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SEXUAL HEALTH

Prevalence of bacterial vaginosis in postmenopausal women: a systematic review and meta-analysis

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ABSTRACT

Bacterial vaginosis (BV), the most common cause of vaginal discharge in women of reproductive age, is associated with considerable reproductive and gynaecological sequelae and increases the risk of acquiring sexually transmissible infections including HIV. Although we understand the burden of BV in women of reproductive age, much less is known about the burden of BV in postmenopausal women. We undertook this systematic review and meta-analysis to estimate the prevalence of BV in postmenopausal women. The electronic databases PubMed, EMBASE, Web of Science, and The Cochrane Library were searched for English-language papers reporting on the prevalence of BV in postmenopausal women and published up until the end of July 2020. Search terms included: (prevalence OR survey OR proportion) AND 'bacterial vaginosis'. Meta-analysis was used to calculate pooled estimates of prevalence. We identified 2461 unique references and assessed 328 full-text articles for eligibility, with 13 studies included in the meta-analysis. The prevalence of BV ranged from 2.0 to 57.1%, with a summary estimate of 16.93% (95% CI: 8.5–27.4; $I^2 = 97.9$). There was considerable heterogeneity between studies and quality varied considerably. Further research is needed to provide a better understanding of the condition in postmenopausal women and understand its effect on their lives.

Keywords: bacterial vaginosis (BV), menopause, postmenopausal, prevalence, sexually transmissible, symptoms, vaginal discharge, vaginosis, women.

Introduction

Bacterial vaginosis (BV) is the most common cause of abnormal vaginal discharge in women of reproductive age. Characterised by a disturbance of vaginal microbiota, there is a marked depletion of *Lactobacillus* species and an increase in diversity of organisms including *Gardnerella vaginalis*, *Atopobium vaginae*, and genital mycoplasmas.[1–6] The symptoms can include a thin homogeneous vaginal discharge and fishy odour and are accompanied by an increase in vaginal pH. Symptoms can be very distressing for some women, and recurrent BV can have a significant effect on a woman's self-esteem and intimate relations, substantially affecting quality of life.[7] However, a significant number of cases are asymptomatic.[8]

BV has been associated with poor obstetric and gynaecological sequelae in premenopausal women including preterm birth,[9–15] spontaneous abortion,[10,15] postpartum endometritis,[16] and pelvic inflammatory disease (PID).[16] There is considerable observational evidence that BV is sexually transmissible;[8,17] therefore, sexually active postmenopausal women continue to be at risk of acquiring BV. Furthermore, women diagnosed with BV are at an increased risk of acquiring sexually transmissible infections (STIs) including HIV.[8,18] Recurrence is common after treatment.[19]

BV is commonly diagnosed by one of two gold standard diagnostic methods: the Nugent score,[20] or Amsel criteria.[21] The Nugent score is based on counting bacterial morphotypes identified under a microscope. Amsel criteria are based on the presence of at least three of the four following signs and symptoms: a thin homogenous discharge, raised pH, detections of amines, and presence of Clue cells seen in a wet preparation viewed under a microscope.

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These two methods were developed in women of reproductive age and there is ongoing debate about whether these are appropriate for diagnosing BV in postmenopausal women where the absence of oestrogen effect the vaginal epithelium and microbiome.[22]

The global burden of BV in women of reproductive age is high. General population prevalence estimates range from 23 to 29% globally,[23] with a higher burden in women who have sex with women,[24–27] women of African ethnicity[28–33] and women who engage in intravaginal practices (e.g. douching or insertion into the vagina of items or products for hygiene, enhancement of sex or treatment of symptoms).[8,34] In contrast, there is very little prevalence data and no real understanding of the effect of BV in postmenopausal women. Women continue to be sexually active after menopause and are at risk of acquiring BV, so it is important to understand the burden of BV among these women. We undertook this systematic review and meta-analysis to determine the prevalence of BV in postmenopausal women.

