

GYNECOLOGY

Association between obesity and bacterial vaginosis as assessed by Nugent score



Rita T. Brookheart, PhD; Warren G. Lewis, PhD; Jeffrey F. Peipert, MD, PhD; Amanda L. Lewis, PhD; Jenifer E. Allsworth, PhD

BACKGROUND: Bacterial vaginosis is 1 of the most common vaginal conditions in the United States. Recent studies have suggested that obese women have an abnormal microbiota reminiscent of bacterial vaginosis; however, few studies have investigated the prevalence of bacterial vaginosis in overweight and obese populations. Moreover, despite the increased prevalence of obesity and bacterial vaginosis in black women, it is not known whether racial disparities exist in the relationship between obesity and bacterial vaginosis.

OBJECTIVE: The objective of this study was to examine the relationship between body mass index and bacterial vaginosis as determined by Nugent score and to determine the influence of race in this context.

STUDY DESIGN: We performed a cross-sectional study using patient data and vaginal smears from 5918 participants of the Contraceptive CHOICE Project. Gram-stained vaginal smears were scored with the Nugent method and categorized as bacterial vaginosis—negative (Nugent score, 0–3), bacterial vaginosis—intermediate (Nugent score, 4–6), or bacterial vaginosis—positive (Nugent score, 7–10). Body mass index was determined with Centers for Disease Control and Prevention guidelines, and obese individuals were categorized as class I, II, or III obese based on National Institutes of Health and World Health Organization body mass index parameters. Linear regression was used to model mean differences in Nugent scores; Poisson regression with robust error variance was used to model prevalence of bacterial vaginosis.

RESULTS: In our cohort, 50.7% of participants were black; 41.5% were white, and 5.1% were of Hispanic ethnicity; the average age of 25.3 years old. Overall, 28.1% of participants were bacterial vaginosis—positive. Bacterial vaginosis was prevalent in 21.3% of lean, 30.4% of overweight, and 34.5% of obese women ($P < .001$). The distribution of bacterial vaginosis—intermediate individuals was similar across all body mass index categories. Compared with the scores of lean women, Nugent scores were highest among overweight and obese class I women (adjusted mean difference: overweight women, 0.33 [95% confidence interval, 0.14–0.51] and obese women, 0.51 [95% confidence interval, 0.29–0.72]). Consistent with this, overweight and obese women had a higher frequency of bacterial vaginosis compared with lean women, even after adjustment for variables that included race. Among white women, the prevalence of bacterial vaginosis was higher for overweight and class I and class II/III obese white women compared with lean white women, which is a phenomenon not observed among black women and suggests an effect modification.

CONCLUSION: Overweight and obese women have higher Nugent scores and a greater occurrence of bacterial vaginosis compared with lean women. Black women have a greater prevalence of bacterial vaginosis independent of their body mass index compared with white women.

Key words: bacterial vaginosis, body mass index, Nugent score, obesity, overweight, race

Bacterial vaginosis (BV) is 1 of the most common vaginal conditions in the United States and is present in approximately 1 of every 3 women.¹ BV is characterized by lower levels of beneficial *Lactobacilli* and an overgrowth of fastidious anaerobic bacteria, such as *Gardnerella vaginalis*, *Atopobium vaginae* and species of *Prevotella* and *Mobiluncus*.² Women with BV are at an increased risk for sexually transmitted infections (STIs; eg, gonorrhea, chlamydia, HIV, and trichomoniasis), urinary tract infection, pelvic inflammatory

disease, and adverse pregnancy outcomes that include preterm birth.^{3–13}

Nugent scoring is the gold standard for laboratory-based BV diagnosis and uses morphotype evaluation of Gram-stained slides to quantify the representation of Gram-positive (*Lactobacillus*), small Gram-negative or -variable (*Gardnerella*, *Bacteroides*), and curved organisms (such as *Mobiluncus*) in vaginal fluid smears.¹⁴ These measurements are reported as a score that ranges from 0–10; scores of 0–3 indicate a “normal” *Lactobacillus*-dominant microbiota and of 7–10 indicate a positive BV diagnosis. Women with a score of 4–6 have an “intermediate” microbiota and, similar to BV-positive individuals, may be at greater risk for acquiring STIs compared with women with a “normal” *Lactobacillus*-dominant microbiota.^{8,15–17} Although the pathologic significance of BV-intermediate status is still not clear in all situations,

this type of vaginal microbiota is often considered along with BV as an “abnormal microbiota.”^{8,18,19} It is known that several factors that include menstruation,^{20,21} douching,^{1,22,23} and high numbers of sexual partners²⁴ are associated with disruptions of the vaginal microbiota. Many questions still remain about how BV negatively influences women’s reproductive health. Unfortunately, there is little mechanistic information about how the dysbiotic BV microbiome develops or how individual bacteria interact with the host to produce disease. However, recent studies in mouse models have further implicated *G vaginalis* as a cause of features related to BV.^{25,26} These unknowns and the fact that BV is a common condition in the United States underscore the importance of the identification of BV-associated risk factors to identify women at high risk for adverse gynecologic and obstetric

Cite this article as: Brookheart RT, Lewis WG, Peipert JF, et al. Association between obesity and bacterial vaginosis as assessed by Nugent score. Am J Obstet Gynecol 2019;220:476.e1-11.

0002-9378/\$36.00

© 2019 Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.ajog.2019.01.229>

AJOG at a Glance

Why was this study conducted?

Although several risk factors for bacterial vaginosis have been identified, whether obesity/overweight is a risk factor for bacterial vaginosis is not clear. This study was conducted to determine whether an association between obesity/overweight and prevalence of bacterial vaginosis exists and to examine the role of race in this context.

Key findings

Key findings of this study are that obese and overweight women have higher Nugent scores and increased prevalence of bacterial vaginosis. We also show that race is an effect modifier of the relationship between body mass index and prevalence of bacterial vaginosis.

What does this add to what is known?

This study uncovered an association between obesity/overweight and frequency of bacterial vaginosis and demonstrates that, unlike white women, black women exhibit higher Nugent scores and increased prevalence of bacterial vaginosis, regardless of body mass index.

outcomes and to design more effective treatments and prevention strategies.

