	Low	Low	High	Low
Balkus et al[40]	Low	Low	Low	Low	Moderate	Low
Brahmbhatt et al[30]	Low	Moderate	Low	Low	Moderate	Moderate
Brotman et al[33]	High	Moderate	Low	Low	Moderate	High
Brotman et al[34]	Low	Moderate	Low	Moderate	Moderate	Low
Fichorova et al[38]	Low	Moderate	Low	Low	Moderate	Moderate
Jarrett et al[31]	Moderate	Moderate	Low	Low	High	Moderate
Kapiga et al[32]	Moderate	Moderate	Low	Low	Moderate	Low
Kaul et al[41]	Low	Low	Low	Low	Moderate to High	Low
Kenyon et al[35]	Low	Moderate	Low	Moderate	Low	Low
Martin et al[42]	Moderate	Moderate	Moderate	Moderate	Low	Low
Nijhawan et al[36]	Low	Moderate	Low	Moderate	Moderate	Low
Rathod et al[39]	Moderate	Moderate	Low	Low	High	Moderate

*"High" risk: the relationship between the prognostic factor and the outcome is *very likely* to be different for the domain of interest.
†"Moderate" risk: the relationship between the prognostic factor and the outcome *may* be different for the domain of interest.
‡"Low" risk: the relationship between the prognostic factor and the outcome is *very unlikely* to be different for the domain of interest.

population by clearly describing the eligibility criteria. Most studies had adequate participation (>70% in most) and adequately described patients' baseline characteristics. Most studies (11 of 14) were rated as moderate for study attrition,[28,30–36,38,39,42] as loss-to-follow-up rates were relatively low, and the reasons for loss to follow-up were described. With 1 exception (Martin et al[42]), all studies were rated as low risk for bias for the prognostic factor measurement (BV). Most studies were rated as having a low risk for bias for the outcome measurement (incident TV).[28–33,38–41] Most studies were retrospective analyses and did not adequately control for all potential confounders (age, education, birth control, HIV status, STI coinfections, number of sexual partners, and unprotected sex/condom use). These were rated as having a Moderate or High risk of bias for confounding.[28–34,36,38–41] Overall, the statistical models were adequate, and selective reporting was not observed by the rater. However, several studies did not account for multiple comparisons or had other issues that, in the rater's opinion, reduced the strength of the analysis. These were rated as having a Moderate or High risk of bias.[30,31,38,39]

Meta-Analyses

Eleven studies contributed unadjusted effect size measures[28–35,38–40] and 10 contributed adjusted effect sizes.[28–30,32–36,39,40] Nine studies contributed both unadjusted and adjusted values.[28–30,32–35,39,40] Odds ratios were the most commonly reported effect size (6 unadjusted[29,32,33,35,38,39] and adjusted[29,32,33,35,36,39]), followed by HRs (3 unadjusted[28,34,40] and adjusted[28,34,40]). The overall unadjusted HR was 2.45 (95% CI, 1.89–3.19) (Fig. 2), and the overall unadjusted OR was 2.27 (95% CI, 1.74–2.96) (Fig. 3). As expected, the adjusted effect sizes, regardless of the original metric, reflected a reduced magnitude of effect. The overall adjusted HR was 2.08 (95% CI, 1.69–2.56) (Fig. 2), and the overall adjusted OR was 1.87 (95% CI, 1.45–2.40) (Fig. 3). The remaining 2 studies reported either an incidence rate ratio (unadjusted and adjusted)[30] or a risk ratio (unadjusted).[31] All stratified summary estimates (with >1 effect size) were statistically significant (unadjusted and adjusted). Heterogeneity I^2 statistics were 56.7% for unadjusted HRs and 70.8% for unadjusted ORs; corresponding values were 31.1% for adjusted HRs and 67.7% for adjusted ORs. Approximately 30% versus 70% of the variance would remain if sampling error was removed among HR versus OR effect sizes. The HR τ^2 values were 0.03 unadjusted and 0.01 adjusted. The OR τ^2 values were 0.07 unadjusted and 0.06 adjusted. Both measures of heterogeneity reflect the importance of using adjusted effect sizes controlling for other outcome-related factors.[43]

For the subgroup meta-analysis of studies by region, the overall unadjusted effect size calculated for 5 African studies[28–32] was 1.71 (95% CI, 1.22–2.39); the corresponding unadjusted effect size calculated for 3 US-based studies[33–35] was 2.37 (95% CI, 1.71–3.27) (Figure, Supplemental Digital Content 4, http://links.lww.com/OLQ/A739). The overall adjusted effect size calculated for 4 African studies[28–30,32] was 1.67 (95% CI, 1.25–2.23); the corresponding adjusted effects size calculated for 4 US-based studies[33–36] was 1.64 (95% CI, 1.36–1.99) (Figure, Supplemental Digital Content 5, http://links.lww.com/OLQ/A739). Tests of subgroup (region) differences were not statistically significant for the unadjusted ($P = 0.17$) or adjusted effect sizes ($P = 0.94$).