Methods

Protocol and registration

The PRISMA statement was used to guide the reporting of results in this review and meta-analysis.[35] Our review protocol is registered on the International Prospective Register of Systematic Reviews (PROSPERO), registration no.: CRD42019146598 (https://www.crd.york.ac.uk/PROSPERO/).

Search strategy

The electronic databases PubMed, EMBASE, Web of Science, and The Cochrane Library were searched for English-language studies that provided BV prevalence data, published before 20 July 2020. The search terms included (prevalence OR survey OR proportion) AND 'bacterial vaginosis' (Supplementary Table S1). Citation lists were examined for additional references.

Eligibility criteria

Studies were eligible for inclusion if they included BV prevalence data for postmenopausal women and the study was published in English. Women were defined as postmenopausal if they had not had a menstrual period for ≥12 months or were aged >50 years if menopausal status was not specified. Studies had to report on the prevalence of BV using an established, diagnostic method such as the Nugent score,[20] Amsel criteria,[21] or Hay/Ison criteria.[36] Studies reporting on BV exclusively in women of reproductive age were excluded. Letters to the editor, reviews, editorial and discussion articles, conference abstracts without subsequent publication, or studies where the target population (postmenopausal women) sample size was <10 were excluded. Studies were reviewed by two authors (LLS and JC). Differences in opinion were resolved by consensus with other authors (JSH, LAV, CSB).

Authors were contacted if it was unclear whether the study included BV prevalence data for postmenopausal women. Given the timeframe of the search and that email addresses of authors were not available for several older publications, an *a priori* decision was made to only contact authors of papers published since 2009, focusing on the most recent decade of publications.

In addition, if the paper reported prevalence data on a sample of women across a broad age range, authors were only contacted if the study included either >100 total participants across all ages or if the sample size of postmenopausal women was ≥10. Fourteen authors were contacted, six responded and three were able to provide additional data eligible for inclusion (see Supplementary Table S3).

Data extraction

The data extracted included: (1) study details (author and year of publication reported); (2) country of study; (3) study population and setting (e.g. clinic or hospital or general population); (4) ethnicity; (5) study design (cross-sectional, cohort, case–control, randomised controlled trial); (6) age range of participants; (7) total sample size across all ages; (8) number of postmenopausal women; (9) number of postmenopausal women who tested positive for BV; (10) diagnostic method used; (11) BV prevalence in postmenopausal women; and (12) reason for visit. For the two community-based cohort studies and the randomised controlled trial, baseline data were extracted. For the population-based cohort study, the most recent data were used. One author (LLS) extracted the data, and a second author (JC) checked the extracted data. Discrepancies were resolved by consultation with a third author (JSH).

Outcome

The primary outcome was BV prevalence among postmenopausal women. This was measured as a proportion, with the numerator being the number of women diagnosed with BV and the denominator being the number of women tested for BV.

Analysis

Meta-analysis was used to calculate summary estimates of BV prevalence; random effects models were used. Where studies did not report 95% confidence intervals (CIs), these were calculated using available data. The I^2 test was used to calculate the proportion of total variability in prevalence

estimates that could be attributed to underlying study heterogeneity alone and not simply due to chance. An I^2 value was considered moderate if >50% and high if >75%.[37] Subgroup analyses were undertaken to investigate factors associated with heterogeneity. Subgroup analyses included assessing BV prevalence by diagnostic method (Nugent score or Amsel criteria) and population type (classified as gynaecology populations, general population-based or screening populations [e.g. cervical cancer or employment health screening] or HIV-positive population). To investigate the effect of individual studies on the overall summary estimate, a sensitivity analysis was undertaken in which the effect of removing each study on the summary estimate was explored. Data were analysed using Stata 16 (Version 16; StataCorp) applying the Metaprop syntax using the Freeman–Tukey double arcsine transformation.