Although a relationship between increased body mass index (BMI) and gut dysbiosis has been studied widely,^{27–32} little is known about the relationship between BMI and BV prevalence. Most recently, it has been reported that the vaginal microbiota of overweight and obese Korean women exhibited a larger proportion of *L iners* and *Prevotella* compared with lean women.^{33,34} This is of interest because both of these taxa previously have been associated with BV.^{35,36} Although these studies suggest that there may be an increased prevalence of BV in overweight/obese women, participant BV status was not reported.^{33,34} One study conducted among US women reported a positive correlation between high BMI and BV; however, after multivariable modeling, this study showed BMI was not associated independently with BV.³⁷ This study had several caveats that included that less than one-third of the women who were examined were black, and that it did not examine the relationship between BMI and women with an “intermediate” microbiota (Nugent score, 4–6). Moreover, all obese women were categorized into a single BMI group, regardless of the subclass of obesity. Both the National Institutes of Health and the World Health

Organization categorize obese individuals into 3 subclasses based on BMI: class I (30–34.9 kg/m²), class II (35–39.9 kg/m²), and class III (≥ 40 kg/m²).^{38,39} Reports have shown an association between obesity class level and an increased prevalence of disease.^{40,41} Given the racial disparities among overweight and obese women and the higher prevalence of BV in black women, an understanding of the relationship between BV and BMI and the role of race is highly warranted.^{1,42–44}

To increase our understanding of the vaginal microbiota among overweight/obese women and the extent to which this association may be influenced by race, we examined the correlation between BMI, Nugent score, and BV prevalence among women in the St. Louis region. Specifically, we examined whether BMI positively correlated with higher Nugent scores and increased BV prevalence. To test whether factors such as race influenced the proposed relationships, we performed multivariable modeling using information gathered from 5918 reproductive aged women, of whom 50.7% were black.

Materials and Methods**Study design**

We conducted a cross-sectional substudy of participants from the Contraceptive CHOICE Project (CHOICE).⁴⁵

CHOICE obtained written informed consent from all participants before enrollment in accordance with its approved Institutional Review Board protocol from Washington University in St. Louis, MO. CHOICE participants consented to the use of questionnaire data and stored vaginal samples by future substudies. The current substudy obtained Institutional Review Board approval (ID# 201108155) from Washington University in St. Louis and followed the principles outlined in the Declaration of Helsinki for human research.

Over a 4-year period, CHOICE enrolled 9256 women from the St. Louis region and provided Food and Drug Administration–approved reversible contraceptive methods at no-cost.⁴⁵ Eligibility criteria included women 14–45 years of age, self-reported sexual activity in the past 6 months or plans to become sexually active with a male partner, and a desire to prevent pregnancy through the use of a reversible contraceptive method. Participants with a history of tubal ligation or hysterectomy were excluded from the study. The CHOICE cohort predominantly consisted of black and white participants, which is representative of the racial make-up of the St. Louis region. The current substudy included only women with a complete baseline questionnaire survey, BMI measurement, and Nugent score (n=5918). The baseline questionnaire included age, self-reported race and ethnicity, highest level of education obtained, monthly income, receipt of public assistance, difficulty paying for basic necessities, tobacco history, number of sexual partners, history of douching in last 30 and 180 days, history of STIs, or positive for an STI at enrollment. Menstrual status was estimated as last menstrual period within 6 days of enrollment, and a flag for recent hormonal contraceptive method use was created for those who reported contraceptive pills, patch, ring, or injection, the levonorgestrel intrauterine system, or subdermal implant. History of STI was defined as ever told by a healthcare provider that she had 1 of

the following sexually transmitted infections: chlamydia, gonorrhea, trichomoniasis, syphilis, human papillomavirus or genital warts, human immunodeficiency virus or herpes; current STI was defined as positive test for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Trichomonas vaginalis* at enrollment.

Assessment of BV

At the time of CHOICE enrollment and before long-acting reversible contraceptive method insertion, participants were instructed by a medical professional for self-collection of vaginal fluid from a mid-vaginal site (approximately 2 inches into the vagina) using a double-headed rayon swab (Starplex Scientific Inc, Etobicoke, Ontario, Canada). Vaginal swabs were rolled immediately onto glass slides to create vaginal smears, which were Gram-stained and scored with the Nugent method.¹⁴ The Nugent method consisted of microscopic evaluation of bacterial morphotypes to score the overall character of the vaginal flora.¹⁴ Nugent scores range from 0–10, based on the prevalence of 3 bacterial morphotypes that roughly correspond to *Lactobacillus*, *G vaginalis* or *Bacteroides*, and *Mobiluncus*. The number of long rod-shaped Gram-positive bacilli are scored 0–4, where 0 indicates high numbers of *Lactobacillus*; small Gram-negative and Gram-variable rods and coccobacilli (*Bacteroides* and *G vaginalis*) are scored 0–4, with 4 denoting the highest observed number of these bacteria; and curved rods (eg, *Mobiluncus* spp.) are scored 0–2, where 2 indicates the highest observed numbers. To ensure consistency in the amount of vaginal fluid on each slide and Gram-staining and Nugent scoring, all swabs were rolled by the same technician, and all slides were stained and scored by the same technician. To assess the reliability of our scoring, a subset of smears was also scored by the laboratory of Dr Sharon Hillier (who established the Nugent score method¹⁴) at the Magee-Womens Research Institute, University of Pittsburgh, and was reproducible between both research groups. Samples were categorized as BV-negative (score, 0–3),

BV-intermediate (score, 4–6), or BV-positive (score, 7–10).

BMI determination

Weight and height of participants were measured at the clinics by research personnel who used a standardized protocol at the time of enrollment. Weight was recorded in pounds, and height was recorded in feet and inches. Participants removed shoes and heavy outer clothing before being measured. These data were converted to BMI with the use of the formula published by the Centers for Disease Control and Prevention⁴⁶: $(\text{weight [pounds]} / [\text{height(inches)}]^2) \times 703$. Women were categorized by BMI based on National Institutes of Health and World Health Organization recommendations: underweight ($<18.5 \text{ kg/m}^2$), lean ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$), class I obese ($30\text{--}34.9 \text{ kg/m}^2$), class II ($35\text{--}39.9 \text{ kg/m}^2$) obese, and class III ($\geq 40 \text{ kg/m}^2$) obese.^{38,39}

Statistical analysis

Participant characteristics were described for all women and among strata of BMI categories. Probability values for these comparisons were estimated with chi-square tests (all categorical variables) or linear regression (age). We examined multiple metrics of BV in relation to BMI: Nugent score category (including intermediate), Nugent-defined BV, and symptomatic BV (report of discharge, itching, odor, or pain during urination⁴⁷ during the 7 days before the clinic visit and sample collection).