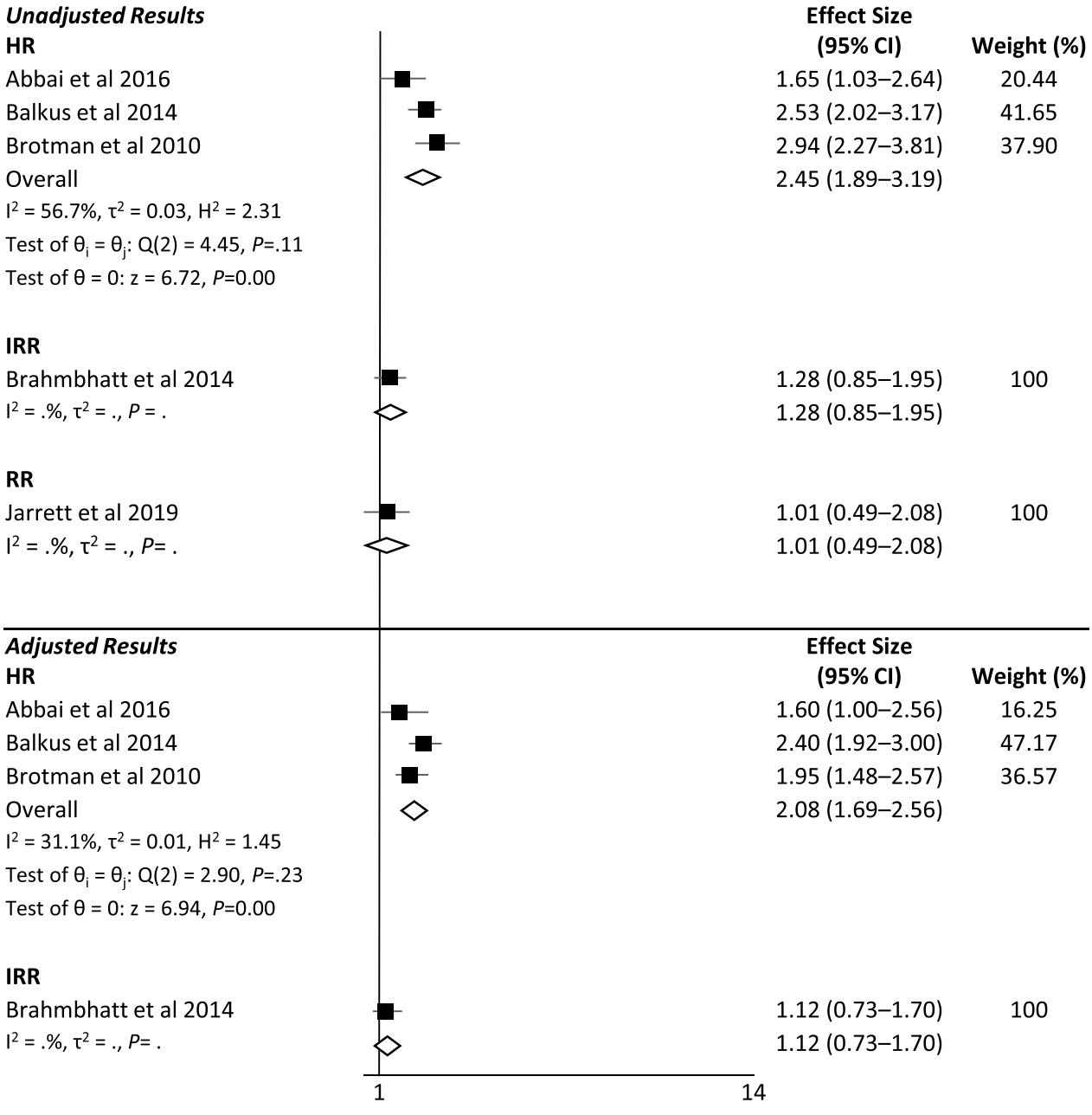
Adjusted Covariates

Data extraction included notations for potential confounding factors adjusted for in each study's multiple regression analyses (Table 3). Eight studies adjusted for at least 7 potential confounders.[28–33,39,42] Age, education, birth control, HIV status, STI coinfections, number of sexual partners, and unprotected sex/condom use were the most commonly identified confounders. No study included in the meta-analysis adjusted for male partners' circumcision status, although 6 studies were conducted in Africa.[28–32,38] Only 1 study not included in the meta-analysis adjusted for female circumcision.[42]