Assessment of study quality

We assessed within-study bias using a combination of the following: evaluation criteria suggested by Sanderson *et al.*[38] and AXIS, the critical appraisal tool for cross-sectional studies developed by Downes *et al.*[39] We assessed the following parameters: (1) selection bias: setting and source population, the reporting of inclusion/exclusion criteria, sample representation of the source population/the use of consecutive sampling, reporting of response fraction, missing data; (2) measurement bias: appropriate diagnostic method, experience with diagnostic method; and (3) statistical bias: sample size and reporting of sample size calculations. Publication bias, assessed by funnel plot analysis, was not performed because of the low number of eligible studies.

Results

Study selection and characteristics

Overall, 5693 articles were identified, of which 2461 were unique studies. A total of 328 full-text articles were assessed for eligibility, with 13 studies eligible for inclusion in the review (see Fig. 1). Table 1 shows that of 13 eligible studies, eight were cross-sectional studies,[22,40–46] three were cohort studies,[47–49] one was a nested case–control study[50] and one was a randomised controlled trial.[51] Three studies were from the USA,[47–49] three were from Italy,[22,45,46] and one study from each of the UK,[41] Kenya,[40] South Africa,[50] Brazil,[51] Greece,[44] China[43] and India.[42] The populations included were ethnically diverse, including Afro-Caribbean,[41] Asian[46], Caucasian,[22,41,51] Central West African[46], East European[46], Han Chinese,[43] Hellenic,[44] Hispanic or Latina,[47,49] Indian subcontinent,[41] Italian,[46] Non-Hispanic African American,[49] Non-Hispanic Black,[47] Non-Hispanic White,[47,49] North African,[46] South American[46] and West European.[46] Four studies recruited participants from gynaecological clinics or inpatient gynaecological wards,[41,44,45,51] two were from community screening programs (cervical screening, employment screening),[22,43] three were from HIV-positive populations,[40,42,50] one was a population cohort,[48] two were community-based cohorts[47,49] and one used archived laboratory data.[46] Seven studies used the Nugent score as the diagnostic method,[22,40,42,47,48,50,51] four used Amsel criteria,[41,43,46,49] one required both the Nugent score and Amsel criteria to be positive to make a diagnosis of BV,[44] one used modified Amsel criteria,[45] and none used Hay/Ison criteria. Sample sizes of postmenopausal women varied from 14 to 1732 with an overall total of 4092 women.

BV prevalence

Prevalence estimates ranged from 2.0 to 57.1%. The overall summary prevalence estimate for BV among postmenopausal women was 16.93% (95% CI 8.45–27.4%; I^2 = 97.9%; $P < 0.01$) with marked heterogeneity (Fig. 2).

Subgroup analyses found that BV prevalence was higher in studies that used the Nugent score to diagnose BV (22.90%; 95% CI 8.64–41.18; I^2 = 98.15; $P < 0.01$) than in those that used Amsel criteria (7.92%; 95% CI 4.05–12.76; I^2 = 74.64; $P < 0.01$). BV prevalence was highest among HIV-positive women (25.06%; 95% CI 7.49–48.27; I^2 = 94.6; $P < 0.01$) (Table 2).

The sensitivity analysis found that removing each study had little effect on the summary estimates, with the overall summary BV prevalence estimates for the remaining studies ranging from 14.50 to 18.64% with marked heterogeneity for each estimate (I^2 > 93%).

Assessment of within-study bias

Risk of bias is summarised in Table 3 and Supplementary Table S2. Overall, the included studies were at very high risk of selection bias with all but one[48] set in specialist clinic settings or high-risk populations (e.g. HIV-positive patients). Even the one population-based study had oversampled women of African American or Hispanic ethnicity.[48,52] Only two (15.4%) studies reported consecutive recruitment of patients[22,41] and none reported the retention of all data. Inclusion and exclusion criteria were described in four (30.8%) studies[22,43,45,51] and a further four (30.8%) studies[42,48–50] reported inclusion criteria alone. Overall, measurement bias was considered low because all studies used gold standard diagnostic methods. However, the risk of measurement bias was considered moderate in one study, which required that the Nugent score and Amsel criteria were both positive.[44] Only three studies focused on postmenopausal women,[45,48,51] with all other studies including adult women of all ages, reducing the available sample size for our target population.[22,40–44,46,47,49,50] None of the studies reported any sample size calculations.

