

Table 1. Overview of literature reviewed, BV, 2009-2013

Year	Author	Title / Journal	Study Population	Intervention	Main Finding; Grade (if applicable)	Strengths / Limitations	Implications for Guidelines
Systematic Reviews							
2009	Abad	The role of lactobacillus probiotics in the treatment or prevention of urogenital infections: a systematic review. J Chemotherapy				Less robust methodology than subsequent ones	None
	Honest	Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling. Health Tech Assessment			No effect on PTB <34 wk; PTB <37 wk lower with intermediate flora and BV (RR 0.53, 95% CI 0.34, 0.83, based on 2 studies with 894 ppts)	Delineated symptomatic vs. not; extensive analysis; no newer data	Agrees with USPSTF with no benefit for screening asymptomatic; treat symptomatic
	Oduyebo	The effects of antimicrobial therapy on BV in non-pregnant women. Cochrane Database of Systematic Reviews			Clinda = MTZ, with less AEs; vaginal LB effective	1981-2008; most in symptomatic women. Probiotic studies were Erikson 2005; Anukam 2006 so not new	Efficacy generally similar, AE profiles differ. Role of LB still unclear.
	Senok	Probiotics for the treatment of BV. Cochrane Database of Systematic Reviews			Cure with oral MTZ/probiotic regimen (OR 0.09 (0.03-0.26)) & probiotic / estriol (OR 0.02 (0.00-0.47))	1966-2008	Evidence insufficient to recommend; larger RCT of potential regimens needed
2010	Cottrell	An updated review of of evidence to discourage douching. Am J Maternal Child Nursing			AE's of douching	2002-8	Counsel cessation for prevention; emphasize lack of benefit
	Hilber	Intravaginal (IV) practices, vaginal infections and HIV acquisition: systematic review and meta-analysis. PloS One			Link biologically plausible; conclusive evidence lacking.	Included only longitudinal studies	No HIV protection from IV practices; some might be harmful
	Marrazzo	BV: identifying research gaps proceedings of a workshop sponsored			Research overview		Definitions for

		by DHHS/NIH/NIAID. Sex Transm Dis					clinical trial outcomes
2011	Gillet	BV is associated with uterine cervical human papillomavirus infection: a meta-analysis. BMC Infectious Diseases			Overall OR 1.43 (1.11-1.84); FAIR	Most cross-sectional (except Mao '03), heterogeneous studies; possible reverse causation bias	Potential new consequence of BV; requires confirmation in prospective studies
	Low	Intravaginal practices, BV, and HIV infection in women: individual participant data meta-analysis. PLoS Medicine			Individual practices associated with HIV acquisition (ORs 1.24-1.47); FAIR	Analyzed ppt-level data from 13 prospective cohort studies; low heterogeneity	No HIV protection from IV practices; some might be harmful
2012	Gillet	Association between BV and cervical intraepithelial neoplasia: systematic review and meta-analysis. PloS One			Overall OR 1.51 (1.24-1.83); FAIR	Cross-sectional, heterogeneous studies; possible reverse causation bias	Potential new consequence of BV; requires confirmation in prospective studies
	Mehta	Systematic review of randomized trials of treatment of male sexual partners for improved BV outcomes in women. Sex Transm Dis			Data not conclusive; need for BVAB transmission study	Reviewed 6 RCTs to date	Data inconclusive; no evidence to support routine tx
	Verstraelen	Antiseptics and disinfectants for the treatment of BV: a systematic review. BMC Infectious Diseases			Non-inferiority of chlorhexidine & PHB	Rigorous inclusion criteria; bias assessed; Novakov '10 only new study	Data insufficient to recommend
Diagnosis / Physical Examination							
2009	Anderson	Are a speculum examination and wet mount always necessary for patients with vaginal symptoms? A pilot RCT. J Am Board Fam Med	46 family practice clinic patients with acute vaginal symptoms	Control had exam and microscopy; intervention syndromic mgmt		Symptom resolution was main outcome and assessed by phone	None
	Bravo	Validation of an immunologic diagnostic kit for infectious vaginitis by T vaginalis, Candida spp., and G vaginalis. Diag Microbiol Infect Dis				Depends on detection of antibody to TV, C albicans, G vaginalis	None
	Dumonceaux	Multiplex detection of			Another way of	Heterogeneous	None—see below