Crude and adjusted mean differences and 95% confidence intervals (CIs) were estimated with linear regression stratified by BMI among all participants and by self-identified race group (black or white). Potential confounders (Table 1) were evaluated for association with BMI and Nugent score. All variables that were significant at the alpha level $<.05$ were retained for inclusion in the fully adjusted model. Hispanic ethnicity and ever use of tobacco were not associated with Nugent score and were excluded. Variables that were significant in the fully adjusted model (public assistance,

education, current smoker, douching in the last 30 days, sexually transmitted infection at baseline, and current hormonal contraception) were included in the final adjusted model. The all participant models were also adjusted for race. Prevalence ratios of BV were estimated with Poisson regression with robust error variance. This approach provides an unbiased estimate of the prevalence ratio in the instance of a common binary outcome. The probability value for the interaction term for BMI and race served as an indicator of effect modification. Probability values for 2-tailed tests less than alpha .05 were considered statistically significant. All analyses were conducted in Stata software (version 13.0; StataCorp LP, College Station, TX).

Results

Participant characteristics

Of the 9256 CHOICE participants, 6022 (65.1%) had a baseline questionnaire survey, BMI measurement, and Nugent score. The main reason for missingness ($n=2417$; 26.1%) was the absence of a vaginal smear for Nugent scoring, which is an element that was added to the protocol after enrollment began. Of the 6022 eligible participants, 5918 (98.3%) had complete data and were included in the current analysis. Participant data and vaginal specimens were obtained at the time of enrollment. Participants averaged 25.3 years old, and 50.7% of them self-identified as black (Table 1). Over one-half of participants (53.1%) reported a monthly income of $\leq \$800$, and 38.1% reported some form of public assistance at enrollment. One-third of participants (33.9%) reported a high school diploma as the highest degree obtained. Most women reported multiple lifetime sexual partners (median, 3); 27.5% of participants reported 2–4 partners; 29.2% reported 5–7; 14.2% reported 8–12, and 19.7% reported ≥ 13 lifetime sexual partners. Forty-six percent had a history of smoking, with 23.1% self-reporting as current smokers at the time of enrollment.

In this cohort, 27.3% of women were BV-intermediate, and 28.1% were BV-positive (Table 2). Of the women diagnosed as BV-positive, 17.2% reported

TABLE 1
Demographics of Contraceptive CHOICE Project participants by body mass index category, N = 5,918

Demographic	Participants by body mass index category, kg/m ²						Pvalue ^a
	All participants (N=5918)	Underweight <18.5 (n=174)	Lean 18.5–24.9 (n=2312)	Overweight 25–29.9 (n=1540)	Class I obese 30–34.9 (n=934)	Class II/III obese ≥35 (n=958)	
Mean age, y (standard deviation)	25.3±5.9	23.2±4.7	24.1±5.4	25.6±6.0	26.1±6.2	26.9±6.1	<.001
Race, n (%)							
Black	3001 (50.7)	72 (41.4)	870 (37.6)	809 (52.5)	570 (61.0)	680 (71.0)	<.001
White	2457 (41.5)	84 (48.3)	1250 (54.1)	604 (39.2)	296 (31.7)	223 (23.3)	
Other	460 (7.8)	18 (10.3)	192 (8.3)	127 (8.3)	68 (7.3)	55 (5.7)	
Hispanic	300 (5.1)	9 (5.2)	105 (4.5)	99 (6.4)	53 (5.7)	34 (3.6)	.014
Monthly income, n (%)							
None	1226 (20.8)	35 (20.1)	524 (22.7)	304 (19.8)	187 (20.1)	176 (18.4)	<.001
\$1–800	1903 (32.3)	75 (43.1)	780 (33.9)	494 (32.1)	258 (27.7)	296 (31.0)	
\$801–1600	1666 (28.2)	45 (25.9)	587 (25.5)	436 (28.4)	295 (31.7)	303 (31.7)	
≥\$1601	1106 (18.7)	19 (10.9)	413 (17.9)	304 (19.8)	190 (20.4)	180 (18.9)	
Receiving public assistance, n (%)	2250 (38.1)	48 (27.8)	639 (27.7)	625 (40.6)	445 (47.7)	493 (51.5)	<.001
Trouble paying for basic necessities, n (%)	2393 (40.5)	62 (35.6)	828 (35.9)	625 (40.6)	433 (46.4)	445 (46.5)	<.001
Education, n (%)							
≤ High school	2007 (33.9)	71 (40.8)	734 (31.8)	535 (34.8)	345 (37.0)	322 (33.6)	<.001
Some college	2512 (42.4)	67 (38.5)	895 (38.7)	670 (43.5)	408 (43.8)	472 (49.3)	
College graduate	1396 (23.6)	36 (20.7)	683 (29.5)	334 (21.7)	179 (19.2)	164 (17.1)	
Smoking							
Ever	2765 (46.7)	79 (45.4)	1123 (48.6)	731 (47.5)	514 (55.0)	546 (57.0)	.037
Current	1367 (23.1)	48 (27.6)	550 (23.8)	374 (24.3)	199 (21.3)	196 (20.5)	.044
Sexual partners last 30 days							
None	1125 (19.2)	21 (12.4)	390 (17.1)	316 (20.7)	191 (20.7)	207 (21.8)	.004
1	4356 (74.5)	136 (80.0)	1750 (76.8)	1124 (73.6)	673 (72.8)	673 (70.9)	
≥2	370 (6.3)	13 (7.7)	139 (6.1)	88 (5.8)	61 (6.6)	69 (7.3)	

Brookheart et al. Obesity and the prevalence of bacterial vaginosis. Am J Obstet Gynecol 2019.