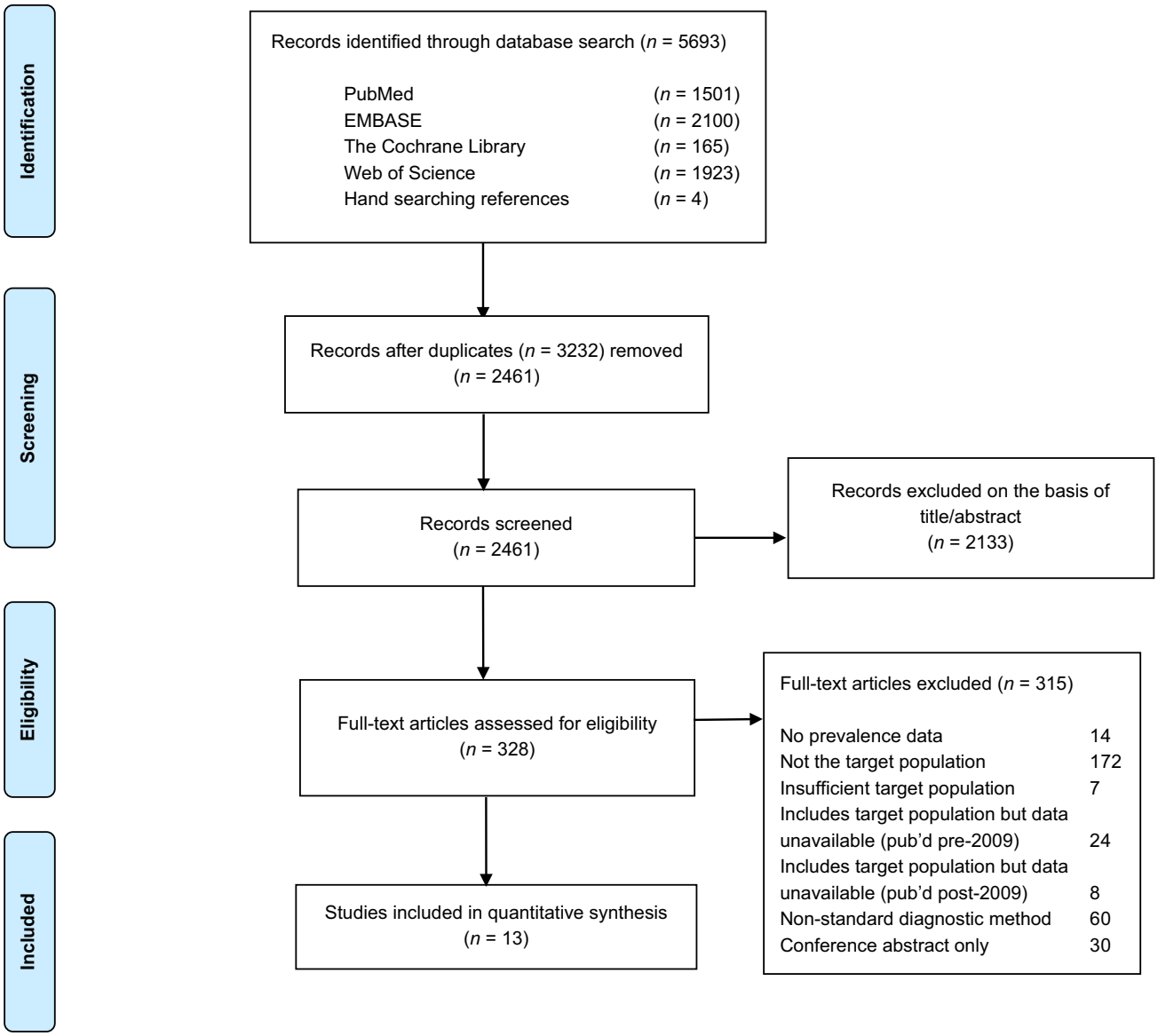

Fig. 1. Flowchart of study selection.

