TV Reporting

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Hoots (2013)[3]	Review	CDC commentary	Should TV infection be reportable in the United States?	Reviewed indices of public health importance: frequency, severity, disparities, costs, preventability, communicability, and public interest	**TV should not be a nationally reportable condition at this time**, because it clearly meets only 3 of 7 criteria warranting additional surveillance (frequency, disparities, and communicability)	Recommendation could change with new data on costs, severity, preventability, and/or public interest	B
Owusu-Edusei (2013)[4]	Economic model	United States men and women	Estimated costs of 8 major STIs in the United States (chlamydia, gonorrhea, HBV, HIV, HPV, HSV-2, syphilis, and trichomoniasis) based on incidence estimates from 2008	Lifetime cost per case	All 8 STIs: total lifetime direct medical costs estimated at $15.6 billion in 2008. **Direct costs per year for incident TV cases in the United States: $24 million** (range, $12–36 million) **This is the lowest estimated cost of any of the 8 major STIs in the United States** Estimated lifetime cost per case of trichomoniasis: $22 (range, $11–$33)	Assumed no sequelae of untreated cases Assumed that 30% of infections are symptomatic and only 85% of these will be treated Assumed average direct cost of trichomoniasis: $121 in private settings, $69 in public settings	C

0. Epidemiology of TV

a. Women

CITATION	STUDY DESIGN	STUDY POPULATION TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Satterwhite (2013)[5]	Meta-analysis	TV estimates from national projections based on data from NHANES, NDTI, and ADD Health studies	Estimated burden of 8 STIs in the United States as of 2008	TV prevalence and incidence among U.S. men and women age 15-49	All 8 STIs: 110 million prevalent and 19.7 million incident infections in the United States in 2008. **TV is the most prevalent curable (non-viral) STI** **Estimated TV prevalence: 3.7 million** (= 2.3 million women + 1.4 million men) **Estimated TV incidence: 1.1 million** (= 680,000 women + 415,000 men)	Prevalence based on NHANES but few reliable sources of incidence data. Estimates of infections in males projected based on female data.	C
Sutton (2007)[6]	National cross-sectional survey N=3,754	Nationally representative sample of women age 14-49 who consented to participate NHANES 2001-2004	ACASI interview Self-collected vaginal swab TV PCR at CDC	TV prevalence and risk factors	**Prevalence in U.S. adult women 3.1%** (CI:2.3-4.3) - **Black women, 13.3%** (CI:10-17.7) - Mexican-American, 1.8% (CI:0.9-3.7) - White women, 1.3% (CI:0.7-2.3) Risk factors: race, older age, born in US, less education, douching, more lifetime sex partners **85% of TV-infected women asymptomatic**	Testing by in-house PCR research test Symptoms not assessed by STD clinicians	A
Ginocchio (2012)[7]	Cohort study N=7,593	Women age 18-89 undergoing GC/CT testing	Discarded urogenital samples tested for TV using APTIMA NAAT	TV prevalence	TV prevalence overall: **8.7%** - **Women in jails: 22.3%** - Black women: 20.2% - Women in family planning clinics: 5.4% **Higher TV prevalence in women >40 years (>11%),** unlike GC/CT prevalence higher in younger women.	Higher prevalence in older women may reflect screening bias since older women more likely to be tested for symptoms (rather than screened)	B

Nijhawan (2011)[8]	Prospective cohort study (HIV Epidemiology Research Study) N=1310 (871 HIV+ and 439 high-risk HIV- women)	Women in 4 urban centers (Bronx, NY; Detroit, MI; Providence, RI; Baltimore, MD) recruited during 1993-1995, with	Interviews and physical exams q6months for up to 7 years. Testing for TV by saline wet mount and/or Pap smear, then by culture starting at visit 4	Association between history of incarceration with and STI (TV, CT, GC, or syphilis)	724 (55%) were found to have a sexually transmitted infection on at least one occasion during the study and 427 (33%) reported being incarcerated on at least one occasion. TV 21%, CT 4.3%, GC 0.6%, syphilis 8%. **Incarceration was significantly associated with TV infection (between-subject, OR 2.4; CI:1.85–3.14)** and (within-subject, OR 1.56; CI: 1.26 –1.92), even after adjusting for age, race, HIV status, enrollment risk group, number of sexual partners, marital status, education, BV, vaginal candidiasis, drug use (crack, cocaine, heroin), alcohol use, health insurance, receipt of public assistance, employment status, visit number, and study site.	Neither CT, GC, nor syphilis was significantly associated with incarceration in this study.	B
Meites (in preparation)[9] (unpublished)	Cross-sectional N=59,176	Women visiting 15 U.S. STD clinics in 6 geographically disparate states (SSuN) in 2010-2011	Routine clinical care by STD clinicians. Nearly all used wet mount testing. None used NAATs routinely.	TV prevalence	**Prevalence in women at U.S. STD clinics**: - HIV-infected women tested/screened: **29.3%** - Symptomatic women tested for TV: **26.2%** - Asymptomatic women screened for TV: **6.5%** Geographic disparities (increased in south) Most SSuN STD clinics use wet mounts and clinical factors to diagnose TV, despite CDC guidelines to test symptomatic women.	Not nationally representative	B

Gaydos (2011)	Cross-sectional survey N=1525	Sexually active women age ≥14 requesting free STD test kit online between 2006-2012	Self-collected vaginal swab returned by US mail APTIMA NAAT	TV prevalence	**TV prevalence in participating women: 10%** Risk factors included: - lacking bachelor's degree (aOR 5.53) - residence in Illinois (aOR 3.85) - having ≥16 sex partners in past yr (aOR 3.51) - not always using condoms (aOR 3.04) - black race (aOR 2.69) - being bisexual (aOR 2.0) - having a partner with a previous STI (aOR 1.71) - having 2-15 sex partners in past yr (aOR 1.60) - lacking health insurance (aOR 1.57)	Internet participation may not be representative	B
Sutcliffe (2010)[10]	Cross-sectional N=624	Female inmates age 18-45 were recruited at 2 female-only prisons in the Midwest and New England in 2001	Participants completed a self-administered questionnaire and provided self-collected first-catch urine and vaginal swab specimens. Thawed specimens were tested for TV DNA by PCR	Prevalence of TV among incarcerated women	**Overall TV prevalence in female prisoners 8.5% (prison 1: 8.5%; prison 2: 8.3%)** Urine PCR sensitivity 66.7% Vaginal swab PCR sensitivity 84.4%. The only significant positive correlate of TV infection was lower household income before arrest. No differences were observed by age, race/ethnicity, education, marital status, or length of incarceration.	Did not assess douching Testing thawed rather than fresh specimens might underrepresent the true number of TV infections	

Freeman (2010)[11]	Cross-sectional N= 713 men, 297 women, and 5 trans	Incarcerated persons in the San Francisco county jail, tested diagnostically because of symptoms or routinely screened for CT and GC (in men age 18-30 and women age 18-35) during Jan-April 2008.	APTIMA NAAT on urine specimens also tested for CT/GC	Prevalence of TV among incarcerated individuals	**Prevalence among incarcerated women:** **- TV: 32.0% (95/297)** - CT: 3.4% - GC: 1.7% Prevalence among incarcerated men: **- TV: 2.1%** (15/713) - CT: 4.3% - GC: 1.1% TV was detected in 24.8% of women ≤25, compared with 38.1% of women >25 (P=0.015)	Unknown what proportion of specimens were submitted for screening versus diagnostic testing	B
Miller (2008)[12]	Cross-sectional N=135	African American women age ≥16 who used drugs (heroin, crack, or noncrack cocaine in the past 30 days or used marijuana daily) were screened for Trichomonas vaginalis by PCR during 2003-2005	Women were administered a structured questionnaire in a community-based research center, underwent serological testing for HIV and HSV-2 and were screened for GC and CT	Incidence and risk factors for TV among African-American women who use drugs	51 women (38%) screened positive for TV at baseline. Twenty-nine (31%) of 95 women with negative results of baseline tests became infected, for an incidence of 35.1 cases per 100 person-years at risk (CI: 23.5– 49.0). Prevalent infection was associated with crack use in the past 30 days, and incident infection was associated with having >1 male sex partner in the past 30 days. Women who reported having >1 partner were more likely to acquire TV (HR 4.3; CI: 2.0 –9.4).	Self-reported behaviors in past 30 days only	B

Willers (2008)[13]	Cross-sectional analysis, data from Project CONNECT N=205 of 1086 eligible	Women age <35 at risk for unplanned pregnancy entering jail in Rhode Island	Incarcerated women were interviewed by a research assistant. Self-collected vaginal swabs were tested for STIs, including NG and CT by PCR and TV by InPouch culture.	Factors associated with prevalent STIs among incarcerated women	**68/205 (33%) incarcerated women had an STI** **- TV: 45 (26%) positive for TV** - CT: 27 (14%) positive for CT - GC: 21 (11%) positive for GC On bivariate analysis, factors associated with STI included 6 or more sexual partners in the last year (RR 1.84; CI:1.01-3.36), exchanging sex for drugs/money (RR 1.65; CI 1.01-2.69), and homelessness (RR 1.82; CI 1.07-3.09).	Of 1086 eligible, 707 were released before evaluation and 155 refused to participate	B
Shuter (1998)[14]	Prospective study N=213	Pregnant prisoners attending prenatal clinic at Rikers Island jail for women in New York City in 1996-1997	Patients participated in an interview regarding sexual and drug-related behaviors, and underwent direct culture for TV in addition to routine testing for syphilis, GC, and CT.	Prevalence of TV among incarcerated female prisoners in New York City	**TV prevalence among pregnant incarcerated women was 46.9%. 61% African-American.** On univariate analysis, there was a significant association between TV and older age, crack use, prostitution, known HIV infection, and positive serological test for syphilis. Multivariate analysis showed a significant association of TV with crack use and positive serological test for syphilis.	TV tests by culture only since study performed too early for NAAT	B

b. Men

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Satterwhite (2013)[5] (duplicate)	Review	TV estimates from national projections based on data from NHANES, NDTI, and ADD Health studies	Estimated burden of 8 STIs in the United States as of 2008	TV prevalence and incidence among U.S. men and women age 15-49	All 8 STIs: 110 million prevalent and 19.7 million incident infections in the United States in 2008. **TV is still the most prevalent non-viral STI** **Estimated TV prevalence: 3.7 million** (= 2.3 million women + 1.4 million men) **Estimated TV incidence: 1.1 million** (= 680,000 women + 415,000 men)	Prevalence based on NHANES but few reliable sources of incidence data. Estimates of infections in males projected based on female data.	C
Munson (2013)[15]	3-year retrospective N=622	Men within a regional health care system in Miwaukee, WI	Urethral swab and first-void urine screening for TV tested by ASR, TMA-based assay	TV prevalence in males	**6.6% of men were positive for TV** Average age of a TV-infected male (39.9 years) was significantly greater than those for CT or GC (27.6 and 25.9 years, respectively; P<0.001). Delineation of all specimens by ZIP code of patient residence revealed 11 predominant ZIP codes with respect to testing volume and detection rates. Seven of these 11 ZIP codes contained majority African American populations. The aggregate TV detection rate trended higher than that of the remaining four ZIP codes, which were comprised primarily of Caucasian populations (8.9% versus 5.0%, respectively; P=0.15).	Race data unavailable for 97% of TV-positive specimens	B

Gaydos (2013)[16]	Cross-sectional survey N=1,699	Sexually active men age ≥14 requesting free STD test kit online between 2006-2012	Self-collected penile-meatal swab returned by US mail APTIMA NAAT	TV prevalence	**TV prevalence in participating men: 3.7%** Risk factors included: - residence in Illinois (aOR 12.02) - age 30–39 years (aOR 6.63) - age >40 years (aOR 5.31) - black race (aOR 2.67)	Internet participation may not be representative	B
Mayer (2012)[17] Includes unpublished data (Brooks, personal communication, 2013)	Prospective observational cohort N=557 (365 MSM, 73 MSW, 119 W)	HIV-infected adults in primary care in 4 US cities (Sun Study) with at least 6 months of followup	ACASI For TV testing, women were screened using self-collected cervicovaginal samples while men were screened using centrifuged urine pellets In-house PCR at Emory	STD prevalence, incidence, and risk factors	Thirteen percent of participants had a prevalent STD at enrollment and 7% had an incident STD 6 months later. Among women: - baseline: 14% had prevalent TV infection - incident infections: 3 (3%) in 6 months Among men: - baseline: 0% had prevalent TV infection - incident infections: 0 (0%) in 6 months In men, only 1 incident TV infection detected at 1 year, and 1 positive at 3 years, both in MSM out of 2,228 visits by MSM (unpublished)	Testing method used in men (centrifuged urine) might have lower sensitivity for TV than testing method used in women (swabs) with this in-house PCR test – reagents not validated on urine	B
Kelley (2012)[18]	Longitudinal cohort N=319 black MSM plus N=281 white MSM	Black and white MSM age 18-39 in Atlanta, GA, not in a mutually monogamous relationship (Emory InvolveMENt study) between July 2010-Feb 2012	Surveyed and tested for urethral TV and other STIs Men were screened using centrifuged urine specimens In house-PCR at Emory	Individual-, dyadic-, and community level factors that may explain disparities in HIV and STI incidence	None of the urine specimens from black MSM (0%, CI:0–0.94%) or white MSM (0%, CI:0–1.06%) tested positive for urethral TV. TV testing was discontinued in this study.	Used same testing protocol as Sun study (above); might have low sensitivity for TV in men	B