(continued)

TABLE 1
Demographics of Contraceptive CHOICE Project participants by body mass index category, N=5,918 (continued)

Demographic	Participants by body mass index category, kg/m ²						Pvalue ^a
	All participants (N=5918)	Underweight <18.5 (n=174)	Lean 18.5–24.9 (n=2312)	Overweight 25–29.9 (n=1540)	Class I obese 30–34.9 (n=934)	Class II/III obese ≥35 (n=958)	
Lifetime sexual partners, n (%)							
None	39 (0.7)	0	12 (0.5)	14 (0.9)	4 (0.4)	9 (1.0)	<.001
1	516 (8.7)	14 (8.1)	253 (10.9)	128 (8.3)	72 (7.7)	49 (5.1)	
2–4	1630 (27.5)	56 (32.2)	680 (29.4)	433 (28.1)	231 (24.7)	230 (24.0)	
5–7	1727 (29.2)	56 (32.2)	646 (27.9)	428 (27.8)	303 (32.4)	294 (30.7)	
8–12	839 (14.2)	15 (8.6)	308 (13.3)	225 (14.6)	136 (14.6)	155 (16.2)	
≥13	1167 (19.7)	33 (19.0)	413 (17.9)	312 (20.3)	188 (20.1)	221 (23.1)	
Douching, n (%)							
In the past 180 days	1340 (22.7)	32 (18.4)	407 (17.6)	354 (23.0)	248 (26.6)	299 (31.2)	<.001
In the past 30 days	590 (10.0)	19 (10.9)	168 (7.3)	162 (10.6)	99 (10.6)	142 (14.9)	<.001
Sexually transmitted infection, n (%)							
Past	2461 (41.6)	63 (36.2)	801 (34.7)	660 (42.9)	441 (47.2)	496 (51.8)	<.001
At baseline	518 (8.8)	17 (9.8)	170 (7.4)	132 (8.6)	85 (9.1)	114 (11.9)	.001
Current menstruation flag, n (%)	856 (14.5)	19 (10.9)	342 (14.8)	216 (14.0)	129 (13.8)	150 (15.7)	.458
Current hormonal contraceptive method before enrollment, n (%)	1520 (25.7)	38 (21.8)	636 (27.5)	412 (26.8)	199 (21.3)	235 (24.5)	.003

^a Determined by chi-square test (all categoric variables) or linear regression (age). For categoric variables, probability values represent the distribution of a given categoric variable for all participants and within a specific body mass index category.
 Brookheart et al. Obesity and the prevalence of bacterial vaginosis. Am J Obstet Gynecol 2019.

TABLE 2
Nugent score and prevalence of bacterial vaginosis by body mass index category

Status	Participants by body mass index category, kg/m ²					Pvalue ^a
	All participants (N=5918)	Underweight <18.5 (n=174)	Lean 18.5–24.9 (n=2312)	Overweight 25–29.9 (n=1540)	Class II/III obese ≥35 (n=958)	
Nugent score, n (%)						<.001
0–3	2639 (44.6)	78 (44.8)	1170 (50.6)	657 (42.7)	370 (39.6)	364 (38.0)
4–6	1618 (27.3)	48 (27.6)	649 (28.1)	415 (27.0)	247 (26.5)	259 (27.0)
7–10	1661 (28.1)	48 (27.6)	493 (21.3)	468 (30.4)	317 (33.9)	335 (35.0)
Bacterial vaginosis, n (%)						<.001
No	4257 (71.9)	126 (72.4)	1819 (78.7)	1072 (69.6)	617 (66.1)	623 (65.0)
Yes	1661 (28.1)	48 (27.6)	493 (21.3)	468 (30.4)	317 (33.9)	335 (35.0)
Symptomatic bacterial vaginosis, n (%)						.371
No	1376 (82.8)	41 (85.4)	406 (82.4)	379 (81.0)	261 (82.3)	289 (86.3)
Yes	285 (17.2)	7 (14.6)	87 (17.7)	89 (19.0)	56 (17.7)	46 (13.7)

^a Determined by chi-square test for categorical variables; probability values represent the distribution of a given categorical variable for all participants and within a specific body mass index category. Brookheart et al. *Obesity and the prevalence of bacterial vaginosis*. *Am J Obstet Gynecol* 2019.

symptoms associated with BV (ie, abnormal discharge, foul odor, and vaginal itching⁴⁷) at the time of enrollment.

BV prevalence by BMI category

Of the 5918 study participants, 2.9% were underweight (BMI, <18.5 kg/m²); 39.1% were lean (BMI, 18.5–24.9 kg/m²); 26% were overweight (BMI, 25–29.9 kg/m²), and 32% were obese (BMI ≥30 kg/m²; Table 1). As shown in Table 2, 34.5% of obese, 30.4% of overweight, and 21.3% of lean women were BV-positive. Given that we observed no relationship between BMI and BV-intermediate scores in this cohort, we examined the number of women below the threshold of BV (BV-negative and -intermediate) and found it to be highest among lean women (78.7%) and lowest among obese women (65.5%; Table 2).

We next examined whether a relationship existed between obesity class and BV prevalence. Because of the limited number of class II and III obese individuals in this cohort, members of these 2 classes (BMI, ≥35 kg/m²) were grouped together (n=958) and members of class I (n=934) remained separate. Nugent scores were higher in the overweight (0.33 [95% CI, 0.14, 0.51]), class I obese (0.51 [95% CI, 0.29–0.72]), and class II/III obese groups (0.37 [95% CI, 0.16–0.59]) compared with lean women (Table 3). Consistent with this observation, the adjusted prevalence ratio of BV was 1.25 (95% CI, 1.12–1.39) for overweight, 1.31 (95% CI, 1.16–1.47) for class I obese, and 1.25 (95% CI, 1.11–1.41) for class II/III obese women compared with lean women (Table 4).

The role of race in the BMI-BV relationship

To determine whether the relationship between BMI and BV was influenced by race, we performed a within-race analysis of the mean difference in Nugent scores and the prevalence ratio of BV among black women (n=3001) in each BMI category. Adjusted Nugent scores were higher in overweight (0.30 [95% CI, 0.01–0.58]) and class I obese (0.41 [95% CI, 0.10–0.73]) black women,

TABLE 3
Mean difference in Nugent score by body mass index category overall and within each race