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis of BV prevalence specifically among postmenopausal women. Our review included a total of 4092 women and found an overall summary BV prevalence of 16.93%. However, the included studies were at considerable risk of bias; only one population-based study was identified,[48] and our pooled estimate had marked heterogeneity, highlighting the scarcity of robust BV prevalence data for postmenopausal women.

There are several limitations present in this review. First, by including studies with women who were aged >50 years and not just those who were postmenopausal, our review will have included some women who are still premenopausal or perimenopausal. However, this highlights the lack of studies that focus specifically on postmenopausal women. Second, by limiting our search to studies published in English, some important studies may have been omitted. Third, there were several studies that we were unable to extract data specifically for postmenopausal women, even after contact with authors, so some important data may have been excluded from our analysis. However, this highlights the need for further studies with a focus on postmenopausal women. Furthermore, our search only identified one population-based study and only three studies specifically focusing on postmenopausal women.[45,48,51] Finally, we chose to only include studies that used either the Nugent score,[20] Amsel criteria[21] or Hay/Ison criteria[36] to diagnose BV.

Table 1. Included studies, their characteristics and BV prevalence.

Study	Country	Study population and setting	Ethnicity	Study design	Age range (years)	Total sample size (*n*)	Women, postmenopausal or aged >50 years (*n*)	Women, postmenopausal or aged >50 years who tested positive for BV (*n*)	Diagnostic method used	BV prevalence in women, postmenopausal or aged >50 years (95% CI)	Reason for visit
de Castro *et al.* (2019)[51]	Brazil	Inpatient elective gynaecology surgery trial	White: 80% Non-White: 20%	Randomised controlled trial, baseline data used	55–75	50	50	1	Nugent scoring	2.0% (0.1–10.6)	Women participating in an elective surgery trial
Brown *et al.* (2013)[47]	USA	Women recruited from the community	Non-Hispanic White: 34% Non-Hispanic Black: 39.7% Hispanic or Latina: 26.2%	Cohort, baseline data used	18–65	141	21	1	Nugent scoring	4.8% (0.1–23.8)	Participation in study
Cauci *et al.* (2002)[22]	Italy	Women recruited from gynaecology clinics presenting for cervical screening	Caucasian	Cross-sectional	40–79	1486	921	55	Nugent scoring	6.0% (4.5–7.7)	Pap smear
Djomand *et al.* (2016)[40]	Kenya	HIV-positive women, screened by mobile unit during community visits	Not stated	Cross-sectional	18–70	1063	89	9	Nugent scoring	10.1% (4.7–1.83)	Participation in study
Hay *et al.* (1992)[41]	UK	Gynaecology clinic/ health service	Caucasian: 78.1% Indian subcontinent: 14.9% Afro-Caribbean: 7%	Cross-sectional	16–65	114	14	1	Amsel criteria	7.1% (0.2–33.9)	Treatment for a gynaecological condition
Hoffmann *et al.* (2014)[48]	USA	Population-based survey of women participating in the National Social Life, Health and Ageing Project (NSHAP Survey)	Not stated	Cohort, most recent data used	62–69 70–79 80–90 62–90	316 325 149 790	316 325 149 790	91 147 71 300	Nugent scoring	28.7% (23.9–34.1) 45.1% (39.7–50.8) 47.7% (39.4–56.0) 38.0% (34.6–41.5)[A]	Participation in study
Joshi *et al.* (2020)[42]	India	HIV-positive women, participating in a study	Not stated	Cross-sectional	21–60	912	61	24	Nugent scoring	39.3% (27.1–52.7)	Participation in study
Li *et al.* (2019)[43]	China	Women presenting for yearly employment examination at Changchun Obstetrics-Gynaecology Hospital	Han: 94.5% Others: 5.5%	Cross-sectional	22–60	511	44	8	Amsel criteria	18.2% (8.2–32.7)	Presenting for yearly employment examination

(*Continued on next page*)

Table 1. (*Continued*).