Kacker (2012)[19]	Markov-based Monte Carlo simulations	Birth cohort of men and women in the United States	Expected change in the prevalence of male circumcision (MC)-reduced infections and resulting health care costs associated with continued decreases in MC rates.	Lifetime direct medical cost (2011 US$) and prevalence of MC-reduced infections	Reducing the MC rate to 10% will increase lifetime health care costs by $407 per male and $43 per female. Among males, lifetime prevalence of human immunodeficiency virus infection is expected to increase by 12.2% (4843 cases), high- and low-risk human papillomavirus by 29.1% (57 124 cases), herpes simplex virus type 2 by 19.8% (124 767 cases), and infant urinary tract infections by 211.8% (26 876 cases). **Among females, lifetime prevalences are expected to increase of trichomoniasis by 51.2% (64 585 cases),** bacterial vaginosis by 51.2% (538 865 cases), high-risk human papillomavirus by 18.3% (33 148 cases), and low-risk human papillomavirus by 12.9% (25 837 cases)..	Model	C
Sosman (2011)[20]	Cohort (part of Project START) N=178	Young men released from prisons in Mississippi, Rhode Island, and Wisconsin	Participants completed ACASI and screening for GC, CT, TV, HBV, HCV, and syphilis 6 months after release. TV PCR on urine	Association between STI and recent incarceration	Of recently incarcerated men, 79% reported unprotected vaginal or anal sex, and 26% tested positive for ≥1 STI: (CT 12%; **TV 8%;** HCV 6%; GC 1%; HBV 1%, syphilis 0%). Mean age 22.5 years, mean incarceration 2.5 years, 46% black. Active STI (GC, CT, or TV) was associated with less education (OR 2.25; P<0.05).	Unclear time period of infection and 5.3% self-reported a prior history of trichomoniasis.	B

Freeman (2010)[11] (duplicate)	Cohort N= 713 men, 297 women, and 5 trans	Incarcerated persons in the San Francisco county jail, tested diagnostically because of symptoms or routinely screened for CT and GC (in men age 18-30 and women age 18-35) during Jan-April 2008.	APTIMA NAAT on urine specimens also tested for CT/GC	Prevalence of TV among incarcerated individuals	Prevalence among incarcerated women: **- TV: 32.0%** (95/297) - CT: 3.4% - GC: 1.7% Prevalence among incarcerated men: **- TV: 2.1%** (15/713) - CT: 4.3% - GC: 1.1% TV was detected in 24.8% of women ≤25, compared with 38.1% of women >25 (P=0.015)	Unknown what proportion of specimens were submitted for screening versus diagnostic testing	B
Sena (2007)[21]	Prospective multi-site study (3 STD Clinics) N=540 women (with and without partners) N=261 men	Male partners of women attending 1 of 3 STD clinics, identified with TV (wet prep or cx), who had had vaginal sex in past 60d, no metro in past 4 wk. Women notified male partners, eligible if presented to clinic with female partner or w/in 30d, ≥18y and spoke English.	Men: urethral gs, syphilis sero, urethral swab for TV cx, 20mL FVU for TV cx, TV PCR, NG and CT PCR; semen specimen (w/in 24h enrollment) for TV cx and PCR. Women: vaginal swab for WM, smear, cx; CT, NG, syphilis testing.	Proportion of concordant TV infections using cultures and PCR of male urine, semen and urethral swabs	540 women consented, 287 male partners consented, analyses limited to 261 most frequent partners. TV prevalence in women 20.6%. Median age females 29 and males 30. Majority AA (>90%). 53.4% women with BV, 13% CT, 10.9% NG. 10.9% males CT, 10.3% NG. **Of 247 male partners who provided urethral cx, urine cx and PCR, 177 (71.7%) had TV**. Only 40 men (15.6%) would have been found to be infected through urethral or urine cx alone. Among 53 men who also provided semen, 81.1% with concordant TV. 76.8% infected men asymptomatic. 21% had urethral d/c on exam and 34% with >/=5 WBC/hpf on gs. Abnormal vaginal pH and younger age of men (<40y) independently associated with concordant infection.	Unable to enroll all eligible men and women. Only 48% male partner enrolled and analyses limited to most frequent sex partner	IIA

Sosman (2005)[22]	Cross-sectional study N=42	STD substudy for men who had completed a 6mo post-release interview as part of prior longitudinal cohort study. 18-29yo, **incarcerated at least 3 mo** during 1999 in CA, MS, RI or WI.	Interview Blood for HBV serologies, HCV Ab, RPR, Urine for NG, CT (LCR) And TV (PCR)	Prevalence of STDs	90 of 106 available for 6mo f/u interview. 15 reincarcerated leaving 75 eligible. Only 42/75 eligible men agreed to participate. No statistical difference between participants and nonparticipants 46%<25yo, 69% AA or hispanic, 66% <hs education. Participants incarcerated mean 2.8yrs since age 18. **9% with TV** 9% with CT 0 with NG 7% previous syphilis All infected men were asymptomatic	Only approx. half of eligibles participated. Specimens were not available for all (i.e. only 32 submitted urine) No info regarding current sexual risk	B

Khan (2005)[23]	Cross-sectional study N=210 hetero dyads (101 males/109 females)	Heterosexual males and females 15-25 yo visiting STD clinic (IN), regardless of sx. Eligibility: Sex/30d, willing to identify all sex partners/30d, English speaking Exclude: Ab use 30d, known HIV/immuno condition, sexual assault, emotional/ MH condition not conducive to partner notification	Enrollment questionnaire, face-to-face interview re: sexual behaviour details. First enrolled subject designated index. Index provided info up to 4 sex partners/30d. A partner could be index for additional partners. TV – PCR vaginal (F)/urine(M) GC Culture (cervical, rectal (F), urethral (M) CT Culture (cervical, urethral (F) NAATS (cerv, vag, urethral, urine (M+F)	Prevlence of TV, CT, NG in partners of index patients infected with TV, CT, NG	Majority black, mean age 21y, 60% only 1 partner/30d, Median coital events 5 (1-73)/30d. **STD prevalence entire popln: 41% CT, 15% GC, 14% TV.** Index: 46% CT, 18% GC, 14% TV – many co-infected 210 Dyads: 55 (26%) uninfected (neither member with any of 3 infections); **155 (74%) had 1 or both members infected** with one or more organisms. 78 dyads with both members infected, 63% with identical infxn. 37% partner had different infxn than index. Of index patients with CT only, 11% were infected with TV. Of index patients with GC only or GC-CT, 20% only had TV. Among 19 TV+ index patients, 6 (32%) partners had TV only, 1 (5%) partner had CT, 1 (5%) partner had GC, and 1 partner with TV-CT coinfection. In 10 partners (53%), no infxn found. 19 /74(26%) partners of Uninfected index patients were infected, mostly with CT (84%)	STD clinic – generalizability issue Women had more specimens/sites collected than males. Gender of partner/index not delineated in paper. Only partners able to be recruited were included, not mentioned in paper how many unable to be contacted, refused, etc.	B

Price (2004)[24]	Cross-sectional survey N=1187	Malawi. Men attending STI clinic with sx urethritis &/or GUD and men attending a derm clinic w/o STI. Enrolled in 2000	TV cx of urethral swab and urine. TV PCR of urine. Gram stain and GC/CT NAAT	Prevalence evaluation	**54 TV+ (13%) at the derm clinic**, and **150 TV+ (20%) at the STI clinic**. 4/54 (7%) TV+ at derm clinic had subclinical urethritis, rate not significantly higher than men w/o TV (21/377 {6%}) . In Derm clinic TV+ significantly assoc. w/older age (>20y) (but not at STI clinic.) Never using condoms was assoc with TV in derm clinic. In STI clinic, lower education, marital status, never using condoms and GUD all assoc w/higher TV rates. HIV at the STI clinic assoc. w/more severe TV.	Prevalence estimate in STD clinic likely overestimate as only patients with GUD or sx or urethritis were enrolled	B
Sturm (2004)[25]	Cross-sectional study N=335 cases 100 controls	Men attending STD clinic w/ sx d/c or dysuria for cases and other sx for controls. Excluded men with abx use in 2wks prior to visit	3 urethral swabs: 1 for chlamydia SDA, one for TV UU and MG PCR then one for Gram stain and GC cx. Evaluated GC cx with GC SDA of subset of 88 cx neg samples	Prevalence of GC, CT, UU, MG, TV, HSV in cases and controls. Risk factors for HIV infection.	HIV more common in cntrls (69%vs.45%; p=0.00005). Previous hx d/c more common in cases and hx GUD more common in cntrls. Cases: GC 52%, CT 16%, MG 5%, UU 36%, TV 6%, HSV 6%. Controls: GC 0, CT 8%, MG 3%, UU 30%, TV 12%, HSV 31%. CT higher in cases than cntrls p=0.04. No difference in prevalence MG and UU. TV and HSV were more prevalent in the cntrls, p=0.03 and p<0.0001.	NGU evaluated by 3rd urethral swab which may have reduced sensitivity. No data on recent contact to an STD.	B
Joyner (2000)[26]	Cross-sectional study N=454	Consecutive men attending an STD clinic in Denver. 6/98-7/98	Urethral swab Gram stain, GC cx, Urine (50ml) 8ml for CT PCR, sediment of $\leq$14ml for TV cx in Diamonds media eval daily for 7d	Prevalence TV and characteristics of TV infection in men	40% Caucasian, 36% black, 23% Hispanic, other. Prevalence GC 5%, CT 7.5%, TV 2.9%. TV associated with sx of D/C, dx NGU, and age >30y. In 214 men $\geq$30yo, prevalence TV 5%, GC 3%, CT 3%. In men >30y TV as common as GC & CT, and in NGU TV as common as CT.	Only one specimen type for TV cx. Not clear if urine was first-fraction. No reported exclusion of men who had recently urinated. No TV PCR.	B

Watson-Jones (2000)[27]	Cross-sectional study N=1004	Community sample of men in Tanzania between 15-54y	First fraction urine for wet prep, TV cx, GC cx,, CT LCR, and LED. Urethral swab for GC cx & Gram stain. TV cx read day3 and 7 only	Prevalence of TV, CT, GC and relationship with LED and risk factors	Lab proven urethritis 249 or 25%. TV+ in 109 (11%). TV + in 14% of 361 men with urethral sx or signs & 9% of 617 men w/ no sx or signs (adjusted for age; p = 0.003.) For 103 TV+ only, 46 (45%) complained of sx urethritis. 37 TV+ cx (54%) were wet prep(-) & 40 (56%) wet prep (+) but cx neg. 22/103 TV+ as only STD had $\geq$5 PMN/hpf vs. 124/855 men w/o CT, TV, or GC (21% & 15% respectively; p = 0.07). LED sensitivity & PPV for TV 70% & 20% respectively. TV increased w/ age, 7% in age 15-19 y to 17% in 35-44 y (p = 0.002). Circumcised men less TV+ (OR 0.37; p = 0.001).	TV cx only read on day 3 and 7. TV cx only from swab of urine pellet. Only one site cultured according to methods.	B

c. Adolescents

CITATION	STUDY DESIGN	STUDY POPULATION TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Satterwhite (2013)[5] (duplicate)	Review	TV estimates from national projections based on data from NHANES, NDTI, and ADD Health studies	Estimated burden of 8 STIs in the United States as of 2008	TV prevalence and incidence among U.S. men and women age 15-49	All 8 STIs: 110 million prevalent and 19.7 million incident infections in the United States in 2008. **TV is still the most prevalent non-viral STI** **TV prevalence among ages 15-24: 500,000** (= 309,000 women + 191,000 men) **TV incidence among ages 15-24: 148,000** (=90,800 women + 56,900 men) Burden among youth: **13% of incident and prevalent TV infections** in the United States	Prevalence based on NHANES but few reliable sources of incidence data. Estimates of infections in males projected based on female data.	C
Mullins (2013)[28]	Secondary analysis of a national, multisite study	U.S. female adolescents age 12-18 who were behaviourally HIV-infected (n = 346) or HIV-uninfected but at-risk (n = 182)	analysis comparing STI incidence between HIV-infected and HIV-uninfected adolescents	Incidence of bacterial STIs (gonorrhoea, chlamydia [CT] and trichomonas [TV; women]) were calculated using Poisson modelling.	TV incidence was 1.3 TV infections per 100 person-months among 257 HIV-infected adolescents, and 0.6 per 100 person-months among 142 HIV-uninfected adolescents (p= 0.002)	Observational	B

Ahrens (2010)[29]	National survey N=7,563 females and 6,759 males	Adolescents participating in waves I-III of the National Longitudinal Study of Adolescent Health ("Add Health"), 1994 -2002	Urine specimens tested for TV by using an in-house PCR ELISA, also tested for GC and CT	Multiple regression analyses were performed to evaluate the association between foster care status and STI biomarkers and risk behaviors	**Female participants who had been in foster care were more likely to have TV (OR 3.23, CI: 1.45-7.23)** but not gonorrhea or chlamydia and reported increased sexual risk behaviors compared with nonfostered peers. Male participants who had been in foster care were more likely to have both GC (OR 14.28, CI: 2.07-98.28) and CT (OR: 3.07, CI 1.36-6.96) but not TV and did not report a higher risk for most sexual risk behaviors than nonfostered peers.	Covariates in all models included baseline age, race, ethnicity, parental education level, parental income level, and average neighborhood household income level.	A
Miller (2005)[30]	National cross-sectional survey N=12,449	Male and female adolescents in school grades 7-12 Add Health 1994-1995	ACASI interview Urine specimens TV PCR	TV prevalence and risk factors	**Prevalence in U.S. adolescents 2.3% (CI:1.8-2.7)** **- Women, 2.8% (CI:2.2-3.6)** **- Men, 1.7% (CI:1.3-2.2)** Prevalence increased with age and varied by region (increased in the southern U.S.) Only 2.3% infected males with urethral d/c or dysuria. In men with TV, 5.6% co-infected with CT	Nationally representative study Testing by in-house PCR for research only	A