		bacteria associated with normal microbiota and with BV in vaginal swabs by use of oligonucleotide-coupled fluorescent microspheres. JCM			detecting and quantifying G vaginalis and A vaginae, and associated with BV by GS	sample sources over long time period	
	Lowe	Accuracy of the clinical diagnosis of vaginitis compared with a DNA probe laboratory standard. Obstet Gynec	535 U.S. military women	Clinical exam, Affirm VPIII; GenProbe CT GC	Exam did not accurately detect most infections	Used unamplified DNA probe, but commonly used in practice	None
	Sobel	Use of the VS-sense swab in diagnosing vulvovaginitis. J Women's Health	193 women with acute vaginitis, 74 controls	VS-Sense swab = pH swab	Worked well as alternative to nitrazine paper		None yet
2010	Menard	Diagnostic accuracy of quantitative real-time PCR assay versus clinical and Gram stain identification of BV. EJCMIID	163 pregnant women		High levels of G vaginalis or A vaginae in BV by GS or Amsel		None yet, but thresholds and species are of interest for targeted BV diagnostics
	Zozoya-Hinchcliffe	Quantitative PCR assessments of bacterial species in women with and without BV. JCM		Applied qPCR to women	High levels of BVAB1 in Nugent score 10; Prevotella genus very common		None yet
2011	Gallo	Accuracy of clinical diagnosis of BV by HIV infection status. STD			No difference in diagnosis of BV by HIV status		Same tests OK for HIV
	Kampan	Evaluation of BV((R)) Blue Test Kit for the diagnosis of BV. J Swed J Midwives	151 women in Malaysia		Good agreement with GS (98.7%)	Disagrees with other evaluations	None
	Levi	Comparison of Affirm VPIII and Papanicolaou tests in the detection of infectious vaginitis. A J Clin Path	431 women undergoing routine Pap smear	Compared yield of these tests		Used unamplified DNA probe, but commonly used in practice; no gold standard	None
2012	Cartwright	Development and validation of a semiquantitative, multitarget PCR assay for diagnosis of BV. JCM			BV PCR assay had sens 95.6%, spec 92.2%; used A vaginae, BVAB2, Megasphaera		None yet, see below
	Mlisana	Symptomatic vaginal	242 women		Vaginal discharge		Confirms need for

		discharge is a poor predictor of sexually transmitted infections and genital tract inflammation in high-risk women in South Africa. JID	followed for 2 y with q 6 mo STD and BV assessment		was only 12.3% sensitive for and 93.8% specific for lab-diagnosed STI (similar for BV)		workup of vaginal discharge and routine STD screening
	Sobel	Diagnosing vaginal infections through measurement of biogenic amines by ion mobility spectrometry. Eur J Ob Gyn Repro Biol		Applied ion mobility spectrometry to women with vaginitis	Sensitivity for BV 95.5%; specificity 98.9%; accuracy 94.4%	Novel method for detecting amines	None yet
2013	Singh	The role of physical examination in diagnosing common causes of vaginitis: a prospective study. STD	197 women with vaginal discharge in STD clinic	Women collected SOV; non-examining clinician based presumptive diagnosis on that and history	High prevalence of BV (63%), TV (19%). Poor correlation between diagnoses; 34% of BV missed.		Confirms need for exam in women c/o vaginal symptoms
Management: Antimicrobials							
2009	Bunge	The efficacy of retreatment with the same medication for early treatment failure of BV. STD	119 women with early treatment failure	Nested cohort study observed outcome with retreatment with same vs. other IV (MTZ/clind)	Cure rates similar	Included follow up over 4 visits; small nos. in final analyses; relatively short follow up period (3 mo)	Limited support for using same regimen in early treatment failure
	Chen	Treatment considerations for BV and the risk of recurrence. JWH	Insurance claims data	Assessed BV recurrence	Oral MTZ, single-dose clind had less recurrence	Diagnosis not confirmed; analysis not controlled for other risks	None
	Perioli	FG90 chitosan as a new polymer for MTZ mucoadhesive tablets for vaginal administration. I J Pharmaceutics	No human involvement	In vitro assessment of new delivery model	Possible new mucoadhesive delivery system for MTZ		None
	Reichman	Boric acid addition to suppressive antimicrobial therapy for recurrent BV (RBV). STD	Uncontrolled non-randomized retrospective chart review of RBV	Women treated with 7 days of oral MTZ; followed by 21 days of IV BA 600 mg/day and if in remission	58 women treated for 77 episodes of RBV. 60 episodes with follow-up. Cure after MTZ and BA therapy 88% - 92%, 7 and 12 wk.	Not controlled or randomized; women with very challenging BV enrolled	Clinical experience with a triple phase maintenance regimen for women with RBV was encouraging