DISCUSSION

This systematic literature review and meta-analysis synthesized evidence from observational studies regarding the relationship between BV and the risk for incident TV infection. Our meta-analyses found a moderate relationship between BV and incident TV, with overall adjusted ORs and HRs of 1.87 and 2.08. There was diversity in the measures of association used, so an overall effect size was not calculated. However, these results suggest that women with BV are twice as likely to acquire TV compared with women without BV.

Research evaluating the relationship between BV and the development of HIV or other STIs report similar findings. Meta-analyses of 4 to 23 studies (~7000–31,000 patients) reported a 41% to 60% increase in risk for HIV among women with BV versus

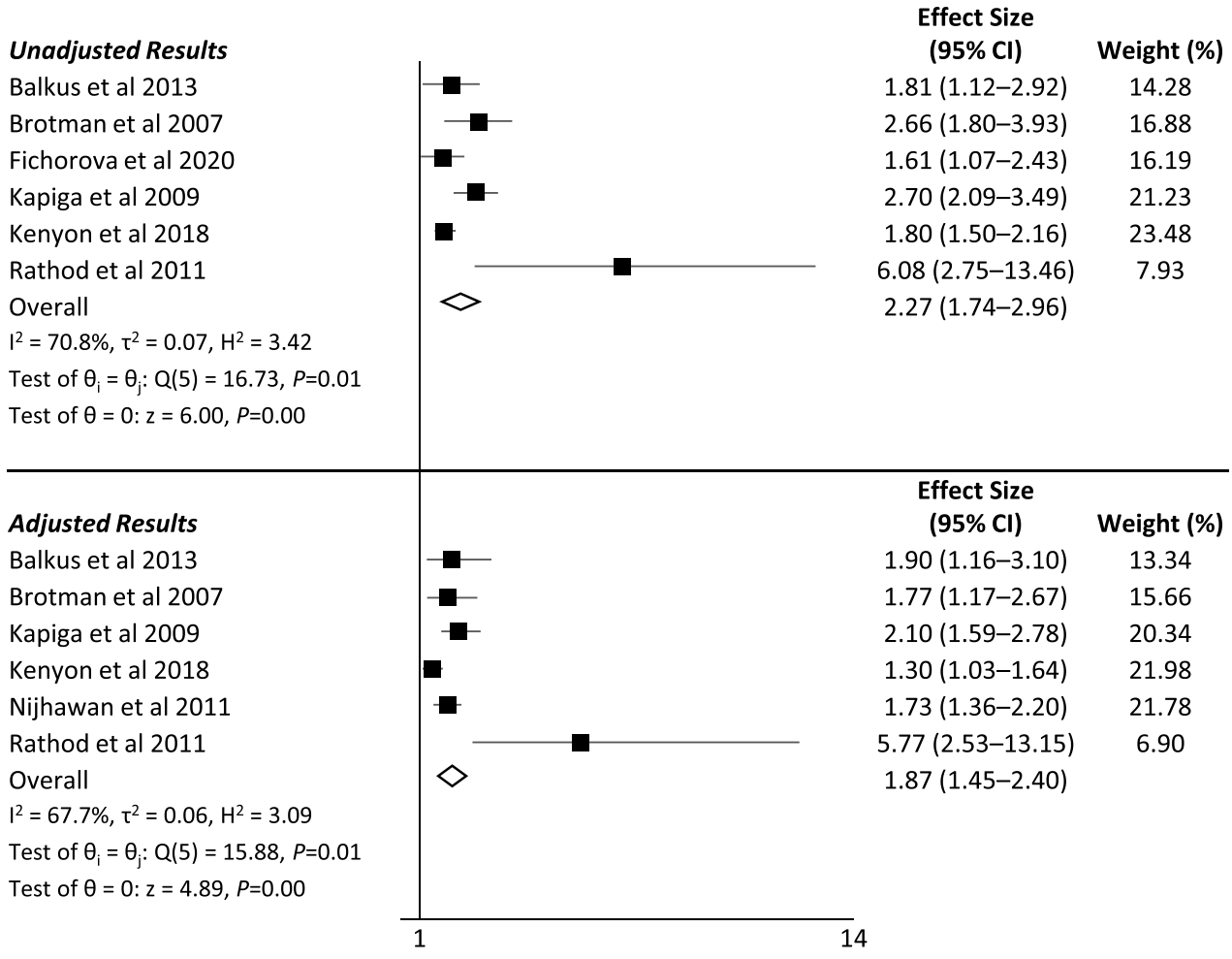


CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio; RR, relative risk.

Figure 2. Forest plot for unadjusted and adjusted HRs, IRR, and RR.

without BV (risk measures ranged from 1.41 [95% CI, 0.96–2.06] to 1.60 [95% CI, 1.20–2.10]).[8–10,44] A meta-analysis of 3 studies reported a 70% higher risk for *C. trachomatis* among women with BV versus without BV (effect size, 1.69; 95% CI, 1.33–2.04).[6] Finally, a meta-analysis of 4 studies reported a 33% increase in human papillomavirus risk among women with versus without BV (RR, 1.33; 95% CI, 1.18–1.50).[7] Clinical studies have shown that the absence of lactobacilli and the presence of diverse facultative and strict anaerobic bacterial species in BV are associated with increased risk of STIs.[45–48] *Lactobacillus* species produce substances with antimicrobial properties (hydrogen peroxide, lactic acid, bacteriocin-like substances) that may play a key role in inhibiting the growth of cervicovaginal pathogens.[49,50] Bacteria frequently associated with BV produce sialidases and mucinases, damage genital epithelia, and disrupt innate immunity, compromising these physical and immune barriers to infection.[51,52]

The 12 studies included in the meta-analysis were of sufficient quality to provide a measure of risk for statistical analysis. The meta-analyses were stratified by type of measure and whether they were reported as unadjusted or adjusted values. The current recommendation is not to combine different measures of effect size in prognostic factor meta-analyses.[25] However, our summary



CI, confidence interval; OR, odds ratio.

Figure 3. Forest plot for unadjusted and adjusted ORs.