Goyal (2011)[31]	Prospective study N=203 tested for TV (of 276 eligible)	Symptomatic adolescent females age 14-19 presenting to a pediatric ED with lower abdominal pain and/or genitourinary (GU) complaints	Patients were tested for TV, Neisseria gonorrhoeae (GC), and Chlamydia trachomatis (CT)	TV prevalence and risk factors	**TV prevalence among symptomatic adolescents: 9.9% (CI:5.7-14.0).** Prevalence of any STI: 22.5% (CI:17.5-27.4) Sensitivity analysis revealed a minimum TV prevalence of 7.2% (95% CI = 4.2% to 10.3%). Vaginal discharge was a significant predictor (OR 3.7, CI:1.1-11.3).	Not representative	B

1. Extra-genital TV

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
Cosentino (2012)[32]	Cross-sectional study N=497	Men and women reporting receptive anal intercourse at 3 clinical sites in Pittsburgh (health department, women's hospital, and AIDS center) in 2009-2010	Evaluation of rectal NAAT (SDA v TMA)	Prevalence of rectal TV by Aptima NAAT, also CT and NG	**Rectal TV: 26 (5.2%)** Rectal CT: 41 (8.2%) Rectal NG: 21 (4.2%)		B
Oud (2009)[33]	Case report N=1	Previously healthy 17yoM in ICU following trauma including skull fractures. Purulent **sinusitis** and fever developed day 4. Microscopic examination revealed motile TV.	Preceding frequent oral sex with girlfriend with recent vaginal discharge diagnosed with trichomoniasis.		Resolved with 15 days of IV metronidazole	Critically ill patient; cannot rule out incidental finding	C
Francis (2008)[34]	Cross-sectional study N=500	MSM at STD clinic in San Francisco in 2005-2006	Remnant rectal specimens tested for TV and NG using TMA	Prevalence of rectal TV and NG	**Rectal TV: 3 (0.6%)** Rectal MG: 27 (5%) None of the specimens from patients presenting with proctitis were TV+	Remnant material used	B

2. Partner Management for TV

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJ QUALITY RATING
Mohammed (2010)[35]	Two randomized trials N=977 men (1991 sex partners) N=463 women (521 sex partners)	Data were obtained from two intervention trials at public clinics in New Orleans, LA, during 2001-2004 to determine the ideal means of partner referral. Data on men and women were analyzed separately.	Men diagnosed with urethritis and women diagnosed with trichomoniasis were randomly assigned to partner referral (PR), booklet-enhanced partner referral (BEPR), or **patient-delivered partner treatment (PDPT).** ACASI re sex partners at baseline, and then whether they had disclosed to them at follow-up.	The objective of this research was to determine the factors associated with disclosure of three treatable STDs	Of men, 57.8% disclosed to their partners. Most men (68.3%) reported having two or more partners and **disclosure was more likely to occur in: those assigned PDPT (OR 2.71, CI:1.93-3.82)**, those who reported only one sex partner (aOR 1.54, CI:1.10-2.16); and those in steady relationships (OR 1.37, CI:1.08-1.74). Of women, 87.3% disclosed to their partners. Most women reported having only one partner (86.8%) and disclosure was more likely to occur in steady relationships (OR: 2.65, CI: 1.24-5.66), and when sex was reinitiated with partners during the follow-up period (OR 3.30, CI: 1.54,7.09).	Different selection criteria for men and women. Self-reported disclosure status.	B

Schwebke (2010)[36]	Randomized trial N=484 women	A single-site study among women age ≥19 in Alabama with a culture or wet prep positive for TV during 2003-2008	Test-of-cure visits were conducted at 5 to 9 days after enrollment. Repeat infections at 1 and 3 months of follow-up were the measure of effectiveness.	Effectiveness of 3 methods of partner notification: self-referral of partners (PR), partner-delivered therapy (PDPT), or public health disease intervention specialists (DIS) locating partners and delivering medication in the field, if needed.	Cure rates with the standard 2-g stat dose of metronidazole were 95% and the repeat infection incidence rate for a 3-month period was 7.0%. Reinfection rates at 1 month (p=0.09): PDPT: 5.8%. PR: 9.8%. DIS: 15.0% Reinfection rates at 3 months (p=0.17): PR: 5.0%. DIS: 7.8%. PDPT: 14.3% **80% of women randomized to PDPT reported delivering medication and 89% thought it likely that partners took the medication. Treatment could be verified for only 25.1% and 56.5% of men in the PR and DIS arms, respectively**. No serious adverse events were reported.	Recruitment 50% less than originally intended according to power calculations Lower than expected repeat infection rate in all arms. When PDPT was compared to DIS or PR/DIS combined, at 1 month the PDPT group had a lower repeat infection rate (5.8 vs. 15% and 5.8 vs. 12.5%, respectively).	A

Gatski (2010)[37]	Multicenter cohort study N=252 women	Women coinfected with HIV and TV at public HIV clinics in New Orleans, LA, Houston, TX, and Jackson, MS. Mean age=40 yrs, 92.5% black, 58.3% taking ART, 34.1% had plasma viral loads >10,000 copies, 26.2% had CD4 cell counts <200, 15.1% had multiple partners	Women were treated with metronidazole (randomized to 1 or 7 days) and given treatment (2 g single dose of metronidazole) to deliver to all reported sex partners. A test-of-cure visit was conducted 6 to 12 days post index treatment completion and behavioral data were collected by CASI.	Evaluate adherence to PDPT and possible causes of repeat TV infection among HIV-infected women	Of 183 women reporting any partners, 138 (75%) provided PDPT to all partners; of those, 113 (82%) were sure all of their partners took the medication. Factors associated with not giving medications to all partner(s) were multiple sex partners, being single, and having at least one partner unaware of the index woman's HIV status. At test-of-cure, 10.3% were TV-positive and 16.7% reported having sex since baseline. Of the 24 repeat infections, 21 (87.5%) reported adherence to medication and no sexual exposure.	**HIV-infected women with TV reported high adherence to PDPT. Treatment failure was the most common probable cause of repeat infection.**	B
Kissinger, (2006)[38]	RCT N=458 (N=155 patient referral arm; N= 147 booklet enhance partner referral; N=156 patient delivered partner therapy)	Women attending New Orleans womens health clinic between 12/01 and 8/04 with culture confirmed trich, non-pregnant, no contraindication to metro and at least 1 male partner/60d	Women treated with metro 2g x 1 or 500mg BID x 7d (if concurrent BV) Randomized to 3 conditions	Recurrent TV at 4 wk (if still + at 4 wk they had subsequent visit at 1mo) Cost-effectiveness of PDPT	81% received repeat TV testing at f/u and 8.2% positive. No difference between study arms. No specific characteristics predictive of TV positivity at f/u. PDPT did not result in more partners taking meds (by woman's report). 30/31 women positive at f/u denied reexposure since treatment. 26/30 responded to higher doses metro. 4/30 had specimens sent for susceptibility testing and demonstrated mild resistance. PDPT less costly than other 2 arms using sensitivity analyses with broad variation	Partner status (whether told, presented for treatment, etc) based on participant's report. No contact of study staff with male partners.	A

3. Treatment options

a. Metronidazole

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
U.S. FDA (2010)[39]	Package insert for Flagyl/metronidazole: http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/012623s061lbl.pdf						
Vickovic (2010)[40]	Prospective randomized trial N=61	Men with prostatitis caused by TV, but no GU abnormalities on ultrasound, in Zagreb, Croatia, 2006-2008	TV had been initially diagnosed in expressed prostatic secretions or voided bladder urine after prostate massage. For this study, TV assessed by urine and urethral swab specimen by microscopy and culture	Randomized to receive metronidazole 1.5g PO either for 7 days or else 14 days. Assessed after therapy and 4-6 weeks later.	A higher percentage of clinical cure (96.7% v 67.7%, p=0.006) and TV eradication (93.3% v 71.0%, p=0.043) occurred in the group that received a longer treatment course (14 days instead of 7).	Female sex partners treated with metronidazole 2g PO x 1. 8 participants in each group complained of nausea (no significant difference)	A

Price (2003)[41]	Single blind placebo control trial N=411	Malawi men with urethritis at STD clinic HIV+ men at Derm clinic for control of HIV seminal VL	Urethral swab and urine cx for TV & TV PCR of urine. Gram stain GC & PCR GC/CT. Gent/ doxycycline to all patients (GUD PCN/Erythro). Group 1: metronidazole 2g once Group2: placebo	F/u 7d post treatment sx, signs, Gram stain. IF initial TV cx+ then Urethral swab, semen, urine for TV cx. Semen collected if TV+, HIV+ and no metronidazole rx	More men in the metronidazole group TV+ (45/205 {22.%} vs. 26/206 {12.6%};*P* =0.01). 71 subjects (17.3%) TV+. 19 men were TV cx+ but neg for GC/CT. Of these, 16 (84.2%) had >4 WBCs/hpf in Gram stains; of 83 TV/GC/CT- men only 42 (51%) had >4 WBCs/hpf *(P* = 0.01). At f/u, 58/366 men (16%) had persistent urethritis, 110/ 373 (30%) reported sx, 59/371 (16%) had d/c on exam. 156 subjects (42%) had at least 1/3 at f/u. Of those who received metronidazole, 16% (29/179) had persistent urethritis, vs. 15% (29/187) placebo. No difference observed in sx (RR, 1.05; CI:0.77–1.44) or d/c on exam (RR, 0.90; CI:0.56 –1.43) between 2 groups at f/u. In TV+ men at baseline who returned for f/u (n= 65), rx did not affect presence of persistent urethritis	Significant loss to f/u. No data on abstinence or partner rx in those completing f/u. Not clear if metronidazole was directly observed.	A
Schmid (2001)[42]	Cohort study N=911	Women attending urgent gynecology clinic, Atlanta in 1997	Wet prep, TV cx in Diamond's media read 7-10d. If wet prep+, metronidazole 2g once & partner rx.. Aerobic drug sensitivity testing.	F/u 1wk w/ wet prep and TV cx	TV cx + 82/911 (9%). Wet prep + 42/82 (51%). 2/82 women(2.4% (95%CI, 0.3-8.5%) had aerobic MLC 50ug/ml. No isolates had higher-level resistance (100->=400 ug/ml). 26/42 (62%)wet prep+ women returned for f/u including ½ w/ resistant isolate –all had wet prep (-) and TV cx.	Only 82 samples tested at a single site in U.S. Limited f/u of TV cases.	B

Spence (1997)[43]	Randomized, blinded trial N=167	Inner city STD clinic in Philadelphia Women with TV diagnosed by WP.	500mg vs 1gm vs 1.5gm vs 2gm metronidazole Each packet with 4 identical pills with varying combinations in each packet. DOT. Subjects, investigators and lab techs blinded to condition. Advised to abstain from sex and to refer partners for therapy. F/U at 7-10days after therapy	Presence of TV by WP and culture	3 individuals vomited meds and were excluded from analyses. Mean age 25+/-8.4y. 82% with only one partner, 9% with >1 partner, 4% no sexual partner, 5% UK partner #. 39% taking antibiotic for other STD (not TV). 66% with d/c, 35% with pruritis. No differences across assignment group. 40% LTF. 500mg (N=8/23): 35% cured 1gm (N=18/29): 62% cured 1.5gm (N=23/27): 85% cured 2gm (N=16/19): 84% cured	Inadequate power. Significant differences: 1.5gm sign higher than 1gm and 500mg; 2gm sign higher than 500mg. Sign LTF: 44% 500mg 34% 1gm 36% 1.5gm 49% 2gm No info on partner therapy or interim sex.	A-B
Viitanen (1985)[44]	Cohort	Male patients subjected to elective gonadal surgery	Nitroimidazoles were administered orally at 500 mg every 8 h, beginning 5 days before the operation.	The steady-state concentrations of metronidazole and tinidazole in male genital tissues	Eight hours after the last dose, the concentrations of tinidazole were 24.1 +/- 2.5 micrograms (mean +/- standard error of the mean)/g of prostatic tissue, 29.1 +/- 2.9 micrograms/g of vas deferens, 22.1 +/- 2.1 micrograms/g of epididymis, and 18.6 +/- 2.3 micrograms/g of testis. The corresponding values of metronidazole were 14.3 +/- 1.8 micrograms/g, 15.9 +/- 1.2 micrograms/g, 14.0 +/- 1.2 micrograms/g, and 12.5 +/- 1.7 micrograms/g, respectively.		B