Study	Country	Study population and setting	Ethnicity	Study design	Age range (years)	Total sample size (*n*)	Women, postmenopausal or aged >50 years (*n*)	Women, postmenopausal or aged >50 years who tested positive for BV (*n*)	Diagnostic method used	BV prevalence in women, postmenopausal or aged >50 years (95% CI)	Reason for visit
Massad *et al.* (2017)[49]	USA	Participants in the Women's Interagency HIV Study (WIHS)	Non-Hispanic White: 4.8% Non-Hispanic African American: 78.6% Hispanic: 13.1% Other: 3.5%	Cohort, baseline data used	<25 to 45+	3730	149	12	Amsel criteria	8.1% (4.2–13.6)	Participation in study
Myer *et al.* (2005)[50]	South Africa	HIV-positive women, participating in a study	Not stated	A case–control study nested within a randomised controlled trial	35–65	410	38	21	Nugent scoring	55.3% (38.3–71.4)	Participation in study
Sianou *et al.* (2017)[44]	Greece	Recruited from females presenting to a gynaecology clinic	Hellenic: 90.80% Other: 9.2%	Cross-sectional	All ages	163	35	20	Nugent scoring and Amsel criteria were both required to be positive for a diagnosis of BV	57.1% (39.4–73.7)	Treatment for a gynaecological condition
Spinillo *et al.* (1997)[45]	Italy	Recruited from women presenting to a gynaecology clinic	Not stated	Cross-sectional	21–70	1712	148	14	Modified Amsel criteria	9.5% (5.3–15.4)	Treatment for a gynaecological condition
Tibaldi *et al.* (2009)[46]	Italy	Archived laboratory data from females presenting to a gynaecology clinic	Italian: 92.2% West European: 1.7% East European: 1.6% South American: 1.4% North African: 1.5% Central West African: 1.1% Asian: 0.4%	Cross-sectional	<13 to 66+	27 172	1732	83	Amsel criteria	4.8% (3.8–5.9)	Treatment for a gynaecological condition

[A]Calculated using available data.