Body mass index category, kg/m ²	Nugent score, mean (standard deviation)	Difference in Nugent score, mean (95% confidence interval)			Black vs white interaction <i>P</i> value
		Crude	Fully adjusted ^a	Final adjusted ^b	
All women^c					
<18.5	4.27 (3.01)	0.30 (−0.14–0.73)	0.15 (−0.29–0.58)	0.19 (−0.24–0.62)	.557
18.5–24.9	3.90 (2.85)	Referent	Referent	Referent	Referent
25–29.9	4.53 (2.94)	0.40 (0.22–0.59) ^d	0.29 (0.11–0.48) ^d	0.33 (0.14–0.51) ^d	.891
30–34.9	4.87 (2.99)	0.61 (0.39–0.83) ^d	0.44 (0.23–0.66) ^d	0.51 (0.29–0.72) ^d	.401
≥35	4.93 (2.96)	0.53 (0.31–0.75) ^d	0.28 (0.07–0.50) ^d	0.37 (0.16–0.59) ^d	.064
Black women					
<18.5	5.08 (3.02)	0.10 (−0.62–0.83)	0.00 (−0.72–0.72)	0.00 (−0.72–0.71)	
18.5–24.9	4.98 (3.01)	Referent	Referent	Referent	
25–29.9	5.24 (3.01)	0.26 (−0.03–0.55)	0.23 (−0.06–0.52)	0.30 (0.01–0.58) ^d	
30–34.9	5.37 (3.06)	0.39 (0.07–0.71) ^d	0.34 (0.02–0.66) ^d	0.41 (0.10–0.73) ^d	
≥35	5.19 (3.00)	0.21 (−0.09–0.51)	0.07 (−0.23–0.38)	0.18 (−0.12–0.48)	
White women					
<18.5	3.63 (2.79)	0.43 (−0.15–1.01)	0.23 (−0.34–0.81)	0.30 (−0.28–0.87)	
18.5–24.9	3.21 (2.51)	Referent	Referent	Referent	
25–29.9	3.62 (2.70)	0.42 (0.16–0.67) ^d	0.24 (−0.02–0.49)	0.24 (−0.01–0.49)	
30–34.9	3.99 (2.78)	0.78 (0.45–1.11) ^d	0.51 (0.18–0.84) ^d	0.56 (0.23–0.89) ^d	
≥35	4.08 (2.71)	0.88 (0.50–1.25) ^d	0.51 (0.13–0.88) ^d	0.58 (0.21–0.95) ^d	

^a Included income, public assistance, trouble paying for basics, education, number of sex partners in the last 30 days, lifetime number of sex partners, current tobacco use, douching in last 30 days, douching in last 180 days, history of sexually transmitted infection, current sexually transmitted infection; ^b Adjusted for public assistance, education, current smoker, douching in the last 30 days, and sexually transmitted infection at baseline; ^c The All Women model was also adjusted for race; ^d Statistically significant value.

Brookheart et al. Obesity and the prevalence of bacterial vaginosis. *Am J Obstet Gynecol* 2019.

compared with lean black women (Table 3). However, the adjusted Nugent scores of class II/III obese black women were not significantly different compared with lean counterparts. Among white women (n=2457), Nugent scores were higher for class I (0.56 [95% CI, 0.23–0.89]) and class II/III (0.58 [95% CI, 0.21–0.95]) obese white women compared with lean white women. We observed no significant difference in Nugent scores for overweight white women compared with lean white women (Table 3).

We next examined the adjusted prevalence ratio of BV for black women across all BMI categories. We observed that only class I obese black women had an increased occurrence of BV (1.14 [95% CI, 1.00–1.31]) compared with lean black women, although the

prevalence of BV for overweight and class II/III obese black women was not statistically different than lean black women (Table 4). Among white women, the adjusted prevalence ratio of BV was greater in overweight (1.44 [95% CI, 1.16–1.79]), class I (1.73 [95% CI, 1.35–2.22]), and class II/III (1.63 [95% CI, 1.23–2.15]) obese white women compared with lean white women (Table 4). We next examined the effect modification of race on the BMI-BV relationship. The statistical interaction of increasing BMI and race in relation to BV prevalence was significant for overweight ($P=.024$) and obese (class I [$P=.001$] and class II/III [$P=.002$]) women (Table 4). No interaction of race was observed in the association of BMI and Nugent score (Table 3).

Comment

We report that Nugent scores were higher in overweight (4.53) and obese (class I [4.87] and class II/III [4.93]) women compared with lean (3.90) women. Overweight and obese women also had a higher frequency of BV (overweight [30.4%], obese class I [33.9%], and class II/III [35%]). Because black race is a risk factor for both BV and obesity in women,^{1,44–46} we examined the relationship between BMI and BV by race. Among white women, Nugent scores were higher in obese (class I [3.99] and class II/III [4.08]) women than in lean (3.21) women. White overweight (19.9%) and obese (class I [24.7%] and class II/III [24.2%]) women had a higher prevalence of BV compared with lean (12.5%) white women. However, among black women, this phenomenon was not

TABLE 4
Prevalence ratio of bacterial vaginosis by body mass index category overall and within each race

Body mass index category, kg/m ²	Bacterial vaginosis prevalence, %	Prevalence ratio (95% confidence interval)			Black vs white interaction <i>P</i> value
		Crude	Fully adjusted ^a	Final adjusted ^b	
All women ^c					
<18.5	27.6	1.25 (0.98–1.60)	1.18 (0.92–1.51)	1.20 (0.94–1.54)	.314
18.5–24.9	21.3	Referent	Referent	Referent	Referent
25–29.9	30.4	1.28 (1.15–1.43) ^d	1.23 (1.10–1.36) ^d	1.25 (1.12–1.39) ^d	.024 ^d
30–34.9	33.9	1.36 (1.20–1.53) ^d	1.26 (1.12–1.42) ^d	1.31 (1.16–1.47) ^d	.001 ^d
≥35	35.0	1.31 (1.16–1.48) ^d	1.20 (1.07–1.35) ^d	1.25 (1.11–1.41) ^d	.00 ^d
Black women					
<18.5	38.9	1.11 (0.82–1.50)	1.08 (0.80–1.46)	1.07 (0.79–1.45)	
18.5–24.9	35.2	Referent	Referent	Referent	
25–29.9	39.1	1.11 (0.98–1.26)	1.09 (0.97–1.24)	1.12 (0.99–1.27)	
30–34.9	39.8	1.13 (0.99–1.30)	1.11 (0.97–1.27)	1.14 (1.00–1.31) ^d	
≥35	37.8	1.07 (0.94–1.23)	1.03 (0.90–1.17)	1.07 (0.98–1.18)	
White women					
<18.5	19.1	1.53 (0.96–2.43)	1.37 (0.86–2.18)	1.44 (0.92–2.25)	
18.5–24.9	12.5	Referent	Referent	Referent	
25–29.9	19.9	1.59 (1.28–1.98) ^d	1.42 (1.14–1.76) ^d	1.44 (1.16–1.79) ^d	
30–34.9	24.7	1.98 (1.54–2.53) ^d	1.69 (1.31–2.17) ^d	1.73 (1.35–2.22) ^d	
≥35	24.2	1.94 (1.47–2.55) ^d	1.56 (1.18–2.07) ^d	1.63 (1.23–2.15) ^d	

^a Included income, public assistance, trouble paying for basics, education, number of sex partners in the last 30 days, lifetime number of sex partners, current tobacco use, douching in last 30 days, douching in last 180 days, history of sexually transmitted infection, current sexually transmitted infection; ^b Adjusted for public assistance, education, current smoker, douching in the last 30 days, and sexually transmitted infection at baseline; ^c The All Women models also adjusted for race; ^d Statistically significant value.