Mannisto (1984)[45]	N=67	Female patients subjected to hysterectomy and/or oophorectomy because of myomatosis uteri, carcinoma uteri or endometriosis.	after a single 500 mg intravenous infusion and after three days of treatment with 400 mg t.i.d. of metronidazole or 500 mg b.i.d. of tinidazole	Concentrations of metronidazole and tinidazole in serum and gynecological organs	At the time of organ removal, metronidazole and tinidazole levels in serum were 14.5 +/- 0.45 mg/l and 12.3 +/- 0.38 mg/l, respectively. At steady-state, the concentrations of tinidazole in serum (23.5 +/- 1.0 mg/l) were remarkably higher than those of metronidazole (13.5 +/- 0.84 mg/l) about three hours after the last oral dose. Drug concentrations in organs of the female reproductive tract were 70 to 100% those of the simultaneous serum levels.		B
Hager (1980)[46]	Randomized, controlled, double-blind trial N=468 (176 evaluable)	DeKalb and Fulton Co. STD Clinics Women with signs or symptoms of vaginitis and motile TV on microscopy Excluded <18y, pregnant women/missed last menses, those treated for TV/30d	2gm metro x 1 vs 250mg TID x 7d. ?first dose DOT All patients took 7d of meds but some took placebo Given 2gm metro dose for steady partner(s) Advised to abstain from sex for 14d F/U 7-21d post-rx	Presence of TV by WP and/or culture. Failure = TV by WP and/or culture (regardless of adherence or history of interim sex) Cure = negative WP and culture	468 enrolled, 176 (37.6%) returned 7-21d after therapy. N=93 in 2g regimen N=83 in std regimen No sign difference between groups. GC+: 14% 2g group and 18% std group. 79% 2g group and 87% std group with vaginal sx. 77% study popln with vaginal d/c 80/93 (86%) cured in 2g group and 76/83 (91.6%) cured in std group (p>0.1) 40 (50%) of the 80 cured in 2g regimen and 4 (31%) who failed reported partner rx. 41 (54%) of 76 cured with std and 5 (71%) who failed reported partner rx. Admitted sexual intercourse no more common in failures vs cures.	62.4% LTF. Not clear that study had power to determine differences between treatment regimens.	A-B

Thin (1979)[47]	Randomized, double-blind trial N=192 (96 women in each group)	2 STD Clinic in London Female patients with vaginal trichomoniasis diagnosed via WP and culture. Excluded "itinerant" patients and pregnant women	Metro 2g po x 1 vs Metro 400mg po BID x 5d F/U 7days and 14days First dose under DOT, rest taken at home (all patients took 5d of antibiotics but some took placebo)	RX failure: reappearance of TV within 14d of start of treatment in patient who denied interim sexual contact Reinfection: reappearance of TV in patient who admitted sexual contact between assessments	2gm group: 73% assessed at 7d with 1.4% failure and 1.4% reinfection; 54.2% seen at 14d with 0 additional failures but 2 (3.8%) reinfection. Overall cure 92.3% at 14d. 400mg BID x 5d group: 78% with 7d f/u with 1.3% failure and no reinfection. 68.8% seen at 14d with 2 additional failures (3%) and 2 reinfections (3%). Overall cure rate 92.4%.	Reasonable blinding of condition. No details regarding randomization except that it was randomized. No study popln details except that they were similar across groups. f/u only out to 2weeks.	B
Wood (1975)[48]	Cross-over study	Healthy female volunteers who	Received a single dose of 2g of each drug	Serum concentrations of tinidazole and metronidazole	Bioassays against T. vaginalis showed that metronidazole achieved higher peak concentrations (mean 81 mug./ml.) than did tinidazole (mean 67 mug./ml.), while assays for unchanged drug showed higher peak concentrations of tinidazole)mean 51 mug./ml;) than of metronidazole (mean 40 mug./ml9).	The longer half-life of tinidazole led to significantly higher serum concentrations (by bioassay and chemical assay) of tinidazole than of metronidazole from 6 hrs onwards.	B

b. Tinidazole

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
Forna (2005)[49]	Meta-analysis N-54 studies total	Analysis of randomized trials of TV rx in women	Search of Cochrane central register of Controlled Trials, MEDLINE, EMBASE, Informal discovery	Clinical cure, parasitologic cure, side effects	Summary of trials involving tinidazole: 8 trials comparing tinidazole w/ metronidazole. All but 1 trial compared short regimens. Significantly higher rx failure/parasitological cure (RR 3.2, 95%CI 1.66 to 6.32), higher clinical failure (RR 3.8, 95% CI 1.8-7.9), and higher side effect (RR 1.65, 95%CI 1.35 to 2.0) w/ metronidazole. Only 1 trial w/ blind outcome assessment and no outcome differences in this trial. Side effects of nausea and vomiting greater in metronidazole groups.	Meta-analysis includes 8 trials that reportedly compare tinidazole w/ metronidazole. Unfortunately included article (lean 1972) actually compares ornidazole w/ metronidazole. This article not included in any of meta-analysis RR calculated for parasitologic cure, clinical cure, or any side effects.	A
Crowell (2003)[50]	In vitro study	TV isolates clinically resistant to metronidazole	Activity of tinidazole and metronidazole	MLCs	MLCs of tinidazole were significantly lower than MLCs of metronidazole. Increased metronidazole resistance correlated with increased tinidazole resistance.		C

Prasertsawat (1992)[51]	Double-blind Randomized trial N=132	Nonpregnant women w/ sx TV on wet prep attending a gynecology clinic in Thailand 9/90-8/91	Group 1: metronidazole 1.6g PO twice q12h to patient and partner Group 2: tinidazole 2g PO once to patient and partner	F/u between 6-16d w/ wet prep and TV cx. Rx failure treated w/ metronidazole 200mg tid x 7d w/ f/u at 14d	Cure 66/67 (98.5%) w/ metronidazole and 65/65 (100%) w/ tinidazole. Clinical improvement in 94% of patients in single day split dose group and 94% of patients in single dose group. Side effects were minimal. Drop out in 16.3% and 18.8% in metronidazole and tinidazole groups	Unusual metronidazole dosing. Significant drop out but unclear how these were included in efficacy calculations.	A
Bloch (1985)[52]	Randomized controlled trial N=161	Non-pregnant Women w/ TV on wet prep	Directly observed PO metronidazole tablets, benzoyl metronidazole suspension and tinidazole tablets each given as single 2g dose. Partner rx given to patient for delivery	F/u at 7 d intervals. Cure = 2 wet preps (-) at 7d intervals. If wet prep (+) retreated once w/ same drug then switched to other drug if (+) at next 7d eval	81 to 84.7% of partners rx. At 7d 1.7, 4.5, 1.7% of patients had TV in metronidazole tab, metronidazole susp, & tinidazole. At 14d, no patients rx w/ metronidazole had TV but 5.1% of tinidazole rx patients had TV(p=0.05). vaginal d/c persisted in .1, 34.1, 42.4% at 14d in metronidazole tab, metronidazole susp, & tinidazole. Repeat rx needed in 1,2,3 patients in metronidazole tablet, metronidazole suspension, and tinidazole groups. Only 1 patient in tinidazole group required a switch to metronidazole	Not blinded. No cx may explain the persistence of sx in many patients. Persistence of sx unclear as patients received incomplete STD evaluation	A
Gabriel (1982)[53]	Randomized single blind trial N=95	Nonpregnant women w/ TV	Tinidazole 2 g PO as single dose or metronidazole 2g PO as single dose	F/u 1-2wks with Wet prep and TV cx	6/46 patients defaulted after metronidazole rx 7/49 defaulted after tinidazole rx. 39/40 (97.5) rx w/ metronidazole cleared TV. 40/42 (95%) patients in tinidazole group cleared TV	No documentation of partner rx. No description of wet prep vs. cx results. No data on side effects. Default comprised $\leq$14 % of patients	A

Lyng (1981)[54]	Randomized controlled trial N=149	**Male partners** of 149 women dx by cx. Most women w/ baseline gyn conditions including induced/spontaneous abortion, metorhagia, fibroids, cervical dx, adnexitis, etc.	All women rx w/ 2g tinidazole. Partners randomized to tinidazole 2g or placebo. Women seen in f/u 1-2 wks post rx w/ TV cx. 2nd f/u about 1 mo after resuming sex w/ TV cx.	TV clearance	Average age 35 yrs (16-64 years). F/u 1: 5/137 women TV(+). Cure rate 96%. F/u 2: (ave 61 days post-rx). 17/118 women TV(+) (14%). TV(+) in 24% placebo and 5% rx group (p=0.01) No suggestion of influence of difference in time from rx, time from 1st intercourse after rx, or differences in sexual activity.	No information on number of partners. Small study but **statistically significant results at 2nd f/u**. No data on adherence to rx of partners.	A
Manorama (1978)[55]	Randomized trial N=60	Women w/ sx of vaginitis and TV on wet prep seen at an outpatient clinic in India. Exclusion criteria included pregnancy, GC or candida or hx of antiTV rx w/i 2 w	Group 1: Tinidazole 2g PO as a single dose. Group 2: Metronidazole 2g PO as a single dose. Partners rx when possible.	f/u w/ vaginal smear and hanging drop prep on initial evaluation, and days 4,8,and 12. Hgb WBC, urine before and after rx. Cure defined as (-) TV smear and drop and near or complete resolution of sx.	1 drop out/loss to f/u. All patients both groups TV smear (-) at f/u. Tinidazole group had significantly more clinical improvement than metronidazole group (p<0.01). More side effects in metronidazole group and significantly more side effects per patient and significantly more severe in metronidazole group. No lab abnl in either rx group. Group 1: 18/29 (62%) cured of clinical sx. 11/29 (38%) markedly improved. 10/29 (34.5%) had side effects. Group 2:Only 4/30 (13%) cured of clinical sx; 23/30 (77%) marked improvement; 3/20 (10%) slight improvement. 24/30 (80%) had side effects	No cx. Incomplete partner rx and difficult to interpret clinical response w/ indeterminate testing for other STDs. Not blinded and may have effected report of sx or side effects.	A

Apte (1978)[56]	Open multicenter trial in 8 countries N=859 for TV rx	Nonpregnant women w/ TV on vaginal smear and sx of vaginitis	Rx of TV, giardiasis, or amoebic liver abscess. TV rx w/ single 2g dose of tinidazole to patient and partner when available	F/u between 8 to 21 days w/ microscopy of vaginal smears	Overall cure 818/859 (95.2%) by site 86.2-100%. Side effects in 82/859 (9.5%) by site 5-45.5%.	No cx data. Not clear how cure was defined.	B
Anjaeyulu (1977)[57]	Randomized trial N=100	Women w/ TV on hanging drop prep	Directly observed metronidazole 2g or tinidazole 2g as single PO dose. Majority of partners rx (87.5%)	Response to rx by hanging drop prep for TV and testing for GC and candida at entry and q4 d for 3 visits. Adverse effects monitored hgb, WBC, Bililrubin, alkphos, LFTs, BUN, UA	39/50 and 36/50 partners received rx in tinidazole and metronidazole groups, respectively. 1 mo before trial 14 tinidazole and 4 metronidazole patients received metronidazole. Tinidazole vs. metronidazole groups: Parasitologic cure 47/50 (94%) and 32/50 (64%) ($p<0.01$). Clinical cure in 42/50 (84%) 25/50 (50%) ($p<0.01$). Side effects 52% and 82% ($p<0.01$). Moderate to severe side effects in 8 and 19 persons ($p<0.05$). Metronidazole more GI side effects	Incomplete partner rx and unclear if partner rx observed. No report of TV cx. Not blinded. Greater number of metronidazole failures or relapse in the tinidazole group.	A
Rees (1974)[58]	Placebo controlled Randomized trial w/ blinding of microscopist and f/u nurse N=29	Women in Nairobi prison w/ vaginal smear w/ TV. Exclusion criteria: pregnancy, coexisting infection	Group 1 tinidazole 2g Group 2: Ascorbic acid placebo	F/u day 4,5, & 7 and 2 mo later w/ vaginal smear eval for TV. Cure defined as all 3 post rx exam negative.	9/29 did not have all 3 vaginal swab exam. 5 in Group 1 neg on single eval. 3/4 inadequately evaluated patients in Group 2 were still TV (+). In those w/ 3 f/u, 8/10 in Group 1 cured and 0/10 in Group 2 cured. At 2mo f/u all 6 patients in Group 1 TV (-). 4/6 in Group 2 TV (+). Side effects similar in both groups except 5 in Group 1 reported headache. Only 1 reported headache in Group 2.	No cx. No mention of blinding of patients to drug taken. Considerable loss to f/u.	A