				treated with MTZ gel twice weekly for 16 wk	Cumulative cure at 12, 16, and 28 wk was 87%, 78%, and 65%. Failure of 50% by 36 wk. No AEs of BA.		but requires validation
	Sharma	Phase II clinical trial with Praneem polyherbal tablets for assessment of their efficacy in symptomatic women with abnormal vaginal discharge (an ICMR task force study). Trans Royal Soc Trop Med Hygiene	130 women with symptomatic vaginal discharge (India)	Uncontrolled study of effect of polyherbal IV tablets on symptoms and micro outcomes	65% resolution of small number of women with BV	Uncontrolled study	None
2010	Bohbot	Treatment of BV: a multicenter, double-blind, double-dummy, randomised phase III study comparing secnidazole and MTZ. IDOG	577 ppts with BV (France)	MTZ 500 mg bid x 7 days vs secnidazole 2 g once.	60.1% cure women vs 59.5% ; 95% CI with non-inferiority margin of 10%:[-0.082; 0.0094]). Safety profiles comparable.	Good definition of therapeutic cure; RCT	Supports efficacy of this regimen; not approved in U.S. but widely used in Europe
	Novakov	Comparison of local MTZ and a local antiseptic in the treatment of BV. Arch Gynecol Obstet	“As much as 450 women treated with either 7 days MTZ vaginal tablets, 7 days OHP, or 14 days OHP”			Poorly conducted, poorly described study	None
	Zeng	Directed shift of vaginal flora after topical application of sucrose gel in a phase III clinical trial: a novel treatment for bacterial vaginosis. Chin Med J	560 ppts with BV at 8 hospitals in China	Randomized, double-blinded, multi-center, parallel-group, placebo-controlled phase III clinical trial of vaginal sucrose, MTZ, placebo gel bid x 5 d.	By Nugent score at 7-10 and 21-35 d, cure for sucrose, MTZ, and placebo gel groups were 83.13%, 71.30% and 0.92%, at 1st TOC, and 61.04%, 66.67% and 7.34%, at 2nd TOC. Sucrose gel was more effective than	Paper not available in English; can't assure appropriate conduct	None; biological plausibility is questionable and results not replicated

					MTZ gel at 1st TOC (P = 0.009).		
2011	Bukusi	Topical penile microbicide use by men to prevent recurrent BV in sex partners: a randomized clinical trial. STD	236 women with BV of whom 223 (94.3%) randomized to intervention (male partners apply gel qAM, before, after sex)	Randomized, single-masked clinical trial evaluated the efficacy of topical application of 62% ethyl alcohol in emollient gel to penis by male partners of women with BV for preventing post-treatment BV recurrence	BV more frequent in intervention arm (HR: 1.44, 95% CI: 1.01–2.04). After adjustment HR was 1.39 (95% CI: 0.98–1.99). At 2-mo visit, prevalences of any vaginal lactobacilli or of H2O2-producing lactobacilli did not differ in study arms (P 0.81 and 0.32).		Daily topical use of EtOH gel by male partners significantly increased women's risk of BV
	Schwebke	TNZ vs MTZ for the treatment of BV. AJOG	593 women with BV	Randomized trial of MTZ 500 bid, TNZ 500 bid, or TNZ 1 g bid for 7 days followed up at 14 and 28 d	Overall cure rates were 76.8% at 14 days and 64.5% at 1 month and did not differ by arm; no significant differences in AEs across arms.		No differences in these regimens, with shorter-course TNZ already in guidelines.
	Shaaban	Pilot randomized trial for treatment of BV using in situ forming MTZ vaginal gel. J Ob Gyn Res	42 women with BV	Randomized to MTZ gel or experimental product (MTZ hydrogel)	Cure 71.4% vs. 85.4% for standard vs experimental gel	Very small sample; no power calculations	None
2012	Boselli	Efficacy and tolerability of fitostimoline (vaginal cream, ovules, and vaginal washing) and of benzydamine hydrochloride (tantum rosa vaginal cream and vaginal washing) in the topical treatment of symptoms of BV.	291 women	See title		Very vague inclusion criteria and non-standard endpoint assessment; standard treatment not used as comparator	None