effect sizes were comparable between HR and OR, suggesting that if they were pooled to increase the number of effect sizes, at least as a hypothesis-generating exercise, it would be possible to use additional stratified analyses or meta-regression to explore study-level factors that might further explain heterogeneity.[25]

All studies included in our meta-analysis were rated as low risk for bias in the QUIPS prognostic factor measurement domain (for BV). This was not surprising, as most of the studies used a Nugent score of 7 to 10, the criterion standard to diagnose BV. Most studies included in the meta-analysis were rated as low risk for bias in the outcome measurement domain (for TV). Most studies used wet mount microscopy and/or TV culture to diagnose TV, likely due to older study enrollment dates and/or available resources in the clinical setting. Wet-mount microscopy has the poorest sensitivity (51–65%),[53,54] followed by culture (81–94%) for detection of TV.[55,56] Only 2 studies used TV NAATs with high sensitivity (95.3–100%) and specificity (95.2–100%).[57,58] Most studies were rated as moderate risk for study attrition and for adjustment for other prognostic factors.

The majority of studies were conducted in Africa, limiting the generalizability of the results. Sub-Saharan Africa has higher BV prevalence compared with North America and Asia.[1] However, even within the United States, there can be large differences in BV prevalence related to race, number of sexual partners, having a female partner, socioeconomic status, and personal hygiene practices.[3] For TV, another study reported the annual incidence as 119.4 of 1000 women in sub-Saharan Africa compared with 52.4/1000 women in North America (1990–2006).[59] Despite these geographical differences in prevalence rates of BV and TV worldwide, the subgroup meta-analysis of the African and US-based studies did not reveal statistically significant differences in risk.

Risk factors for BV were regarded as potential confounding variables in our meta-analyses. Confounding due to unprotected sex is probably the most important limitation. Although many of the studies included adjustment for unprotected sex, data for these variables are subject to recall and social desirability biases. Incomplete adjustment for differences in unprotected sex tends to increase observed associations between BV and TV acquisition. Of the 12 studies included in the meta-analysis, 7 explicitly adjusted for the number of sexual partners,[28–32,34,40] which is an important risk factor associated with increased risk for both infections.[60,61] No study adjusted for whether partners were circumcised.