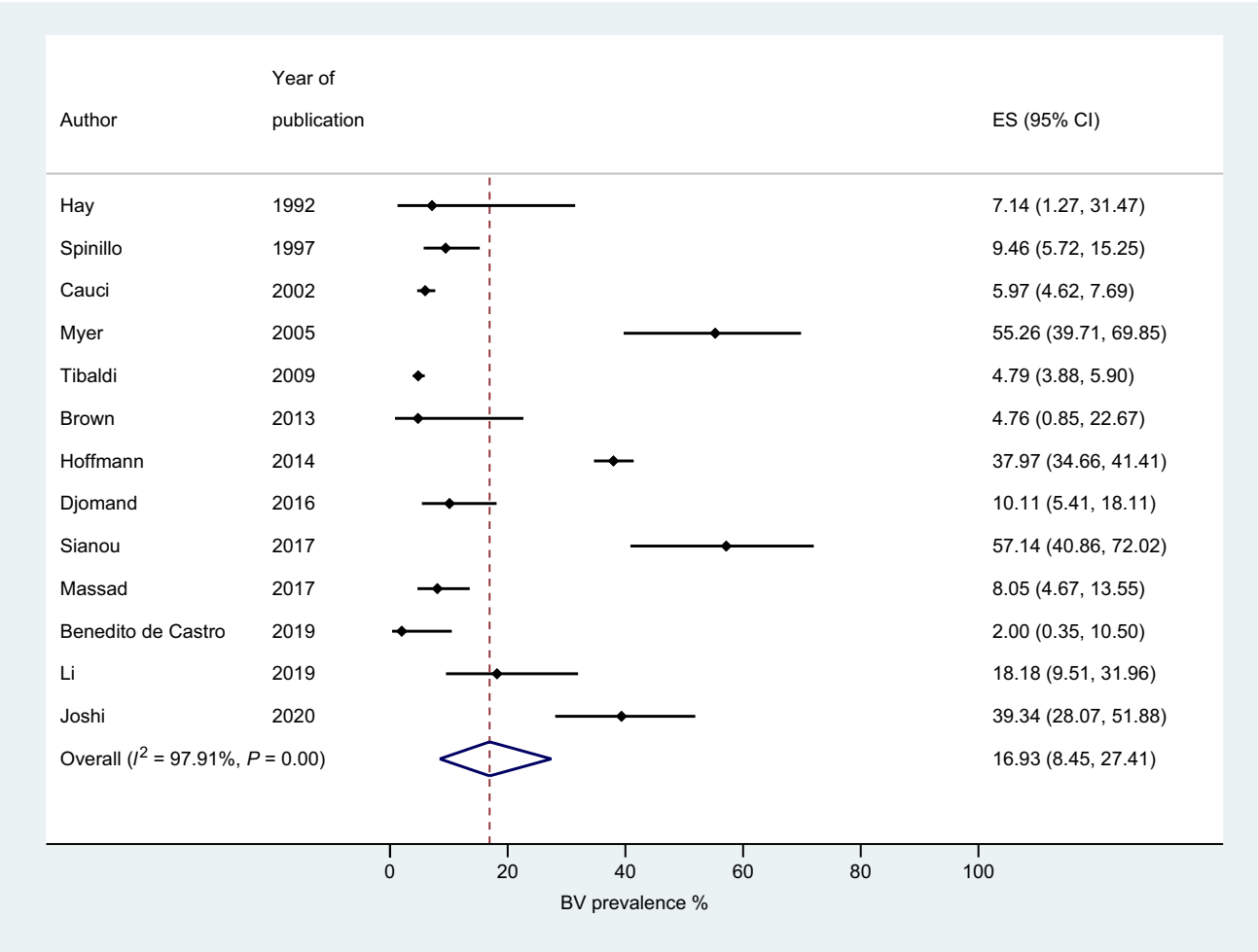

Fig. 2. Forest plot of BV prevalence. ES, effect size (prevalence). Studies ordered by year of publication.

Table 2. Subgroup analyses – BV prevalence.

Subgroup	Number of studies	Summary prevalence estimate % (95% CI)	I^2% (P-value)
BV test type			
Nugent score[A]	8	22.90 (8.64–41.18)	98.15 ($P < 0.01$)
Amsel criteria	5	7.92 (4.05–12.76)	74.64 ($P < 0.01$)
Population group			
Gynaecology	5	12.02 (2.86–25.49)	93.45 ($P < 0.01$)
Population/ Screening	4	15.25 (0.90–40.35)	98.99 ($P < 0.01$)
HIV-positive	4	25.06 (7.49–48.27)	94.60 ($P < 0.01$)

[A]Includes the study by Sianou *et al.*[44] that required both a positive Nugent score and Amsel criteria to be classified as BV.

Table 3. Summary assessment of study quality and bias.