Mati (1974)[59]	Randomized double blind placebo controlled trial N=31	Nonpregnant women w/ TV on wet prep attending gynecology clinic in Nairobi	Directly observed Tinidazole 2g PO as a single dose or placebo w/ rx	Wet prep and cx for GC and candida at initiation and at 7d f/u. If TV persisted rx w/ tinidazole ?1g daily x 7d for patient and partner	Clinical cure was resolution of sx and wet prep in 12/15 (80%) 2/13(15%) in placebo group w/ exclusion of those w/ candidiasis Clinical cure rate in tinidazole group increased to 92.3%. 16/16 patients rx w/ tinidazole neg. microscopy vs. 4/15 (26.6%) placebo group. 12/15 (80%) and 5/13 (38%) patients in tinidazole and placebo groups were sx free.10/16 and 1/15 in tinidazole and placebo groups were d/c free on exam after rx.	No TV cx. Incomplete evaluation for other causes of sx and signs.	B
Milek (1974)[60]	Open label trial N=386	Women w/ TV on ?microscopy? were enrolled at 8 Swiss gynecology clinics	Tinidazole as single oral dose: 1500mg in 98 patients; 1600mg in 75 patients; 1800mg in 79 patients; 2000mg in 134 patients. 123 partners rx concurrently	Wet prep at 7-10d and 4-6 wk. Evaluation of lactobacillus, pathogenic bacteria, fungi and leucocytes.	Cure rates at 1st and 2nd f/u for 2000mg, 1800mg, 1600mg, and 1500mg were 94% and 93.5%, 92.4% and 92.4%, 88% and 88%, and 84.5% and 83.7%, respectively. 27 patients lost to 2nd f/u in 2000mg group. In 2000mg group 2/8 failures at 1st f/u did not have partner rx and 5/7 failures at 2nd f/u were probable reinfections. 123/134 patients (92%) receiving 2000mg reported no side effects. Majority of reported side effects were nausea and vomiting	No cx data. Not all partners rx. No comment if rx was directly observed. Considerable loss to f/u on 2nd f/u visit in 2000mg group	B

c. Alternatives

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Obiero (2012)[61]	Meta-analysis of 9 RCTs including a total N of 31,941 women	RCTs of topical microbicides (except Nonoxynol-9) in sexually active, HIV-negative women or MSM by 2011	Specifically assessed Carraguard (Skoler-Karpoff 2008, n=6202) and a cellulose sulfate gel (Van Damme 2008) against TV Carraguard (1 trial)	Effects of topical microbicides for prevention of the acquisition of STIs	**No evidence of an effect of any topical microbicide on the acquisition of trichomoniasis,** gonorrhoea, syphilis, condyloma acuminatum, or human papillomavirus (HPV) infection	Not enough evidence to recommend topical microbicides for HIV or STI prevention at present	A
Moraes (2012)[62]	Randomized, double-blind, and controlled clinical trial N=60	Nonpregnant women age ≥18, BMI 19-30, with symptomatic TV (e.g. vaginal discharge, odor, itching, irritation). TV test by wet mount only.	Women were randomized to a treatment group, either a single dose of Mentha crispa (24 mg) or a single dose of secnidazole (2,000 mg)	Efficacy of a single oral dose of **Mentha crispa (peppermint)** compared to secnidazole for the treatment of women with TV	After treatment, **97% of women in the secnidazole group were cured, as were 90% of women in the Mentha crispa group** (P=0.6). Symptoms improved in both groups. Adverse effects, mostly nausea and metallic taste, were more common in the secnidazole group (67%) than in the M. crispa group (20%), (P<0.001).	Wet mount testing only for TV diagnosis	B

Tweats (2012)[63]	Genotoxicity evaluation	Fexinidazole, a 2-substituted 5-nitroimidazole rediscovered by the Drugs for Neglected Diseases initiative (DNDi) after mining public and pharmaceutical company databases, has potential to become a short-course, safe and effective oral treatment	Many nitroimidazoles possess antibacterial and antiprotozoal activity and examples such as tinidazole are used to treat trichomoniasis and guardiasis, but concerns about toxicity including genotoxicity limit their usefulness.	Genotoxicity evaluation of **fexinidazole** and its two active metabolites, the sulfoxide and sulfone derivatives	Mutagenic in the Salmonella/Ames test; all mammalian cell assays to detect genetic toxicity, conducted for this study either in vitro (micronucleus test in human lymphocytes) or in vivo (ex vivo unscheduled DNA synthesis in rats; bone marrow micronucleus test in mice), were negative. Thus, fexinidazole does not pose a genotoxic hazard to human patients and represents a promising drug candidate in clinical development for human African trypanomiasis	Fexinidazole is expected to enter Phase II clinical trials in 2012.	C
Khryanin (2007)[64] (poster)	Randomized study N=427	Males 20-48 attending Russian STD Clinic, with TV, 2000-2004	250mg TID metro vs **500mg ornidazole BID both x 10d** F/u 1, 2 and 3 wk post treatment for exam, gram stain and TV cx	Cure of TV	217 subjects in metro group and 210 subjects in ornidazole group. Clinical efficacy 57.6% metro and 94.5% ornidazole Microbiologic efficacy 77.1% metro and 98.2% ornidazole Side effects 59% metro and 3.7% ornidazole	Culture and WP used to define cure (suboptimal sensitivity) Not blinded to condition Insufficient detail in poster	B

Muzny (2012)[65]	Case report N=1	A 37-year-old African-American woman, severely allergic to metronidazole, history of hypertension and diabetes with end-stage renal disease (on dialysis) presented c/o severe vaginal pruritis and profuse green discharge x6months starting after unprotected sex with a new male partner. Wet prep positive and InPouch culture confirmed TV.	Unsuccessful treatments (>12 months): - oral clindamycin and topical 2% clotrimazole cream - paromomycin cream 250mg/1g intravaginally x 3 wweeks - furazolidone intravaginally x 2 weeks - betadine douches BID twice a week x 4 months - oral nitazoxanide x 2 weeks	Successfully treated with: **Boric acid,** 600mg gel capsule intravaginally BID x 2 months Resulted in symptomatic cure and patient also remained wet prep- and culture-negative 60 days after treatment.	Case report	C
Subramanian (2011)[66]	Case report N=1	36-year-old woman at 16 weeks of pregnancy presented with persistent, profuse, foul-smelling vaginal discharge for 18 months. She had been treated with multiple courses of oral metronidazole in several dose combinations and tinidazole 500 mg twice daily for 7 days with no relief.	Saline microscopy of the discharge showed motile trichomonads with increase in polymorphonuclear leukocytes. Review 3 weeks after treatment revealed decreased discharge with negative smears and culture for Trichomonas using Diamond medium.	Successfully treated with a **high dose of oral tinidazole**, 1 g BID x 2 weeks, plus tinidazole vaginal tablets 500 mg inserted BID x 1 week. Smear and culture remained negative at repeat evaluation 2 weeks later.	Delivered term infant with no complications	C

Nyirjesy (2011)[67]	Case reports N=2	I) 54-year-old woman with vaginal burning, irritation, discharge, and dysuria x 7 years. Trichomonads visualized by wet mount of discharge. Partner had outside partners, was treated in the past. Sensitivity testing at CDC found moderate resistance to both MTZ and TDZ. II) 29-year-old woman with 2-year trichomonas infection. Partner treated with a course of metronidazole and relationship ended. Results of sensitivity testing by the CDC concluded that the organism was "highly resistant" to metronidazole and "moderately resistant" to tinidazole. Many trichomonads were seen on microscopy.	I) Failed treatments included multiple courses of metronidazole and tinidazole, paromomycin intravaginal cream x14d + gentian violet 1% topically, furazolidone 100 mg in 5 g of 3% nonoxynol-9, for topical vaginal application BID x14d tinidazole (1 g orally TID with 500 mg vaginally BID x14d), povidone-iodine suppositories vaginally x14d, nitazoxanide cream 500 mg/5 g vehicle BID x14d, metronidazole/ miconazole/ lidocaine pessary x14d, and potassium permanganate (1:2500 dilution) vaginal douches x14d II) Failed treatments included 6 courses of metronidazole, 3 courses of tinidazole (including a 14-day regimen with 3 g orally and 1 g vaginally per day), and zinc supplements; 14-day course of 2% furazolidone cream course BID x14d	Successful treatments: I) Intravaginal paromomycin, 5 g of a 5% cream inserted nightly, along with concomitant oral tinidazole 1 g 3 times daily for 14 days was given. At 1 and 6 weeks after the treatment was completed, the patient returned with no signs or symptoms of infection; urine, saline wet mount, and Diamond's culture were all negative. II) A course of 5% intravaginal paromomycin, 1 applicator full (5 g) inserted vaginally nightly for 14 days with concomitant oral tinidazole 1 g 3 times daily for 14 days. At 6 weeks and 3 months after treatment, there was no evidence of infection, and cultures for T. vaginalis were negative at each visit.	Case reports	C

Bhaduri (2010)[68]	Case report N=1	44 year-old woman with vaginal discharge and a vulval itch. TV diagnosed by wet mount and treated with MTZ 400mg BID x5d. TOC after 2 weeks showed continued infection; repeat treatment course achieved clinical and microbiologic cure. 3 years later, represented with similar symptoms and no vaginal sex for >1 year. TV diagnosed by wet mount and a third course of MTZ was prescribed. Symptoms recurred when antibiotics stopped and additional treatments were attempted despite no reported risk factors for reinfection.	Alternative therapies attempted without success: - erythomycin 500mg BID x 14d - metronidazole 400 mg BID x 28d plus metronidazole gel daily x 3w - tinidazole 2 g twice a day for 14 days	Clinical and microscopic cure achieved with **acetarsol vaginal pessaries**, 500mg nightly x 2 weeks. No reported side effects.	Higher doses of acetarsol have been associated with systemic reactions including rigors and confusion.	C
Tayal (2010)[69]	Case Report N=1	49-year-old UK woman with 5-year history of persistent TV with intermittent symptoms. Last sex several years ago. TV diagnosed both on wet mount and culture.	Unsuccessful treatments (>13 months): - metronidazole 400mg BID x 1 week (numerous courses) - clotrimazole (Canesten) pessary 500 mg x 1 - metronidazole 2 g x1 - fluconazole 150 mg x 1 - erythromycin 250 mg 4x/day x 1 week. - tinidazole 2 gm BID x 1 week and chlorphenamine 4 mg as necessary	Successfully treated with: - **paromomycin (Gabbroral) intravaginal tablets** 250 mg BID x 2 weeks. Oral tablets were used intravaginally because pessaries were not available. Patient stopped treatment after 10 days due to vaginal soreness. Urinary tract infection developed but was treated with a three-day course of cefalexin 500 mg twice daily. Symptoms resolved within 3 weeks; tests of cure performed during subsequent visits clear of TV.	Paromomycin is not licensed in the UK	C

Helms (2008)[70]	Observational. N=127 (N=59 with follow-up)	Clinicians reporting suspected metronidazole hypersensitivity to CDC were provided options and asked to report outcomes.Women reported by providers to CDC Div. STD Prevention or Division of Parasitic Diseases from 9/1/03-9/30/06 with follow-up information available.	Choice of RX up to provider though **desensitization strongly recommended**. 1) RX utilized 2) If desensitization occurred, presence of adverse response 3) Cure defined as microbiological (culture or wet prep) or clinical (based on provider impression) for all treatment regimens	Avg age 36. Avg wt 171lb. 10% pregnant. 50% (64/127) of rxn directly observed by provider (48% urticaria, 16% pruritic, 9% facial edema, 7% GI, 2% anaphylactic, 9% erythematous rashes and 10% other. 41/59 with follow-up info were treated. 15/41 (36.6%) Rx oral or IV metro. Desensitization. 15/15 (100%) were cured (3 cx, 9 wet prep, 3 clinical). 1 on oral and 1 on IV with minor reactions. Of 26 not RX with desensitization, 9 (22%) received std rx with 85.7% cure and 17 (41.5%) received alternative RX (with 41.7% cure)	Observational nature of study. Treatment regimens not standardized. Microbiologic test of cure not uniformly available. No follow-up on >50%.	B

Kissinger (2008)[71]	Secondary analysis of 2 cohort studies	HIV- female cohort (RCT of EPT for TV), conducted 9/01-12/03, >/=16, denied HIV+, scheduled for pelvic, not in first trimester pregnancy, named at least 1 partner to be included in study. HIV+ female cohort, >/=18, not pregnant, scheduled for pelvic	Tested via wetprep and f/u culture for TV. + treated with 2g metro DOT. f/u in 1 mo for interview/retest. If positive 1mo, higher dose metro given (500mg BID x 7-10d) and return 2 wk retesting. If + and no unprotected sex, specimen sent to CDC for susceptibility test. MLC50-100ug/mL mild resistance; 101-199ug/mL mild-mod; 200-400ug/mL mod; >400ug/mL high. Outcomes: probable reinfection, probable infection by new sexual partner, probable treatment faiure	HIV+ - N=60, 92% AA, 20% <30yo, 30% CD4<200, 68% report partner took TV meds, 35% reported unprotected sexu during 1 mo f/u, 18.3% (11/60) positive TV at 1mo. **Of those, 27% probable reinfection, 18% probable infection by new partner**, 55% (6/11) probable rx failure. Of 6 rx failure, 3 (50%) respond to higher doses metro. Other 3 tested and 2 with mild resistance, other susceptible. HIV- N=301, 99% AA, 74%<30yo, 69% reported partner took TV meds. 8% (24/301) TV+ 1mo. **Of those, 8% probable reinf, 92% (22/24) probable RX failure.** 17/22 probable rx failure responded to higher dose metro. Remaining 5, 4 able to be tested with 1 susceptible, 2 mild resistance and 1 mod resistance.	Data from 2 separate cohorts. Potential overlap between outcome categories. Susceptibility testing conducted on very small subset. Partners not tested for TV	IIB vs C