		ISRN OB GYN					
	Cruciani	Efficacy of rifaximin vaginal tablets in treatment of BV: a molecular characterization of the vaginal microbiota. AAC	102 European patients with BV	Multicenter, double-blind, randomized, placebo controlled study of 3 doses of rifaximin vaginal tablets (100 mg/d for 5 d, 25 mg/d for 5 d, and 100 mg/d for 2 d)	By qPCR and PCR-DGGE, increase in members of genus Lactobacillus and decrease in the BV-related bacterial groups after treatment. Rifaximin 25 mg/day for 5 days represents an effective treatment of BV	No comparison to standard treatment but did use placebo. Cure rates detailed in Donders 2013.	None; may be a future option for study for BV.
	Thulkar	A comparative study of oral single dose of MTZ, TNZ, secnidazole and ornidazole in BV. Ind J Pharmacol	344 women with BV by Amsel	See title		Inappropriate statistical tests used; single-dose MTZ (2 g) used as comparator	None
	Weissenbacher	A comparison of dequalinium chloride vaginal tablets (Fluomizin(R)) and clindamycin vaginal cream in the treatment of BV: a single-blind, randomized clinical trial of efficacy and safety. Gynecol Obstet Invest	321 women with BV	Multicenter, single-blind, randomized trial in 15 centers, randomized to vaginal DQC (quaternary ammonium compound) tablets or vaginal clinda cream. Follow-up 1 wk and 1 mo	Cure with DQC (C1: 81.5%, C2: 79.5%) was similar to clinda (C1: 78.4%, C2: 77.6%). [ClinicalTrials.gov, Med380104, NCT01125410].	Thorough analysis of outcomes by Amsel criteria	Preliminary data; no immediate ramifications
2013	Donders	A multicenter, double-blind, randomized, placebo-controlled study of rifaximin for the treatment of BV. Intl J Gyn Obstet	114 white, non-pregnant premenopausal women with BV; 103 evaluable	Randomly assigned to rifaximin at 100 mg for 5 d (100 mg/5 d), 25 mg/5 d, or 100 mg/2 d, or placebo. Cure assessed at 7–10 and 28–35 d.	Cure at 1 st follow-up higher in rifaximin 25 mg/5 d (48%, P=0.04), 100 mg/2 d (36.0%), and 100 mg/5 d (25.9%) groups than placebo (19.0%). At 2 nd follow-up, cure was 28.0%,	Involved no standard BV treatment for comparison	Rifaximin at 25 mg/5 days may offer a future option for BV treatment, but requires further validation in clinical trials.

					14.8%, and 4.0% in respective groups vs 7.7% in placebo. No difference in AE		
Management: Probiotics / Other							
2009	Antonio	Vaginal colonization by probiotic <i>Lactobacillus crispatus</i> CTV-05 is decreased by sexual activity and endogenous <i>Lactobacilli</i> . JID	87 women with BV treated with <i>L. crispatus</i> CTV05 & SD MTZ	Evaluated predictors of vaginal colonization, and safety	Of 40 pts without <i>L. crispatus</i> at enrollment, 90% were successfully colonized; only 51% of 47 participants colonized at enrollment were positive for CTV-05 at follow-up ($P < .001$). Ppts engaging in sexual intercourse with condoms (OR 6.3 [1.3–29.4]; having unprotected sex (OR 75.5 [6.9–820.6]; during first week less likely to become colonized.	Intriguing results that align with known risks for failure of BV to resolve (sexual exposures) and that may inform future probiotic research	Probiotic research is still in the early stages. Failure to colonize the vagina with <i>L. crispatus</i> probiotic strain CTV05 included exposure to semen, vaginal intercourse, and the presence of the same species at time colonization was attempted.
	Hemmerling	Phase 1 dose-ranging safety trial of <i>Lactobacillus crispatus</i> CTV-05 for the prevention of BV. STD	12 women without BV	Dose-ranging for CTV-05 (LACTIN-V)	Product safe and acceptable		None
	Martinez	Improved cure of BV with single dose of TNZ (2 g), <i>Lactobacillus rhamnosus</i> GR-1, and <i>Lactobacillus reuteri</i> RC-14: a randomized, double-blind, placebo-controlled trial. CJM	64 women with BV in Brazil	RCT of 2 g TNZ with either 2 placebo capsules or 2 probiotic capsules qD for 4 wk	Cure at 28 d 87.5% in probiotic (<i>L. rhamnosus</i> GR-1, <i>L. reuteri</i> RC-14) vs 50% in placebo	Implications unclear; small nos. with limited power	None
	Mastromarino	Effectiveness of <i>Lactobacillus</i> -containing vaginal tablets in the treatment of symptomatic BV. Clin Micro Infect					
2010	Donders	Effect of lyophilized <i>Lactobacilli</i> and 0.03 mg estriol (Gynoflor(R)) on vaginitis and vaginosis with	46 women in Belgium (private practice) with	Randomized lyophilized LB with 0.03 mg estriol vs MTZ;	Not much difference in outcomes, but...	Poor retention, small nos, limited power	None