Brookheart et al. Obesity and the prevalence of bacterial vaginosis. *Am J Obstet Gynecol* 2019.

present, which suggests that BV occurrence in black women is independent of their BMI. We observed a significant interaction of race and increasing BMI in relation to BV prevalence for overweight ($P=.024$) and obese (class I [$P=.001$] and class II/II [$P=.002$]) women, which suggests that race is an effect modifier of the association of increasing BMI and BV prevalence. Although the interaction of race on the BMI-BV relationship has not been reported previously, studies have shown that obese white women exhibit a higher avoidance of female preventative healthcare services (eg, Papanicolaou test and breast cancer screening), which is a phenomenon not observed in obese black women.^{48,49} Multiple factors likely contribute to the significant interaction among race, BMI, and BV in our study; the previously observed higher level of delay and

avoidance toward preventative genital health services among obese white women may be 1 factor.⁵⁰

Few studies have explored the relationship between BMI and BV prevalence, and a consensus on whether BMI is a risk factor for BV has not been reached. In 1 study of 2906 US women of whom 26.2% were black, 36% of obese women were BV positive; however, after adjustment for confounders, there was no relationship between BMI and BV.³⁷ This apparent discrepancy may be due to our larger sample size ($n=5918$), a larger representation of black women (50.7%), and potential differences in the differential control of confounders and levels of residual confounding between our study and Koumans et al.³⁷ A recent longitudinal study reported obesity was associated with nearly a 20% decrease of BV risk in a cohort of 1946 Kenyan

female sex workers.⁵¹ The longitudinal Kenyan study measured relative risk of BV in obese populations; our cross-sectional study measured prevalence (eg, 1 infers a causal relationship; the other offers association). Differences in the characteristics of the Kenyan cohort and our cohort may also account for the discrepancy between the 2 studies, for example, our larger sample size ($N=5918$ total and $n=3001$ black women vs their $N=1946$). Additionally, their cohort consisted of only African women; our analysis included women of white (41.5%), black (50.7%), and other (7.8%) races. This difference may be important because African and black women exhibit a higher incidence of vaginal microbiota disruption compared with white women^{52,53}; thus, results of 1 race may vary from results of other races. Expanding on this point, our

within-race analyses (Tables 3 and 4) show that, in white women, increasing BMI is associated with a higher incidence of a disrupted vaginal microbiota and increased prevalence of BV; however, for black women, the same comparison did not reach statistical significance. Other differences include a high HIV prevalence (41.8%), and the women studied were sex workers; the obese women in the study also appeared to be more likely to have high CD4 counts compared with normal women. Whether these characteristics influenced BV risk in the Kenyan population was not explored. Additional studies are needed to fully understand the relationship between BMI and BV prevalence in different geographic populations.

Given the complex nature of obesity, mechanisms contributing to the increased occurrence of BV in obese women are expected to be multifactorial. Although reports have shown a positive correlation between overweight/obese women and the presence of BV-associated microbiota,^{33,34} the mechanisms at play remain unknown. Obesity may generate a favorable environment for BV through disturbances in host hormonal, metabolic, and/or immune functions. Diet may also influence the BMI-BV relationship, because certain dietary habits have been associated with BV.^{54,55} A potential role for the gut microbiota in BV is also plausible, because the gut microbiota has been suggested to influence the composition of the vaginal microbiota by serving as an extravaginal reservoir of bacteria.⁵⁶ In addition, given the higher prevalence of menstrual irregularity in obese women, the presence of blood may alter vaginal flora. The role of douching in the BMI-BV relationship should also be considered, because douching is associated with BV and was found in 1 study to be practiced more often among obese women.³⁷ The mechanisms that contribute to the BMI-BV relationship may best be explored via established animal models of obesity and BV,²⁵ which would allow for a causal analysis of the role of specific factors such as obesity-associated hormonal and

metabolic dysfunctions, dietary habits, the gut microbiota, and the synergistic effects these factors may exhibit.

This study had both strengths and limitations. Our 5918 cohort represented a diverse group of women socioeconomically and racially. BMI and Nugent score were determined for each participant by trained clinical staff who used universally approved and established guidelines.^{14,46} Reproducibility of our Nugent scoring was verified by Dr Sharon Hillier's laboratory (developer of the Nugent scoring method¹⁴) for a sample of specimens. In this cohort, 28.1% of women were BV-positive, which is a figure similar to estimates from a representative sample of US reproductive-aged women (29%)⁵⁷; at the time of enrollment, 17.2% of BV-positive women reported symptoms associated with BV, which is a percentage consistent with another report (15.7%),³⁷ thus underscoring the commonly asymptomatic nature of BV from the patient perspective. Limitations in our study included small numbers of underweight and class II and III obese women, a cross-sectional design, and a lack of information on recent antibiotic use. Also, our study focuses on 2 races, black and white, and does not focus on the relationship between BMI and BV in other racial populations, because the sample size of other races in our cohort was small.

Obesity and BV pose serious threats to women's health, and black race is a risk factor for both of these conditions. Our study demonstrates that overweight and obesity are associated with higher Nugent scores and increased prevalence of BV and that the relationship between BMI and BV prevalence varies between black and white women. Our observations indicate additional efforts to understand the relationship between obesity and BV and the influence of BMI on the vaginal microbiome in racially diverse cohorts are highly warranted. ■

Acknowledgments

We thank Jennifer Reed (née Jennifer Bick) for technical assistance with Nugent scoring (employed by Washington University in St. Louis)

and the entire Contraceptive CHOICE Project support staff; Dr Kia Davis in the Division of Public Health Sciences at Washington University School of Medicine for comments on the manuscript. We especially thank Dr Sharon Hillier and her laboratory at the Magee-Womens Research Institute, University of Pittsburgh, for verifying Nugent scoring. We gratefully acknowledge the generosity and commitment of CHOICE participants for their participation in this study.