Aggarwal (2008)[72]	Case reports N=2	1. 58yo F with culture+ TV. Failed 2g metronidazole then developed allergy with reRx 2. 40yo F with culture + TV. Failed 2gm metronidazole dose followed by metronidazole 250mg TID x 7 d followed by metronidazole 2gm qd x 5 d followed by metronidazole 2 gm qd x 7d.	1. Failed saline douches, betadine douches, vaginal clotrimazole (with and without estrogen cream), paromycin cream. Failed conjugated equine estrogen cream (1g) nightly alternating with vaginal clotrimazole for 2 weeks. Failed 4% acetic acid vaginal douche/debridement followed by vaginal clotrimazole alternating with 600mg boric acid in gelatin capsules for 6 weeks. 2. Failed 4% acetic acid vaginal douche/debridement applied followed by alternating vaginal clotrimazole in morning with 600mg vaginal boric acid in gelatin capsules at bedtime. She was given another single dose metronidazole during this course followed by metronidazole 250mg TID x 7d. She underwent further vaginal douche/acidification with 4% acetic acid followed by continuing vaginal clotrimazole in morning and boric acid in evening for 2 more weeks. Failed this and developed yeast infection which was	1. Responded to the boric acid/clotrimazole alternating regimen when extended for 5 months. Has been TV culture – for >5 yrs. 2. Responded to vaginal regimen of 600mg boric acid capsules BID + intravaginal gentian violet applied weekly resumed for duration of 1 month. Patient TV – for 4 months	1. Partner treated with metronidazole at time of initial Rx and not mentioned again. 2. Partner not mentioned.	C

			treated with gentian violet intravaginally and oral fluconazole.			
Dan (2007)[73]	Case reports N=3	1. 43yo failed metronidazole, failed tinidazole 2 total dose regimens of 42-60g orally and vaginally, failed topical paromomycin, thiobendazole, albendazole, atovaquone, zinc bacitracin, furazolidone-nifuratel all in combo with tinidazole. MIC 60ug/mL for metro and 30ug/mL to tinidazole. 2. 61yo Severe urticaria to metronidazole 3. 35yo failed 2 single dose 2gm tinidazole courses, 7 days 500BID metro course then seizures developed.	Case 1 –nitazoxanide 2g BID x 14d followed by 2g BID + oral tinidazole Case 2- nitazoxanide 1gBID x 7d Case 3 – nitazoxanide 1g BID x 7d	0/3 cured. Case 1 – lives with trich Case 2 – desensitized and cured with tinidazole Case 3 – cured with high dose tinidazole (1g po TID + 0.5g intravag TID x 14d)		C

Waters (2005)[74]	Retrospective chart review N=15	Female patients attending UK GU medicine clinic between 1985 and 2002 with two or more positive TV cultures in the microbiology database. Notes reviewed within a 6mo period of micro results Recalcitrant TV = failure to respond to 2g x 1 dose of metro followed by metro 400mg BID x 7 d (everyone received this regimen). Excluded if poor of doubtful compliance per medical record.	15 (1.2%; 95%CI 0.7-1.9) refractory TV cases, out of 1292 total cases seen in clinic All received 2g metro + 7 d metro (400BID) 3 specimens sent for susceptibility testing	All 3 specimens demonstrated aerobic and anaerobic resistance (?MIC cut off) 10/15 with negative TOC end of RX and 5/10 LTF. Patients required RX on 4-12 occasions (median 6) RX resulting in microbiologic cure: 1) Metro 1g BID per vagina x 14d + povidone-iodine vaginal cleansing kit qd x 14d 2) Metro 500mg TID per vagina x 5d + povidone-iodine vaginal cleansing kit qd x 5d 3) Tinidazole 2g po x 1 (2 patients) 4) Tindazole 2g po qd x 10 d + clotrimazole pessary per vagina x 3d 5) Povidone-iodine pessary 250mg per vagina x 14d 6) Acetarsol pessary 250mg per vagina x 7d 7) Acetarsol pessary 250mg per vagina x 14 d (3 patients) 8) Nonoxynol-9 per vagina x 2 d	Case series No uniformity to rx. Reinfection not addressed	C

Mammen-Tobin (2005)[75]	Retrospective chart review N=11	Women in Leeds (UK) clinic between 1994-2002 with documented TV (by wet mount and/or culture) who failed to respond to 2gm oral metro x 1 or 400mg metro BID x 5-7d. Excluded cases of probable reinfection or nonadherence. Failure to respond = persistence or recurrence of signs and symptoms of vaginitis + TV positive WP or culture.	Regimen = tinidazole 2g BID + Amp 500mg TID + clotrimazole pessaries 500mg Qhs x 7-14d (doxy 100mg BID substituted for amp if PCN allergic)	8/11 received all 3 drugs while 3 received tinidazole + broad-spectrum ab (no pessaries). All treated 7-14d. 9/11 cured (6/8 receiving 3 drugs and 3/3 receiving 2 drugs). 1 documented RX failure and 1 LTF Cure rate = 90% (if exclude LTF). Treatment of partners documented in 4 male partners of female patients. 2gm x 1 metro effective in 3 of 4. 1 of 4 cured with tinidazole + doxy	Case series RX more uniform than many but still variable. Cure of male partner based on ability to cure the woman (TV not isolated from male partners)	C

Hager (2004)[76]	Case reports N=3	1. 33yo (164lb) 4mo vaginitis. Failed intravaginal and PO metronidazole rx failed. 2. 38yo (137lb) 6mo vaginitis. Metronidazole PO and PO w/ intravaginal failed. 3. 42yo (176lb) 4.5mo vaginitis. Failed metronidazole PO and PO/vaginal.	1. Tinidazole 500mg PO tidx10d. partner rx w/ metronidazole 2. Tinidazole 500mg PO tid x 7d. partner rx w/ metronidazole 3. Tinidazole 500mg tid PO x7d . Partner rx w/ same tinidazole	1. Cure after tinidazole with f/u at 14d and 1mo w/ wet prep 2. Cure after tinidazole w/ f/u wet prep 14d and 1mo 3. Cure after tinidazole w/ f/u wet prep 10d and 30d. Side effects reported were metallic taste in all 3	Cannot r/o reinfection v. resistance. No data on prior partner rx. No cx MLC/MIC. Clearance evaluated w/ wet prep only	C
Kanno (2003)[77]	Case report N=1	30yo woman presented to clinic in 1999 w/ 4mo hx vaginitis rx w/ 5 courses of metronidazole 500mg bid w/ longest course 10d	Tinidazole 2 g daily PO and 1 g per vagina daily x14d.	Cx+ for TV, MIC metronidazole >100 ug/ml (MIC control 5 ug/ml). At 5wk f/u TV cx (-). Relapsed post 9mo after sexual contact w/ original partner. Retreated tinidazole 3 g PO dailyx14d. Sx freeafter 8 wks, w/ nrml exam. No repeat cx obtained.		C

Sobel (2001)[78]	Retro-spective chart review N=24	Women w/ metronidazole resistant TV (failure to respond to metronidazole 500mg PO BID x 7 days) seen at 2 U.S. clinic between 1/96 and 12/00. Dx confirmed by wet prep & some patients resistance testing on cx	Rx w/ **intravaginal 5g paromomycin (250mg/g) daily x 14 d** or tinidazole 500mg qid PO w/ intravaginal 500mg bid x 14d or tinidazole 1g tid PO w/ intravaginal 500mg tid x 14d. Evaluation after rx and 4-6wks w/ wet prep. Cx done in most	Median duration of vaginitis sx 15.9mo 2 patients responded to high dose metronidazole alone. 12 patients given 13 courses of paromomycin. 7 cured (58%). 22/24 (92%) patients cured (5 who failed paromomycin) w/ tinidazole. Of 2 failures 1 cured w/ tinidazole and paromomycin x 14d. 1 failed multiple courses tinidazole. High frequency of local disease effects w/ paromomycin. 15 patients aerobic metronidazole MLC median 32.5ug/ml, range 6.25-200ug/ml.	Limited resistance testing of organisms. Retrospective. Different doses of tinidazole used at 2 different clinic sites.	B
Lewis (1997)[79]	Case reports N=3	1. 48yo with 3mo hx vaginitis. Failed metronidazole 2g single dose, higher doses metronidazole, clotrimazole pessaries and single dose tinidazole. 2. 37yo with a 20y hx vaginitis Failed multiple courses of metronidazole, clotrimazole pessaries, augmentin, tinidazole, nonoxynol-9 3. 44yo 7w hx vaginitis . Failed metronidazole 400mg bid x5d. higher dose metronidazole, nonoxynol-9, paromomycin, tinidazole 2g once, acetarsol pessaries	1. Tinidazole 2g daily x2d 2. nonoxynol-9 3. acetarsol pessaries 250mg nightly for 14d	1. negative wet prep at 3 and 7w f/u from tinidazole. MIC for metronidazole aerobic 500ug/ml w/ control 2ug/ml 2. responded to prolonged nonoxynol-9 3. responded to acetarsol pessaries. wet prep negative at 6w. metronidazole MIC 16ug/ml w/ control MIC 4ug/ml.		C

Dan (1996)[80]	Case report N=1	40yo w/ 3mo hx of TV that failed 2 courses metronidazole 500 mg qidx14d, metronidazole PO 1gqid and vaginal tablets 500mg bid x 14d w/ recurrence 1wk after completing rx		Tinidazole 2g PO x 14d	Infection cleared and examination normal at 1 and 3 mo.		C
Chunge (1992)[81]	Randomized trial N=153	Non-pregnant women w/ vaginitis and TV on microscopy in Kenya.	Directly observed **Nimorazole 2g, nimorazole 2g x2 doses, nimorazole 3g, tinidazole 2g, ornidazole 1.5g PO** directly observed. 13 to 16 patients in each group by final analysis. Patients not advised to avoid sex before f/u.	f/u day 3 w/ wet prep x 3	121 returned for f/u. 49 dropped b/c of sex after rx. Only 72 included in final analysis. Tinidazole parasitological cure rate 50% (7/14), ornidazole 54% (7/13) , nimorazole 3g 93% (13/14, nimorazole 2gx2 100% (16/16), nimorazole 2g 67% (10/15). Clinical cure for tinidazole 86% range from other rx 80-100%.	Small sample size. No TV cx data. Possible selection bias based on exclusion of women who had sex after rx. No mention of testing for other causes of vaginitis or cervicitis	A
Lossick (1990)[82]	Review	Treatment options for TV vaginitis			Anecdotal experience indicates that urticarial adverse reactions do not always recur if nitroimidazole therapy is repeated		C

Chaisilwattana (1980)[83]	Double-blind N=180	Nonpregnant Thai women w/ TV	Rx w/ tinidazole 2g PO in single dose or **ornidazole 1.5g PO in a single dose**. Partners provided w/ same rx.	Hanging drop microscopic evaluation for TV. F/u on day 4,7, & 14 w/ hanging drop assessment for TV, pH,	13 drop outs. Chronic vaginitis 36.5% and relapsed TV in 20.6%. More recurrent cases in ornidazole group. At 4d after rx, 54/55 TV- in ornidazole group and 52/52 TV- in tinidazole group. 1 tinidazole patient relapsed on 3rd f/u. Side effects in 13.5% and 30.9% w/ tinidazole and ornidazole. Side effects to ornidazole tended to be more severe by report.	Rx was not directly observed. No cx data. No randomization.	A
Chaudhuri (1980)[84]	Double-blind controlled trial N=77	Nonpregnant women w/ TV on wet prep	Tinidazole 2g PO in single dose or **carnidazole 2g PO in a single dose** given to patient and partner	F/u 1 & 2 wks w/ wet prep	39/39 cured w/ carnidazole 36/38 (95%) cured w/ tinidazole ($p>0.1$). 2 failure had TV on all 3 evaluations. 25/78 reported side effects in carnidazole and 12/76 in tinidazole group ($p>0.05$). Nausea and vomiting greater in carnidazole (18) then tinidazole (4) group ($p<0.001$)	Not randomized. No cx.	A

Hillstrom (1977)[85]	Randomized Double blind trial N=88	Nonpregnant women w/ TV on wet prep presenting to gynecology and STD clinics	Tinidazole 2g PO in a single PO dose or **ornidazole 1.5g PO in a single PO dose**. 27 sexual partners in ornidazole group and 25 partners in tinidazole group received corresponding TV rx	F/u 1wk and 1mo w/ TV cx	45/45 (100%) women in ornidazole group TV cx (-) at ~1wk. 41/43 (95%) in tinidazole group TV cx (-) at ~1wk. 2 failures rx w/ ornidazole and 1 cured. Mild side effects reported in 6/45 ornidazole and 9/43 tinidazole patients. 1 reinfection in 1 patient in ornidazole group found at f/u 1 mo later.	Incomplete partner rx could have effected 1mo f/u data	A

4. Epidemiology of Antimicrobial-resistant TV

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Kirkcaldy (2012)[86]	Prospective cohort study N=538	TV isolates from TV+ women at STD clinics in 6 U.S. cities	Swab specimens from women found to be TV+ on routine pelvic exam were cultured and tested at CDC for in vitro resistance at CDC. (minimum lethal concentration MLC>50ug/mL)	Prevalence of in vitro metronidazole and tinidazole resistance among TV isolates	Of 538 TV isolates, **23 (4.3%) exhibited low-level in vitro metronidazole resistance** (minimum lethal concentrations 50-100 microg/mL). No isolates exhibited moderate- to high-level metronidazole resistance nor tinidazole resistance.	Not nationally representative In vitro resistance may not correlate with clinical symptoms. No data on clinical treatment or cure.	B

Bosserman (2011)[87]	Retrospective chart review N=175	In vitro specimens from women with refractory TV (standard therapy failed at least twice) whose clinicians requested consultation and susceptibility testing from CDC between 2002-2008	Alternative treatment recommendations were provided based on susceptibility results. - If isolate susceptible: Metronidazole 3g PO x 14d - If isolate min resistant: Tinidazole 2g PO Tinidazole x 7d - If isolate mod resistant: Tinidazole 3g PO + 1g vaginal tinidazole X 14d - If isolate high resistant: Furazolidone vaginally	Susceptibility testing performed for metronidazole and tinidazole: MLC<50ug/ml =susceptible MLC 50-100ug/ml min. =resistant MLC 200ug/ml =mod resistant MLC >/=400ug/ml =highly resistant	In vitro, 115 of 175 isolates demonstrated metronidazole resistance: 35 (20%) isolates were minimally resistant, 24 (14%) isolates were moderately resistant, and 56 (32%) were highly resistant/ For all isolates resistant to metronidazole, in vitro resistance to tinidazole was similar or lower. Clinical and microbiologic treatment success was attained in 59 (82%) of 72 women whose follow-up information was available. Of the women receiving an alternative recommended nitroimidazole regimen, 30 (83%) of 36 were cured compared with 8 (57%) of 14 women who received a lower dose than recommended.	Potentially biased sample (only have specimens for patients whose providers contacted CDC) Followup available on only 72/175 women (41%)	B