		disrupted vaginal microflora: a multicenter, randomized, single-blind, active-controlled pilot study. Gyn Ob Invest	BV or aerobic vaginitis	vaginal tablets of Gynoflor® or 500 mg MTZsuppositories			
	Ehrstrom	Lactic acid bacteria colonization and clinical outcome after probiotic supplementation in conventionally treated BV and vulvovaginal candidiasis. Microbes Infect	95 women with BV				None
	Hemmerling	Phase 2a study assessing colonization efficiency, safety, and acceptability of Lactobacillus crispatus CTV-05 in women with BV. STD	24 women with BV	Randomized to LACTIN-V or placebo	78% colonized with perfect use at Day 10 or 28	Supports capacity for colonization	None; product safe, but more work needed to demonstrate benefit
	Hummelen	Lactobacillus rhamnosus GR-1 and L. reuteri RC-14 to prevent or cure BV among women with HIV. Intl J Gyn Ob	65 HIV+ women with Nugent >3	Randomized to placebo or probiotic daily x 6 mo	No difference in BV; probiotic associated with normal pH		None
	Marcone	Long-term vaginal administration of Lactobacillus rhamnosus as a complementary approach to management of BV. Intl J Gyn Ob	49 women with BV	Randomized to BID PO MTZ 500 mg for 7 d alone or with once wk vaginal L. rhamnosus x 6 mo	Trend to “Vaginosis-free” state in probiotic group	Small nos; uncertain generalizability; no control	None
	Rossi	The use of Lactobacillus rhamnosus in the therapy of BV. Evaluation of clinical efficacy in a population of 40 women treated for 24 months. Arch Gyn Ob	40 women with BV	Prospective open trial to evaluate L. rhamnosus on pH		Uncontrolled, small	None
	Ya	Efficacy of vaginal probiotic capsules for recurrent BV: a double-blind, randomized, placebo-controlled study. AJOG	120 women with history of recurrent BV in China	Randomized to daily use of IV probiotic for 2 non-consecutive week use vs placebo (L. rhamnosus, L.	Recurrence by ppt report lower in probiotic arm (15.8%) vs. placebo (45%); GV detection lower	Followed women for 11 mo; Small nos; simple statistical analysis; outcomes assessed by self-report (phone)	None

				acidophilus, S. thermophilus)			
2011	Larsson	Extended antimicrobial treatment of BV combined with human lactobacilli to find the best treatment and minimize the risk of relapses. BMC ID	63 women with BV	Treatment with vaginal clinda, LB, IV MTZ, LB, etc	Low levels of LB colonization assessed by repPCR at follow up overall	Mash-up of interventions including male partner treatment; non-randomized/uncontrolled; mix of human LB spp that are well characterized	None from therapy standpoint, but did confirm risk for BV conferred by new partner during follow up
	Lazar	Gynevac-a vaccine, containing lactobacillus for therapy and prevention of BV and related diseases. Akusherstvo i ginekologija	No abstract available				None
	Leite	Randomized clinical trial comparing the efficacy of the vaginal use of MTZ with a Brazilian pepper tree (Schinus) extract for the treatment of BV. Braz J Med Res	277 women with BV	Randomized to 7 d of MTZ IV or 7.4% pepper tree extract	Cure lower with pepper: 12/4% vs 56.4%		Good evidence this product does not work
	Petersen	Efficacy of vitamin C vaginal tablets in the treatment of BV: a randomised, double blind, placebo controlled clinical trial. Arzneimittel-Forschung	277 women with clinical BV	Randomized, double blind, parallel groups, placebo controlled trial on efficacy and safety of 250 mg ascorbic acid in BV (6 d).	In ITT analysis, cure 55.3% with Vit. C (n = 141) and 25.7 % placebo (n = 136). In the per-protocol population, cure 66.4 % with Vit. C (n = 116) and 27.1 % with placebo (n = 118). In a subset with evaluation of vaginal swab, cure in 86.3 % of Vit. C (n = 51) and 7.6 % placebo (n = 53)	No comparison to standard treatment. Abstract only available.	None.
2012	Bohbot	Vaginal impact of the oral administration of total freeze-dried culture of LCR 35 in	20 women	Open label two dose pilot study of oral	Reported improvements in GS score	Uncontrolled	None

		healthy women. IDOG		administration			
	Bradshaw	Efficacy of oral MTZ with vaginal clindamycin or vaginal probiotic for BV: randomised placebo-controlled double-blind trial. PloS one	408 women with symptomatic BV	Double-blind placebo-controlled parallel-group randomization to MTZ-Clind, MTZ-Prob or MTZ-Placebo and assessed at 1,2,3 and 6 months. MTZ and Clind were administered for 7 days and Prob and Placebo for 12 days.	Primary outcome was BV recurrence (NS of 7–10) on self-collected vaginal-swabs over 6-months. Six-month retention rates were 78% (n = 351). One-month BV recurrence rates were 3.6% (5/140), 6.8% (9/133) & 9.6% (13/135) in the MTZ-Clind, MTZ-Prob and MTZ-Placebo groups respectively, p = 0.13. Hazard ratios (HR) for BV recurrence at one-month, adjusted for adherence to vaginal therapy, were 0.43 (95%CI 0.15–1.22) and 0.75 (95% CI 0.32–1.76) in the MTZ-Clind and MTZ-Prob groups compared to MTZ-Plac respectively. Cumulative 6-month BV recurrence was 28.2%; (95%CI 24.0–32.7%) with no difference between groups, p = 0.82; HRs for 6-month BV recurrence for MTZ-Clind and MTZ-Prob compared to MTZ-Plac, adjusted for adherence to vaginal therapy were 1.09(0.70–1.70) and 1.03(0.65–1.63), respectively.	Well conducted study	Good evidence against effect of this particular probiotic in preventing BV recurrence
	Hantoushzadeh	Comparative efficacy of probiotic yoghurt and clindamycin in treatment of BV in pregnant women: a randomized clinical trial. J Mat-Fet & Neonat Med	310 symptomatic pregnant women (third trimester) with BV in Iran			Not well conducted (inadequate statistical methods; endpoint definitions)	None
	Hemalatha	Effectiveness of vaginal	~200 women in			Low power;	None