References

1. Allsworth JE, Peipert JF. Prevalence of bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data. *Obstet Gynecol* 2007;109:114-20.
2. Allsworth JE, Lewis VA, Peipert JF. Viral sexually transmitted infections and bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data. *Sex Transm Dis* 2008;35:791-6.
3. Wiesenfeld HC, Hillier SL, Krohn MA, Landers DV, Sweet RL. Bacterial vaginosis is a strong predictor of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infection. *Clin Infect Dis* 2003;36:663-8.
4. Wiesenfeld HC, Hillier SL, Krohn MA, et al. Lower genital tract infection and endometritis: insight into subclinical pelvic inflammatory disease. *Obstet Gynecol* 2002;100:456-63.
5. Kline KA, Lewis AL. Gram-positive uropathogens, polymicrobial urinary tract infection, and the emerging microbiota of the urinary tract. *Microbiol Spectr* 2016;4.
6. Peipert JF, Lapane KL, Allsworth JE, Redding CA, Blume JD, Stein MD. Bacterial vaginosis, race, and sexually transmitted infections: does race modify the association? *Sex Transm Dis* 2008;35:363-7.
7. Allsworth JE, Peipert JF. Severity of bacterial vaginosis and the risk of sexually transmitted infection. *Am J Obstet Gynecol* 2011;205:113.e1-6.
8. Brotman RM, Klebanoff MA, Nansel TR, et al. Bacterial vaginosis assessed by Gram stain and diminished colonization resistance to incident gonococcal, chlamydial, and trichomonal genital infection. *J Infect Dis* 2010;202:1907-15.
9. Rezeberga D, Lazdane G, Kroica J, Sokolova L, Donders GGG. Placental histological inflammation and reproductive tract infections in a low risk pregnant population in Latvia. *Acta Obstet Gynecol Scand* 2008;87:360-5.
10. Zhang X, Xu X, Li J, Li N, Yan T, Ju X. [Relationship between vaginal sialidase bacteria vaginosis and chorioamnionitis]. *Zhonghua Fu Chan Ke Za Zhi* 2002;37:588-90.
11. Flynn CA, Helwig AL, Meurer LN. Bacterial vaginosis in pregnancy and the risk of prematurity: a meta-analysis. *J Fam Pract* 1999;48:885-92.
12. Holst E, Goffeng AR, Andersch B. Bacterial vaginosis and vaginal microorganisms in