Krashin (2010)[88]	Cross-sectional N=467	Nonpregnant, HIV-seronegative, sexually active females (13–19) visiting an inner city public primary care clinic	Tested for TV by wet mount and culture, and interviewed about risk-taking behavior every 6 months Infected patients were treated with 2g oral metronidazole TV cultures were tested for in vitro resistance to metronidazole and tinidazole	Epidemiology of TV and resistant TV among female adolescents	**Initial prevalence was 14.4%.** Significant risk factors for TV infection were having an older sex partner and concurrent GC. **Incidence was 22.1 cases per 100 person-years.** Among 42 participants who had a prevalent infection and returned for followup, 13 (31.0%) had at least 1 more episode of trichomoniasis. Resistance was uncommon among 78 isolates. 1 (2.7%; CI:0.07–14.2) of 37 first-visit isolates was moderately resistant to metronidazole (MLC=200ug/mL). Of 41 follow-up visit isolates, 1 was moderately resistant to metronidazole and 2 had borderline resistance (MLC=50ug/mL). The prevalence of tinidazole resistance was 0% (CI:0–9.5).	Could underestimate TV prevalence since NAAT was not used. No data on partner treatment.	B

Schwebke (2006)[89]	Cross-sectional study N=209	Women attending Alabama STD clinic between 5/03-5/05. enrolled in TV partner notification study.	All pts rx 2gm metro TV cx (InPouchTV)	Susceptibility according to CDC protocol (modified Meingassner method) Resistance to metro=aerobic MLC>/=50ug/ml/anaerobic MLC >3.0ug/ml	31 isolates lost viability, 178 for analysis. 17/178 (9.6%) resistant to metro (aerobic): 14/17 (82.4%) with MLC 50-100ug/ml; 3/17 (17.6%) with MLC 200-400ug/ml; 1 tinidazole resistant (MLC 50ug/ml). 13/178(7.3%) resistant to metro (anaerobic), 2/178 (1.1%) resistant to tinidazole. No correlation b/t aerobic and aerobic MLCs **Clinical outcomes not correlated with MLCs**. 12/209 women TV+ at 1st f/u and 11 denied reexposure. Among women with TV resistance, 2 failed stat metro, both had MLC 100ug/ml. Neither woman with high level resistance failed therapy.	31 isolates lost viability Limited generalizability.	B

Saurina (1998)[90]	Case report N=1	33yo w/ TV failed multiple courses of metronidazole over 4y w/o recurrent sexual exposure including metronidazole 2.5g/d and intravaginal 0.5g at bedtime x 20d, oral furazolidone 300-400mg qidx7d,intravaginal furazolidone 100mg in 5g of 3% nonoxynol-9one to 3 x daily for 7d. Improved on intravaginal furazolidone for >1mo but recurred	Tinidazole 5 00mg qid w/ 500mg intravaginallly bid x14d. Measurement of MLC.	Metronidazole MLC aerobic/anaerobic were initially 400/12.5 increasing to >400/25. Tinidazole MLC aerobic/anaerobic fluctuated between 100/25 and 400/12.5. Patient responded to rx and had negative vaginal and urinary sediment cxs at 21 and 60 days. Sx free at 5mo.		C
Nyirjesy (1995)[91]	Case report N=1	53yo with 14y hx TV failing metronidazole, clindamycin. Finally w/ metronidazole 3g PO and 1.5g intravaginal daily x 14d. Tinidazole 3g PO 1.5g intravaginally daily x 14d w/ 3w alleviation of sx but recurrence	Cured with paromomycin intravaginal prep.	MLC metronidazole 200mg/l aerobic and 12.5mg/l anaerobic, tinidazole 50mg/l aerobic and 12.5mg/l anaerobic. Control metronidazole 50mg/l aerobic and 6.3mg/l anaerobic.		C
Voolmann (1993)[92]	Case report N=1	54yo with recurrent TV x18mo after $\geq$10 courses of tinidazole and metronidazole. Sexually inactive 8mo after dx. Therapies included clotrimazole 1% pessaries qhs x 14, metronidazole suppositories 2g qhs x 7d. 2.5% nonoxynol-9 cream 1g intravaginal bid x 14d, 5% nonoxynol-9 cream and povidone-iodine douches bid x14d followed by saline douches. + Response to last therapy for 4w. 5% nonoxynol-9 cream w/ trimethoprim/sulfamethoxaole bid x 1mo.	Tinidazole 2g PO bid and 500mg intravaginal qhs w/ 3% acetic acid douches qhs from day 6 x 16d.	MIC to metronidazole anaerobic/aerobic 25-50/400 to tinidazole -/ 12.5-25ug/ml. Control MIC metronidazole anaerobic/aerobic 0.8-1.6/6.25-12.5ug/ml tinidazole -/0.4ug/ml. Negative cx and asx over 6mo after rx		C

Hamed (1992)[93]	Case report N=1	31yo w/ 15mo hx of TV. Failed: metronidazole 750mg PO to 2 g daily for intervals 7d to 14d. High dose PO metronidazole w/ 1g intravaginal tid x 14d. Acetic acid vaginal douches. IV metronidazole 500mg q 6hrs x 14d. Mebendazole 400mg tidx1wk sx would recur soon after rx cessation. No sex since infection.	Tinidazole 2g daily for 2d	MLC for metronidazole aerobic and anaerobic >1000ug/ml and 8ug/ml, tinidazole >400ug/ml and 3.1ug/ml. Control MLC metronidazole and tinidazole 12.5ug/ml and 0.8ug/ml. Asx and negative wet prep after 4 mo f/u		C
Livengood (1991)[94]	Case report N=1	31yo woman seen 3/88 for chronic vaginitis 12mo. Metronidazole 2g once and up to 1.5g PO and 500mg intravaginally both tid x 5d. and metronidazole 1g PO and 1g intravaginally tid failed after 33d rx. Tinidazole 2g once followed by 1g BID for 4d failed. Rx w/ intravaginal sulfonamide, gentian violet, nitrofuantoin, chlorhexidine, clotrimazole, povidone-iodine, 3% acetic acid and H_2O_2 and 20% saline douche also failed	Clearance after 100mg nonoxynol-9 intravaginal twice –confirmed by TV cx.	Aerobic and anaerobic MLCs to metronidazole were greater than 1000ug/ml and 4ug/ml with tinidazole 400ug/ml and 1.6ug/ml and control isolate was 12.5ug/ml and 0.8ug/ml		C
Forsgren (1979)[95]	Case report N=1	25yo w/ TV on wet prep. 14 courses of metronidazole. Tinidazole 2g as a single dose given 6x and 4g single dose given once. Nitrofuratel w/o success	MLC testing. Drug levels	MLC control TV 1.25-10ug/ml mean 3.75ug/ml. MLC patient strain mean 160ug/ml range 80-320. Tinidazole level at 4hrs 40ug/ml and at 48hrs 2.5ug/ml		C

5. Management of TV in Pregnancy and Breastfeeding

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJ. QUAL. RATING
Golightly (2012)[96]	Review	Various			Low doses of metronidazole are compatible with breastfeeding		B
Gulmezoglu (2011)[97]	Meta-analysis of 2 trials with combined N=842 pregnant women	Cochrane Pregnancy and Childbirth Group's Trials Register. Randomized trials comparing anti-trichomonas agents during pregnancy.	Trials including symptomatic or asymptomatic women with trichomoniasis were eligible. Both trials (Klebanoff 2001 and Ross 1983) involved metronidazole.	In both trials around 90% of women were cleared of trichomonas in the vagina after treatment.	**Metronidazole, given as a single dose, is likely to provide parasitological cure for trichomoniasis, but it is not clear whether this treatment will have any effect on pregnancy outcomes** (either helpful or harmful).	Cure rate could probably be higher if more partners used the treatment. Only 2 studies included.	See individual trials below
Stringer (2010)[98]	Randomized trial N=2428 woman-infant pairs, ~86% HIV+	Pregnant women from four sites in Africa enrolled in a randomised trial (HPTN 024) of antenatal and intrapartum antibiotics to reduce chorioamnionitis-related perinatal HIV transmission.	Women were randomised to receive either antibiotics (metronidazole 250 mg and erythromycin 250 mg orally, both 3 times daily for 7 days) or placebo.	Gestational age at the time of delivery or mean birth weight.	428 (18%) mothers had TV at enrollment. Of these, 231 (54%) were randomised to receive the study antibiotics and 197 (46%) were randomised to placebo. Women randomised to receive antibiotics were more likely to have resolution of trichomoniasis at their second visit ($p<0.0001$). There were no differences in mean birth weight between groups. Women with TV who received no treatment were more likely to deliver a preterm infant when the symphysis-fundal height was used to estimate gestational age (36% v. 23%; $p=0.03$), but not when the Ballard score was used (16% v. 21%; $p=0.41$).	A number of women randomised to the placebo arm were exposed to metronidazole, but an actual-use analysis, showed similar results to the the intention-to-treat analysis (**no differences in pregnancy outcomes associated with diagnosis or treatment of trichomoniasis**.)	A

Mann (2009)[99]	Model based on retrospective administrative data N=144,737	Singleton live births in South Carolina from 1996-2002 and their mothers	Medicaid billing data and birth certificate records Excluded women initially diagnosed with trichomoniasis at ≥35 weeks or who delivered <2 days after the diagnosis	Cox proportional hazards regression **to assess risk of preterm birth among women with trichomoniasis who were untreated versus treated** with oral metronidazole	4274 (3.0%) of pregnant women were diagnosed with trichomoniasis and 3579 met inclusion criteria. 1436 (40.1%) filled a prescription for oral metronidazole within 14 days. Of treated women, 12.7% delivered prior to 37 weeks compared with 15.3% of women who were not treated within 14 days. In the multivariable proportional hazards regression, **metronidazole treatment appeared to be protective** both for women with another genitourinary infection at some point during pregnancy (HR=0.69, CI:0.50-0.95) and without (HR=0.69, CI:0.52,-0.92).	Cases of trichomoniasis were identified using billing codes.	B
Kigozi (2003)[100]	Subgroup analysis of nested randomized controlled trial	Pregnant women 1994-99 Rakai Uganda. 5 community clusters randomized to STD intervention and 5 community clusters randomized to control condition. Analysis of women with documented TV infection by cx during pregnancy	Random sample intervention and placebo arms tested w/ TV cx. TV 12% (112/926) intervention arm and 18% (165/926) cntrl arm (P = .0007). Lower TV in intervention arm due to preceding rounds of mass rx . Intervention arm received directly observed azithromycin, cefixime, and 2 g metronidazole. Control arm mothers received Fe, folate and MVI	Mothers and infants followed during 1st wk of life to determine infant wt and gestational age at birth. Low birth wt: <2500g. Prematurity: <37wks gestation. Child mortality rate at 1 and 2 yrs.	Intent-to-treat analysis. Low birth weight more common in rx (18%) than placebo (7%) (RR 2.5; 95% CI 1.1-5.5). Tendency seen regardless of trimester of rx although not statistically significant on subgroup analysis. Prematurity tended more common in rx (24%) than placebo (19%) (RR 1.3; 95% CI 0.8-2.0). Tendency seen only in 1st trimester rx (30% rx vs.15% placebo; RR 2.1; 95% CI 0.9-4.4.) Tendency higher infant and 2yo mortality in rx arm(RR 1.3; 95%CI 0.7-2.2 and RR 1.6; 95%CI 0.9-2.5, respectively.) After controlling for HIV, RR of 2 year mortality rx group declined (RR 1.4; 95% CI 0.7-2.5.)	Lower % of infants in cntrl arm had wt measured w/i 1 wk. Rx group had higher prevalence HIV then controls(29% vs.22%, p=0.18). control arm had higher prevalence TV (p=0.0007)Subanalysis of nested study. Not designed for evaluation of rx during pregnancy of TV. No f/u assess. of TV cure. Effects of other abx unclear. No data on possible confounders such as mother wt, other STDs, smoking, age etc.	A