		tablets containing lactobacilli versus pH tablets on vaginal health and inflammatory cytokines: a randomized, double-blind study. <i>Eu J Clin Micro ID</i>	India with varying GS			attempted to measure cytokines	
	Sudha	Effect of oral supplementation of the probiotic capsule UB-01BV in the treatment of patients with BV. Beneficial microbes	30 women in India, possibly with BV			No abstract available, no comparator arm	None
2013	Ling	The restoration of the vaginal microbiota after treatment for BV with MTZ or probiotics. <i>Microb Ecol</i>				Small nos of women, limited power, heterogeneous group of enrollees	None
Pregnancy: Natural History, Outcome, & Management							
2009	Banhidy	Rate of preterm births in pregnant women with common lower genital tract infection: a population-based study based on the clinical practice. <i>J Mat Fet Neon Med</i>	Population-based data set in Hungary; analysis			Not definitive	None
	Bodnar	Maternal vitamin D deficiency is associated with BV in the first trimester of pregnancy. <i>The Journal of nutrition</i>				Cross-sectional study; causation unclear	None direct
	Diaz-Cueto	Effect of clindamycin treatment on vaginal inflammatory markers in pregnant women with BV and a positive fetal fibronectin test. <i>International journal of gynaecology and obstetrics:</i>			Treatment with oral clinda effected reductions in key cytokines, but not MMP-8 vaginal levels		None direct
	Donders	Predictive value for preterm birth of abnormal vaginal flora, BV and aerobic vaginitis during the first trimester of pregnancy. <i>BJOG</i>	Observational study of 759 women from first prenatal visit	None	Confirmed association between PTB with BV and abnormal flora	Defined aerobic vaginitis; didn't use Nugent	Supports current evidence
	Jesse	Racial disparities in biopsychosocial factors and			Confirmed high prevalence of BV in		None direct

		spontaneous preterm birth among rural low-income women. Journal of midwifery & women's health			A-A women		
Lamont		Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous preterm birth: a systematic review and metaanalysis. AJOG			5 trials with 2346 women included. Clinda given <22 weeks was associated with significantly reduced risk of PTB at <37 wk of gestation and late miscarriage. No differences the risk of PTB at <33 wk, LBW, VLBW, admission to NICU, stillbirth, peripartum infection, and AE.	Note that oral clinda was associated with beneficial outcomes; vaginal wasn't. Moreover, authors note heterogeneity in trials and instability of some estimates (reduction of PTB <37 wk)	Clinda PO in early pregnancy in women with abnormal flora reduces risk of sPTB at <37 wk & late miscarriage. Data to justify further RCT of clinda for prevention of PTB
Lee		A high Nugent score but not a positive culture for genital mycoplasmas is a risk factor for spontaneous preterm birth. The journal of maternal-fetal & neonatal medicine					Confirms prior observations
Mania-Pramanik		BV: a cause of infertility? International journal of STD & AIDS	72 women with infertility; 450 without		Higher BV prev in infertility	Cross-sectional analysis	None
Mitchell		Changes in the vaginal microenvironment with MTZ treatment for BV in early pregnancy. Journal of women's health	126 pregnant women	RCT of oral (250 mg tid) vs vag MTZ in early preg (<20 wk)	33-34% therapeutic cure	Trial stopped early for futility, thus nos. were small; sialidase findings unclear. Blinded study	No concerns for safety, but disappointing levels of cure
Msuya		The effectiveness of a syndromic approach in managing vaginal infections among pregnant women in northern Tanzania. East African journal of public health				Abstract only available	Confirmed poor performance of current symptom-directed approach
Nelson		Preterm labor and BV-associated bacteria among urban women. Journal of	Prospective cohort study of 50 pregnant	Assessed individual levels of BVAB and	High levels of GV and low L crispatus predicted SPTB		Confirmed role of BVAB in AOP