An important limitation is our inability to determine the exact timing of exposure to TV or women's BV status at the time of exposure, which was not uniformly reported across studies. This was true for visits that preceded TV infection and for those when

TABLE 3. Summary of Potential Confounders*

Reference	Age	Marital Status	Education	SES	Birth Control	HIV Status	STI, Comorbid	STI, History	No. Sexual Partners	Sexual Activity	Unprotected Sex/Condom Use	Other
Abbai et al[28]	✓	✓			✓			✓	✓	✓	✓	Age of first sex, sex workers
Balkus et al[29]	✓		✓		✓	✓		✓	✓	✓	✓	Sex workers, years of sex work, vaginal washing
Balkus et al[40]	✓	✓	✓		✓				✓		✓	
Brahmbhatt et al[30]	✓		✓	✓	✓	✓	✓		✓		✓	Religion
Brotman et al[33]	✓					✓	✓	✓			✓	Pregnancy, drug use, follow-up visits
Brotman et al[34]	✓		✓	✓					✓		✓	Ethnicity
Fichorova et al[38]	✓				✓				✓		✓	Pregnancy, breast-feeding status, vaginal hygiene practices
Jarrett et al[31]	✓		✓		✓		✓		✓	✓	✓	Menstrual status, amenorrhea,
Kapiga et al[32]	✓	✓	✓		✓	✓	✓		✓		✓	Anal sex in last 3 months
Kenyon et al[35]	✓		✓				✓		✓		✓	High-risk sex behavior, STI treatment
Nijhawan et al[36]	✓	✓	✓	✓		✓			✓		✓	Study site, number of visits, enrollment risk group
Rathod et al[39]	✓		✓	✓						✓		Age of first sex, years with partner, religion, HSV-2+

*A ✓ denotes that the potential confounder listed, as well as those specified in the other column, were adjusted for in the multivariate regression for each study.

HSV-2, herpes simplex virus 2; SES, socioeconomic status.

TV was not detected (nondifferential misclassification). This type of misclassification of exposure status tends to bias results toward finding no association. Treatment of BV was reported in 5 studies, which could have reduced the association with TV since most antimicrobial agents for BV are also active against trichomoniasis. There was substantial heterogeneity across studies (I^2 = 31–71%), which may reflect different effects in different populations and limit the meaning of quoting 1 summary effect. However, the direction of the effect was consistent across studies in that the presence of BV was always associated with an increased risk for TV (not a decrease). Lastly, non-English language articles were not included in the search, which may affect the generalizability of the findings.

Our review supports BV as a significant risk factor for TV and highlights the importance of BV diagnosis and treatment to reduce the likelihood of acquiring STIs. National guidelines recommend routine evaluation and diagnostic testing for BV among symptomatic women seeking care for vaginal discharge.[22] Antimicrobial therapy is recommended for women with symptomatic BV to relieve symptoms and reduce the risk of transmission and acquisition of TV and other STIs,[22,62] with the primary BV treatment regimen of oral metronidazole 500 mg BID for 7 days. Alternative oral therapies for BV include single-dose secnidazole,[62] tinidazole for 2 to 5 days, or clindamycin for 7 days.[22,62] Fortunately, metronidazole,[63] secnidazole,[64] and tinidazole[65] also have direct effects on TV infections, independent of their effects on BV.

Future studies to evaluate the relationship between BV and TV will need to consider the effect of antimicrobial agents with potential activity against both infections and therapies to prevent recurrent infections, which are common in asymptomatic and symptomatic women. Periodic presumptive treatment and suppressive regimens with oral and intravaginal metronidazole have been shown to reduce BV recurrences.[66,67] Other studies have evaluated the efficacy of intravaginal *Lactobacillus* formulations for BV that restore normal vaginal microbiota.[68–72] The identification of interventions that can restore a healthy vaginal microbiota in women with recurrent or persistent BV may reduce a woman's subsequent risk of TV and other STIs.

Bacterial vaginosis and TV are highly prevalent and frequently occur as coinfections.[23] This is the first systematic review and meta-analysis of the association between BV and incident TV infection. Our results demonstrated that women with BV are twice as likely to acquire TV compared with women without BV. Treating BV with recommended oral and intravaginal regimens could reduce the risk of TV and its sequelae. Future clinical research using novel diagnostic tools, such as genomic-based technology and newer therapeutic options, including single-dose regimens and suppressive therapies, may facilitate more effective management strategies for BV and TV to reduce their transmission and associated risks in women.

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