Author, publication year	Selection	Measurement	Sample size
de Castro (2019)[51]	+++	+	++
Brown (2013)[47]	+++	+	+++
Cauci (2002)[22]	+	+	+
Djomand *et al.* (2016)[40]	+++	+	+
Hay *et al.* (1992)[41]	+	+	+++
Hoffmann *et al.* (2014)[48]	++	+	+
Joshi *et al.* (2020)[42]	+++	+	+
Li *et al.* (2019)[43]	+++	+	+++
Massad *et al.* (2017)[49]	++	+	+
Myer *et al.* (2005)[50]	+++	+	+++
Sianou *et al.* (2017)[44]	+++	++	+++
Spinillo *et al.* (1997)[45]	+++	+	+
Tibaldi *et al.* (2009)[46]	+++	+	+

Note: + = low risk of bias; ++ = moderate risk of bias; +++ = high risk of bias.

Our subgroup analysis found that BV prevalence was higher in studies using the Nugent score than in studies that used Amsel criteria as the diagnostic method. It has been previously shown that the Amsel criteria has a lower sensitivity for BV than the Nugent score, and this may have contributed to the observed difference.[53–55] Furthermore, BV prevalence was highest among HIV-positive women. However, there are concerns about how well these diagnostic methods work after menopause[22,48] when the decline in oestrogen alters the vaginal epithelium and leads to a significant reduction or absence of lactobacilli.[22,56] Currently, there is no standardised recommendation for the diagnosis of BV in postmenopausal women. According to a recent study that compared the relative abundances of vaginal microbiota with Nugent score,[57] classic BV-associated organisms such as *Gardnerella*, *Atopobium*, *Sneathia*, and *Megasphaera* were strongly associated with an elevated Nugent score in premenopausal women, but in postmenopausal women, these same organisms were not. The authors concluded that a high Nugent score should not be used to infer a diagnosis of BV in postmenopausal women.[57] This highlights the challenges with understanding BV in postmenopausal women and may contribute to the heterogeneity in prevalence estimates.

The use of hormone replacement therapy (HRT) is relatively common among postmenopausal women to alleviate the symptoms of menopause.[56] Physiological changes in response to HRT can include significant increases in the relative abundance of *Lactobacillus* spp., a decrease in vaginal pH, as well as increased maturation of the vaginal epithelium.[58] However, it remains unclear how the use of HRT could affect the pathogenesis, symptoms, or diagnosis of BV in postmenopausal women when there are already ongoing concerns about how well diagnostic methods work after menopause[22,48] and, currently, there is no standardised recommendation for the diagnosis of BV in postmenopausal women. Only one study in our review compared the prevalence of BV in postmenopausal women who use HRT with those who did not, with the authors observing that the difference was not statistically significant.[22]

BV is associated with poor reproductive and obstetric outcomes, significant gynaecological sequelae,[9–14,16,41,59,60] and a greater risk of STI acquisition, including HIV[18,61–63] in women of reproductive age, but there is sparse discussion about its impact in postmenopausal women. However, women continue to be sexually active after menopause, often lacking knowledge of STIs and safer sexual practices,[64] and are less likely to use condoms.[65] A recent study found that STIs are increasing at a faster rate among older women than among younger women.[66] Given the considerable evidence suggesting that BV is sexually transmissible,[8,17] and the knowledge that women continue to be sexually active after menopause, postmenopausal women continue to be at risk of acquiring BV, which can increase their risk of other STIs including HIV.[8,18,32,67–70]

This review highlights that there are few quality studies on BV prevalence in postmenopausal women. Most studies were subject to considerable selection bias and lacked sample size calculations. Even the single population-based study had some selection bias with women of African American or Hispanic ethnicity being oversampled.[48,52] A recent systematic review and meta-analysis by Peebles *et al.*,[23] of global BV prevalence and costs among women of reproductive age in the general population, found similar marked heterogeneity. Nevertheless, our review suggests that BV may be highly prevalent among postmenopausal women.

Conclusion

BV is a condition we take seriously in younger women, but know very little about in postmenopausal women. Our review highlights how under-researched and poorly understood this important area of public health is. Quality research is needed to further our understanding of BV in postmenopausal women and understand its effect on their lives.

Supplementary material

Supplementary material is available online.

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