		perinatal medicine	women	LB			
	Shahin	Effect of oral N-acetyl cysteine on recurrent preterm labor following treatment for BV. International journal of gynaecology and obstetrics					
	Uscher-Pines	Racial differences in BV among pregnant women: the relationship between demographic and behavioral predictors and individual BV-related microorganism levels. Maternal and child health journal	Prospective cohort study of 1886 pregnant women, 73% A-A		46% BV prevalence in A-A. Associated BV risks: smoking, mult SP, unmarried	Well designed	Confirmed some risks for BV in important cohort
2010	Digiulio	Prevalence and diversity of microbes in the amniotic fluid, the fetal inflammatory response, and pregnancy outcome in women with preterm pre-labor rupture of membranes. Am J Repr Imm			Detected previously uncultivated BVAB in amniotic fluid in pPROM		None
	Farquhar	Illness during pregnancy and BV are associated with in-utero HIV-1 transmission. Aids	Prospective study of 463 HIV+ mothers/infants		BV at 32 wk had 3x increase (1.2-5.8) after adjusting for viral load		New data to support role of vaginal microbiome in potentiating HIV vertical transmission; note, but require more data
	Lim	Is there a correlation between BV and preterm labour in women in the Otago region of New Zealand? Austral & New Zealand J of obstetrics & gynaecology					Supports previous conclusions
	Luong	Vaginal douching, BV, and spontaneous preterm birth. JOGC	Nested case-control study in a prospectively recruited cohort of pregnant	PTB in 207 of 5092 women (4.1%). In MVA, BV not associated, but a significant			Vaginal douching appears to be an independent and potentially modifiable risk factor for early

			women. Spontaneous preterm births before 37 weeks' gestation were cases. All spontaneous births occurring after 37 weeks were potential controls.	association with early PTB < 34 weeks (OR, 6.9; 95% CI 1.7 to 28.2) and preterm birth due to preterm labour (OR 3.0; 95% CI 1.1 to 8.5) persisted after controlling for BV and placental inflammation.			preterm birth (32-34 weeks)
	Menard	High vaginal concentrations of Atopobium vaginae and Gardnerella vaginalis in women undergoing preterm labor. Ob Gyn	90 women admitted for SPT labor with intact membranes	See title			Limited
2011	Anderson	Effect of antibiotic exposure on Nugent score among pregnant women with and without BV. Og Gyn			No effect on PTD; no change in Nugent score if initially normal		Supports lack of AEs associated with antibiotic treatment in pregnancy
	Briery	Treatment of BV does not reduce preterm birth among high-risk asymptomatic women in fetal fibronectin positive patients. J Mississippi State Medical Association	232 women at high-risk for spontaneous preterm delivery	Tested for BV/fFN at 20-28 weeks gestation & treated with MTZ; no differences in outcomes by BV status	In asymptomatic high-risk women, testing for fFN/BV during mid-pregnancy does not appear warranted.	Abstract only	Supports current guidance
	Cauci	High sialidase levels increase preterm birth risk among women who are BV-positive in early gestation. AJOG	707 BV+ pregnant women		Elevated sialidase levels were associated with early sPTD and late miscarriage	Direct linear associations between sialidase and AOP	None direct
	Hensel	Pregnancy-specific association of vitamin D deficiency and BV. AJOG	NHANES data analysis of Vitamin D		VDD associated with BV only in pregnant women	Cross-sectional analysis; reverse causation possible	Confirms known risks for BV in non-pregnant

			deficiency as BV risk		(AOR 2.87;1.13-2.37). In non-pregnant women, risks were smoking, douching, black race (+) and OCP (-)		women with addition of OCP; new info on VDD in pregnancy
	Krauss-Silva	A randomised controlled trial of probiotics for the prevention of spontaneous preterm delivery associated with BV: preliminary results. Trials	Oral probiotic vs placebo through 24 th -26 th week in pregnancy (644)			Low retention; inconclusive results	None
	Selim	Effect of MTZ to bacterial flora in vagina and the impact of microbes on live birth rate during intracytoplasmic sperm injection (ICSI). Arch Gyn OB	71 women who were undergoing ICSI.	At embryo transfer (ET), all of the women had quantitative vaginal culture, ET catheter-tip culture, and vaginal Gram stain	The overall live birth rate (LBR) was 36.6% (26/71), and the rate of early pregnancy loss was 13% (4/30). In women with BV, intermediate flora and normal flora, the conception rates were 35% (9/26), 42% (14/33) and 58% (7/12), respectively ($p = 0.06$ for trend). The predominant species isolated from the tip of the embryo transfer catheter in negative pregnancy was <i>S epidermidis</i> (7 vs. 15.2%), and <i>S viridians</i> (11 vs. 24%).	Abstract only; not definitive given small numbers.	None
2012	Harper	The interaction effect of BV and periodontal disease on the risk of preterm delivery. Am J Perinatol	Secondary analysis of cohort data (PIPS); 792		No effect of BV or PD on sPTD		None