- idiopathic premature labor and association with pregnancy outcome. *J Clin Microbiol* 1994;32:176–86.
13. McGregor JA, French JI, Jones W, et al. Bacterial vaginosis is associated with prematurity and vaginal fluid mucinase and sialidase: results of a controlled trial of topical clindamycin cream. *Am J Obstet Gynecol* 1994;170:1048–60.
14. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. *J Clin Microbiol* 1991;29:297–301.
15. Balkus JE, Richardson BA, Rabe LK, et al. Bacterial vaginosis and the risk of trichomonas vaginalis acquisition among HIV-1-negative women. *Sex Transm Dis* 2014;41:123–8.
16. Guédou FA, Van Damme L, Mirembé F, et al. Intermediate vaginal flora is associated with HIV prevalence as strongly as bacterial vaginosis in a cross-sectional study of participants screened for a randomised controlled trial. *Sex Transm Infect* 2012;88:545–51.
17. Guédou FA, Van Damme L, Deese J, et al. Intermediate vaginal flora and bacterial vaginosis are associated with the same factors: findings from an exploratory analysis among female sex workers in Africa and India. *Sex Transm Infect* 2014;90:161–4.
18. Donders GGG, Vereecken A, Bosmans E, Dekeersmaecker A, Salembier G, Spitz B. Definition of a type of abnormal vaginal flora that is distinct from bacterial vaginosis: aerobic vaginitis. *BJOG* 2002;109:34–43.
19. Meyn LA, Krohn MA, Hillier SL. Rectal colonization by group B *Streptococcus* as a predictor of vaginal colonization. *Am J Obstet Gynecol* 2009;201:76.e1–7.
20. Srinivasan S, Liu C, Mitchell CM, et al. Temporal variability of human vaginal bacteria and relationship with bacterial vaginosis. *PLoS One* 2010;5:e10197.
21. Gajer P, Brotman RM, Bai G, et al. Temporal dynamics of the human vaginal microbiota. *Sci Transl Med* 2012;4:132ra52.
22. Ness RB, Hillier SL, Richter HE, et al. Douching in relation to bacterial vaginosis, lactobacilli, and facultative bacteria in the vagina. *Obstet Gynecol* 2002;100:765–72.
23. Ocelik V, Furár I, De Hosson JTM. Microstructure and properties of laser clad coatings studied by orientation imaging microscopy. *Acta Mater* 2010;58:6763–72.
24. Schwebke JR, Richey CM, Weiss HL. Correlation of behaviors with microbiological changes in vaginal flora. *J Infect Dis* 1999;180:1632–6.
25. Gilbert NM, Lewis WG, Lewis AL. Clinical features of bacterial vaginosis in a murine model of vaginal infection with *Gardnerella vaginalis*. *PLoS One* 2013;8:e59539.
26. Gilbert NM, O'Brien VP, Lewis AL. Transient microbiota exposures activate dormant *Escherichia coli* infection in the bladder and drive severe outcomes of recurrent disease. *PLoS Pathog* 2017;13:e1006238.
27. Turnbaugh PJ, Hamady M, Yatsunenko T, et al. A core gut microbiome in obese and lean twins. *Nature* 2009;457:480–4.
28. Xu X, Grijalva A, Skowronski A, van Eijk M, Serlie MJ, Ferrante AW. Obesity activates a program of lysosomal-dependent lipid metabolism in adipose tissue macrophages independently of classic activation. *Cell Metab* 2013;18:816–30.
29. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. *Annu Rev Immunol* 2011;29:415–45.
30. Ding S, Chi MM, Scull BP, et al. High-fat diet: bacteria interactions promote intestinal inflammation which precedes and correlates with obesity and insulin resistance in mouse. *PLoS One* 2010;5:e12191.
31. Kim K-A, Gu W, Lee I-A, Joh E-H, Kim D-H. High fat diet-induced gut microbiota exacerbates inflammation and obesity in mice via the TLR4 signaling pathway. *PLoS One* 2012;7:e47713.
32. Cani PD, Amar J, Iglesias MA, et al. Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes* 2007;56:1761–72.
33. Oh HY, Seo S-S, Kong J-S, Lee J-K, Kim MK. Association between obesity and cervical microflora dominated by *Lactobacillus iners* in Korean women. *J Clin Microbiol* 2015;53:3304–9.
34. Si J, You HJ, Yu J, Sung J, Ko G. Prevotella as a hub for vaginal microbiota under the influence of host genetics and their association with obesity. *Cell Host Microbe* 2017;21:97–105.
35. Hillier SL, Krohn MA, Rabe LK, Klebanoff SJ, Eschenbach DA. The normal vaginal flora, H₂O₂-producing lactobacilli, and bacterial vaginosis in pregnant women. *Clin Infect Dis* 1993;16(suppl 4):S273–81.
36. Fredricks DN, Fiedler TL, Marrazzo JM. Molecular identification of bacteria associated with bacterial vaginosis. *N Engl J Med* 2005;353:1899–911.
37. Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the United States, 2001–2004; associations with symptoms, sexual behaviors, and reproductive health. *Sex Transm Dis* 2007;34:864–9.
38. Flegal KM, Carroll MD, Kit BK, Ogden CL. Executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. *Arch Intern Med* 1998;158:1855–67.
39. Bjorntorp P, Bray GA, Carroll KK, et al. Obesity: preventing and managing the global epidemic: report of a WHO consultation. *World Health Organ Tech Rep Ser* 2000;894:(i–xii), 1–253.
40. Nguyen NT, Magno CP, Lane KT, Hinojosa MW, Lane JS. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the national health and nutrition examination survey, 1999 to 2004. *J Am Coll Surg* 2008;207:928–34.
41. Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA* 1999;282:1523.
42. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999–2002. *JAMA* 2004;291:2847.
43. Ness RB, Hillier S, Richter HE, et al. Can known risk factors explain racial differences in the occurrence of bacterial vaginosis? *J Natl Med Assoc* 2003;95:201–12.
44. Goldenberg RL, Klebanoff MA, Nugent R, Krohn MA, Hillier S, Andrews WW. Bacterial colonization of the vagina during pregnancy in four ethnic groups: Vaginal Infections and Prematurity Study Group. *Am J Obstet Gynecol* 1996;174:1618–21.
45. Secura GM, Allsworth JE, Madden T, Mullersman JL, Peipert JF. The Contraceptive CHOICE Project: reducing barriers to long-acting reversible contraception. *Am J Obstet Gynecol* 2010;203:115.e1–7.
46. Prevention C for DC and. About Adult BMI. Available at: https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html. Accessed January 1, 2017.
47. Centers for Disease Control. Bacterial Vaginosis - CDC Fact Sheet. 2017. Available at: <https://www.cdc.gov/std/bv/stdfact-bacterial-vaginosis.htm>. Accessed December 12, 2018.
48. Maruthur NM, Bolen SD, Brancati FL, Clark JM. The association of obesity and cervical cancer screening: a systematic review and meta-analysis. *Obesity* 2009;17:375–81.
49. Wee CC, McCarthy EP, Davis RB, Phillips RS. Obesity and breast cancer screening: the influence of race, illness burden, and other factors. *J Gen Intern Med* 2004;19:324–31.
50. Wee CC, Phillips RS, McCarthy EP. BMI and cervical cancer screening among white, African-American, and Hispanic women in the United States. *Obes Res* 2005;13:1275–80.
51. Lokken EM, Richardson BA, Kinuthia J, et al. A prospective cohort study of the association between body mass index and incident bacterial vaginosis. *Sex Transm Dis* 2019;46:31–6.
52. Ravel J, Gajer P, Abdo Z, et al. Vaginal microbiome of reproductive-age women. *Proc Natl Acad Sci* 2011;108(suppl 1):4680–7.
53. Kenyon C, Colebunders R, Crucitti T. The global epidemiology of bacterial vaginosis: a systematic review. *Am J Obstet Gynecol* 2013;209:505–23.
54. Neggers YH, Nansel TR, Andrews WW, et al. Dietary intake of selected nutrients affects bacterial vaginosis in women. *J Nutr* 2007;137:2128–33.
55. Thoma ME, Klebanoff MA, Rovner AJ, et al. Bacterial vaginosis is associated with variation in dietary indices. *J Nutr* 2011;141:1698–704.
56. Marrazzo JM, Fiedler TL, Srinivasan S, et al. Extravaginal reservoirs of vaginal bacteria as risk

factors for incident bacterial vaginosis. *J Infect Dis* 2012;205:1580–8.

57. Allsworth JE, Peipert JF. Prevalence of bacterial vaginosis. *Obstet Gynecol* 2007;109:114–20.

Author and article information

From the Department of Medicine (Dr Brookheart), Center for Women's Infectious Disease Research (Drs Lewis and Lewis), and the Departments of Molecular Microbiology

(Drs Lewis and Lewis) and Obstetrics and Gynecology (Dr A.L. Lewis), Washington University School of Medicine, St. Louis, MO; Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, IN (Dr. Peipert); Department of Biomedical and Health Informatics, University of Missouri, Kansas City School of Medicine, Kansas City, MO (Dr Allsworth).

Received Oct. 25, 2018; revised Dec. 21, 2018; accepted Jan. 23, 2019.

Funding for the Contraceptive CHOICE Project was provided by an anonymous foundation.

A.L.L. has had consulting relationships with Talis Biomedical Corporation, Tennon Therapeutics, and Toltec Pharmaceuticals. A.L.L. and W.G.L. have performed contract research for Metis Therapeutics. J.F.P. receives research funding from Bayer Healthcare Pharmaceuticals, Teva Pharmaceutical Industries Ltd./CooperSurgical, and Merck & Co, Inc, and has served on an advisory board for TEVA/CooperSurgical. The remaining authors report no conflicts of interest related to this project.

Corresponding author: Jenifer E. Allsworth, PhD. allsworthj@umkc.edu