			women with BV				
	Lamont	Rescreening for abnormal vaginal flora in pregnancy and re-treating with clindamycin vaginal cream significantly increases cure and improvement rates. Intl J STD AIDS	199 pregnant women treated with vag clinda x 3 d vs 205 treated w/ placebo	Repeat treatment with clinda in those who failed or recurred			Similar to Bunge 2009, supports value of repeat treatment with same agent
	Laxmi	Association of BV with adverse fetomaternal outcome in women with spontaneous preterm labor: a prospective cohort study. J Mat-Fet Neonat Med		Neonatal adverse outcomes more common in BV		Small study in India; results c/w other large studies	Not new
	Sioutas	Effect of BV on the pharmacokinetics of misoprostol in early pregnancy. Human reproduction					None
	Sungkar	Influence of early self-diagnosis and treatment of BV on preterm birth rate. IJGO					
2013	Brocklehurst	Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane database of systematic reviews			21 trials with 7847 women; concluded no effect of antibiotics in preventing PTB; did find them to prevent late miscarriage; advantage for oral antibiotics over vaginal with respect to admission to neonatal unit (RR 0.63; 0.42 to 0.92; 2 trials with 156 women, prolongation of gestational age (MD 9.00; 8.20 to 9.80; one trial, 156 women, and birthweight (grams) (MD 342.13; 95% CI 293.04 to 391.22; one	Reasonable discussion regarding exclusion of many symptomatic women from screening studies	Supports no change in current guidelines

					trial, 156 women).		
	Mangot-Bertrand	Molecular diagnosis of BV: impact on IVF outcome. EJCMIID			No differences seen in outcomes		None
	Salah	BV and infertility: cause or association? EJOGRB	Cohort study of 874 infertile women in Egypt & 382 fertile controls	Higher BV prev in infertile (esp PCOD); treatment improved fertility rates		Uncontrolled, complicated sequential design; causality uncertain	Interesting area for future research
Prevention							
2009	Yotebieng	Effect of consistent condom use on 6-month prevalence of BV varies by baseline BV status. Trop Med Intl Health	FSW cohort in Madagascar	BV assessed at baseline & 6 mo	56% BV+ at entry; 72% had BV at 6 mo, compared to 39% incidence in BV- group at that time. Consistent condom use protected vs incident but not recurrent BV (PR 0.57;0.3-0.9)	Vaginal micro assessed at two widely separated time points; self-report of condom use	Supports other observational data that speak to protective effect of condoms in maintaining healthy vaginal flora
2011	Balkus	Establishing and sustaining a healthy vaginal environment: analysis of data from a randomized trial of periodic presumptive treatment for vaginal infections. JID	310 FSW in Mombasa Kenya (secondary analysis)	Oral periodic presumptive treatment with fluconazole and 2 g MTZ given monthly vs placebo	Healthy effect of intervention:		Supports use of antimicrobials to prevent BV, but data are still limited
	Christian	Maternal vitamin A and beta-carotene supplementation and risk of BV: a randomized controlled trial in rural Bangladesh. Am J Clin Nutr			BV prevalence and incidence lower 3 mo postpartum in Vit A rel to placebo	Variable and some low rates of follow-up; no effect in third trimester; BV assessed at only 3 points	Intriguing data; need more
	Marrazzo	A behavioural intervention to reduce persistence of BV among women who report sex with women: results of a randomised trial. STI	RCT of behavioral intervention to reduce risk of sharing vaginal fluid		Despite reduction in targeted behavior, no effect on BV cure 30 d post-treatment	Looked longer out from treatment; no difference	Data insufficient to recommend this

	McElligott	Preoperative screening strategies for BV prior to elective hysterectomy: a cost comparison study. AJOG	Cost minimization model using literature estimates		Optimal strategy was treat all for BV; test all and treat if positive was slightly more		Support for routine or directed treatment
2012	Balkus	The posttrial effect of oral periodic presumptive treatment for vaginal infections on the incidence of BV and Lactobacillus colonization. STD	165 FSW in PPT trial examined for post-PPT cessation BV incidence		Not sustained		Suppressive effect of antibiotic maintenance is not longlasting
	Cohen	Diaphragm used with replens gel and risk of BV: results from a randomized controlled trial. IDOG			No change in risk of BV	MIRA trial	Evidence vs weak acidifying agent
	Coste	Safety and efficacy of an intravaginal prebiotic gel in the prevention of recurrent BV: a randomized double-blind study. Ob Gyn Intl	42 women previously treated for BV	Randomized to active prebiotic gel APP-14 vs placebo for 16 d		Not significant—very small nos	
	Pham	Screening for BV at the time of intrauterine contraceptive device insertion: is there a role? JOGC	Observational prevalence study of 70 women seeking IUD (38 copper, 32 LNG)	Followed for 1 month	The prevalence of BV was 7.1%. 5 women with BV at the time of IUD insertion, and none experienced any clinical no significant relationship between a patient's BV status and any clinical outcome.	Abstract only; low BV incidence	Authors do not recommend BV screening prior to IUD insertion