Czeizel (2003)[101]	Data from Hungarian Congenital Abnormality Registry				The rate of congenital abnormalities was not higher among children born to mothers who had received oral tinidazole during pregnancy (10/22843 cases compared with 16/38,151 controls, OR 1.0, 95%CI: 0.7–1.3)		B
Klebanoff (2001)[102]	Double blind placebo controlled randomized multi-center trial N=617 320 rx 297 placebo	Asymptomatic pregnant women (no sx of vaginitis, chronic medical conditions, GC, CT, syphilis, or abx use) w/ TV cx+ at screening at one of 15 antenatal centers in the U.S.	Screened at 8-22wks, 6d gestation. Randomized to rx or placebo and repeat testing at 16wks and 23wks, 6 d gestation. Rx: metronidazole 2g at randomization and 48hrs later vs. placebo. All partners given 2g metronidazole. F/u at 24 to 29 wks, 6 d gestation, ≥14d after initial rx. Testing and repeat rx as above.	Women with asymptomatic TV between 16-23 weeks were treated with metronidazole on two occasions at least two weeks apart. Preterm birth(<37 wks gestation). Infant birth wt. PROM. Intraamniotic infection. Postpartum endometritis. Neonatal sepsis	Intent to treat analysis, prematurity 19% of rx group and 11% placebo group (RR 1.8, 95%CI 1.2-2.7). Primarily attributable to preterm labor, 10% rx and 3.5% placebo (RR 3.0, 95% CI 1.5-5.9). Tendency to low birth wt in rx group. 72% rx group and 71% placebo group had TV at randomization. In patients w/ TV at randomization prematurity more common in rx than placebo (RR 1.9, 95%CI 1.2-3.0). Birth wt <2500g found in 16% rx and 12% placebo infants (RR 1.4, 95% CI, 0.9-2.1). Birth wt <1500g found in 5% rx and 4% placebo (RR1.4; 95% CI .7-3.0). TV at f/u 7% rx group and 65% placebo group. Additional metronidazole administered to 12%rx group and 26% placebo group (p<0.001).	As treated analysis not available. Repetitive high dose metronidazole non-standard for uncomplicated TV or TV in pregnancy. Significant metronidazole use in placebo group w/ resultant misclassification. Results may not be generalizable to all racial groups. Only assessed asx patients which may select for certain host or pathogen features. Trial was stopped early because women taking metronidazole were more likely to give birth preterm and have low birthweight babies. (RR 1.8; CI 1.2-2.7).	A-

Goldenberg (2006)[103]	Double-blind placebo controlled Phase III trial, 7/01-8/03 N= 2098 HIV+ and 335 HIV-	Zambia; Malawi; Tanzania Prenatal care clinics, enrolled 20-24wk gestation. At ¾ sites, for every 5 HIV+ F enrolled, 1 HIV- F enrolled. ¼ site only HIV+ F Only women with known outcome, singleton delivery in analysis DSMB closed enrolment 2/03 due to NS decrease MTCT HIV. No L and D antibiotics given after 3/03 due to small increase in MTCT in those randomized to receive antibiotics at delivery (NS) All included in analysis as no differences in outcome with or without this group.	Study visit enrolment, 28wk, 36wk (+prenatal visits) Testing for candida, NG, CT, TV, syph, BV (Nugent/Amsel) at enrolment, 28wk Placental samples at delivery (path). Enrollment/random. Visit – metro 250mg + erythro 250mg both TID x 7d or placebo Onset labor or premature ROM, metro 250mg + AMP 500mg both q4 until delivery or up to 7d if undelivered. Questionnaires, blister pack count GA based on fundal ht, LMP (67% missing), and Ballard score (peds assess at birth) 90% HIV+ received single dose NVP (no other ART given)	Birth at <32wk, <35wk and <37wk <1500g, <2500g Infiltration of PMN in placenta (none/slight vs marked)	HIV+ lower educ, less likely to be married/living with partner, greater # pregnancies and stillbirths, had more syphilis, trich, BV than HIV- Infants of HIV+ more likely to weigh <2500g, more likely to be preterm at 32 and 35wk by fundal measurement. HIV+ and HIV- analyzed separately. Placebo and control comparable within each group except RX group more likely TV+ in HIV+ women. HIV+ RX group with 60% reduction TV between visit 1 and 2, 49% reduction in BV b/t visits, compared to placebo HIV- RX group with 51% reduction TV (NS) and 61% reduction BV between visits 1 and 2. **In HIV+ and HIV- group, no sig difference in GA by LMP, fungal height, Ballard score; no sig difference in mean birth weight** and no difference in PMN infiltration by placental site EXCEPT mean GA one week longer in HIV- treatment group by LMP only. HIV+ women had significantly worse birth outcomes than HIV- women Adherence high.	Single pathologist read all slides. Cannot generalize to HIV- popln due to No testing for STDs or other cultures performed at delivery Methodology for TV testing not mentioned (nor for NG and CT). No mention if women tested or treated between visits for pathogens. Results not conclusive for HIV- women Emycin used for 20-24 wk RX then switched to amp for delivery. Unable to assess adherence at delivery after 3/03. GA age not precise (though used multiple measures to get around this. Excluded if antibiotics previous 2 wk (except NG/syph RX), allergy to study meds, other major med problems (ie. DM, CVD), CNS	IB

						disease, obstetrical problems (placenta previa, etc).	
French (2006)[104]	Secondary analysis of combined data from 1 prospective cohort study and 3 clinical trials (1985-1993)	Data from subjects enrolled in previous studies; received care at Univ Colorado affiliated sites with similar prenatal protocols (95% popln on public assistance)	TV (wet prep), NG (culture), CT (culture or EIA), BV (gram stain), M hom cx, G vag cx, u urea cx, GBS cx.	Prevalence infxn black vs NH White/Asian Population Attri FX due to infxn Number needed to treat	Black women had had more pregnancies/deliveries and enrolled significantly later (ie GA 23.3 wk vs 21wk). Black women more likely to have BV (RR 1.6; 95% CI 1.4-1.9), TV (RR 3.7; 95% CI 2.4-5.8), CT (RR 2.4; 95% CI 1.6-3.6), NG (RR 8.4; 95% CI 1.8-40.0), GBS (RR 3.2; 95% CI 1.6-6.6), M. hominis (RR 1.8; 95% CI 1.4-2.1) and U. urealyticum (RR 1.1; 95% CI 1.0-1.2) than non-black. Black women more likely to have preterm birth (RR 1.5; 95% CI 1.0-2.2), premature ROM (RR 2.6; 95% CI 1.2-5.4) and endometritis (RR 2.2; 95% CI 1.2-4.2). Excess risk of preterm birth for BF differed sign based on presence or absence of 1 or more infxn. RR preterm birth from TV 1.4 (0.4-5.5) with PAF 3.4% in black women (in W/Asian women RR 1.7 (0.4-6.4 and PAF 2%). RR combined infxn 3.6 (1.8-7.5) with PAF 26.9% in black women vs RR 2.4 (0.8-6.9) and PAF 4.1% in white/asian. Presence >/=1 infx with RR 2.2 (1.1-4.1) and PAF 42 in black females compared to RR 1.4 (0.8-2.5) and PAF 10% in white/asian females 1 preterm birth prevented for every 6 black female screened/treated for >/1 infxn. For every 12 BF screened, 1 preterm birth prevented with adequate RX	Data collected through different studies with similar but not identical protocols. Some of the studies had treatment arms that were not randomly assigned. Medical record reviews done to classify exposures could lead to misclassification Small # preterm births could lead to loss of precision with estimates. Lack of generalizability	B-C

Morency (2007)[105]	Meta-analysis	Review limited to RCTs 1965-2006 and human females. Women had to have been randomized macrolides or equivalent placebo (or no RX), during second trimester (12-28wk) in order to prevent preterm delivery Excluded studies including women with PPROM, preterm labour or RX beginning at <12wk gestation. Excluded trials with <30 pts, who did not report rate of preterm delivery and who had >5% LTF. Similar procedure for studying clinda and metro use.	61 articles found, only 3 met inclusion criteria for macrolide. N=1807 for macrolide vs placebo 62 articles found, only 5 met inclusion criteria for clinda (N=1523) 62 articles found, 8 eligible for metro (N=5310)	1) Deliver <37wk 2) Mean gestational age at delivery	No sign. Change in rate of delivery before 37wk found in women receiving metro (OR 1.1;95% CI 0.95-1.29) . No change in mean gestational age. When analyses restricted to metro alone during second trimester (vs combined with another antibiotic) – N=3991, Metro use associated with higher rate preterm birth (OR 1.31; 95% CI 1.08-1.58)	Few studies met inclusion criteria. Problems inherent with meta-analysis (i.e. heterogeneity of popln and treatment, different risk factors for preterm delivery amongst study participants). Dose, duration and route of administration of medications different amongst studies.	C

Hitti (2007)[106]	Prospective observational multi-center study N=11,910	Subjects enrolled at 23-26wk gestation in the Vaginal Infections and Prematurity Study between 1984-1989. Women excluded if antibiotic use in past 2 weeks or risk factors for preterm birth (cervical cerclage, tocolytic use prior to enrolment, HTN, renal or autoimmune dx, IDDM)	At enrolment, samples sent for CT (culture), TV (culture), BV (Nugent+pH>4.5) and other genital flora.	Preterm delivery (<37wk) of low-birthwt infant (<2500g) and its association with genital tract infx.	Preterm delivery occurred among 287 (6.4%) of 4479 AA, 135 (3.8%) of 3567 Hispanics, and 171 (4.4%) of 3864 whites (p<0.001). CT, TV and BV and multiple concurrent infxn all more frequent in AA. No difference in preterm delivery rate between those who did and did not receive antibiotics for infxn so data combined. Among AA, CT (AOR 1.23; 95% CI 1.06-1.45), TV (AOR 1.20; 95% CI 1.05-1.37) and presence of multiple infections (AOR 1.28; 95% CI 1.02-1.60) significantly increased rate of preterm birth. Trend for BV (AOR 1.12; 95% CI 0.98-1.23). Trend for TV to increase preterm birth in Hispanics but not significant. No affect in whites. PAR of genital infections to preterm birth in AA = 20.7%, 11.6% in Hispanics, 5% in whites	Insensitive test used for CT which probably underestimates risk assoc. with this infxn. Women with NG excluded due to low numbers.	IIB
Koss (2012)[107]	Retrospective cohort N=2829 singleton/ mother pairs	Chart reviews and an analysis of electronic data from a cohort of women delivering at an urban New York State hospital in Syracuse	Congenital malformations identified at birth or in birth certificates	Potential association between metronidazole during pregnancy and any adverse outcomes (preterm birth, low birth weight, or major congenital anomalies)	922 (32.6%) mothers received any metronidazole, 348 during the first trimester of pregnancy and 553 in the second or third trimester. There were 333 (11.8%) preterm births, 262 (9.3%) infants with low birth weight, and 52 (1.8%) infants with congenital anomalies. In multivariable analysis, **no association was found between metronidazole treatment and preterm birth (OR 1.02, CI: 0.80-1.32), low birth weight (OR 1.05, CI: 0.77-1.43), or congenital anomalies (OR 0.86, CI:0.30-2.45).**	Data dependent on documentation by providers of metrnodazole use and abonrmalities, biasing toward the null	B

Czeizel (1998)[108]	Case-control study	Cases congenital abnormalities (CAs) selected from Hungarian Congenital Abnormality Registry 1980-1996. 2 cntrl infants w/o CAs for every case matching by sex, week of birth, and residence	Exposure data obtained prospectively through antenatal care logbooks and other medical records, and by questionnaires. non-respondents families were visited at home by regional nurses	Effect tinidazole on CA	Exposure info available 86% of cases (response: 73.6%; home visit: 11.9%) and 69% (response: 68.9%; home visit: 0.4%) of controls. 10/22,843 CA cases (0.04%), and 16/38,151 controls (0.04%) had mothers w/ oral tinidazole rx (1-2 g per day for 6-7 days) during pregnancy (crude POR 95% CI: 1.0; 0.7-1.3). Tinidazole used mainly 2nd trimester (4 and 10 in case and cntrl groups. No indication of higher maternal tinidazole use during entire pregnancy or during 2nd-3rd mo gestation among cases	Very few tinidazole exposures for evaluation	B
Passmore (1988)[109]	Cohort N=12 mothers, N=35 infants	Breast-feeding women following multiple doses of metronidazole (400 mg three times daily) and suckling infants		Milk and plasma metronidazole and hydroxymetronidazole concentration	Mean milk to plasma ratio (M/P) was 0.9 for metronidazole and 0.76 for hydroxymetronidazole while the mean milk metronidazole concentrations were 15.5 micrograms ml. The mean milk hydroxymetronidazole concentration was 5.7 micrograms ml. Infant plasma metronidazole concentrations ranged from 1.27 micrograms ml to 2.41 micrograms ml, and the corresponding hydroxymetronidazole concentrations from 1.1 to 2.4 micrograms ml. There were no significant increases in adverse effects in infants which could be attributable to maternal metronidazole therapy. Metronidazole was excreted in milk at concentrations which caused no serious reactions in the infants studied. The drug may therefore be administered at doses of 400 mg three times daily to mothers wishing to breast-feed their infants.		

Erickson (1981)[110]	Cohort N=3	3 women who had been treated with a single 2.0-g dose for trichomoniasis.		Breast milk concentration of metronidazole	Highest concentrations of the drug were found 2 and 4 hours after administration, and they declined over the next 12 to 24 hours. It appears that if breast-feeding is withheld for 12 to 24 hours after the dose, infants will be exposed to a greatly reduced amount of metronidazole.	Small cohort	C

6. Management of TV with HIV Coinfection

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Kissinger (2013)[111] (in press)	Review				Factors that may interfere with standard single-dose treatment for trichomoniasis among HIV-infected women include high rates of BV co-infections, changes in vaginal ecology and impaired immunity		
Balkus (2013)[112] (in press)	Cohort	Female sex workers in Kenya, 1993-2010, with and without HIV coinfection	Treated with 2g metronidazole within 14 days of TV diagnosis	Persistance of TV infection after single-dose treatment	Nearly 1 in 7 had persistent TV infection. No significant difference in persistenceby HIV status. Participants taking ART had a 2.9 times (CI:1.9-7.3) increased risk of persistent TV infection		B

Kissinger (2009)[113]	Prospective cohort with matched controls N=58 treated for TV and 92 TV-negative controls	TV-infected women age ≥18 attending a public HIV outpatient clinic in New Orleans, LA from 2002-2005 Controls matched on matched on ART status (yes/no) and date of enrollment	Women were examined and interviewed at baseline, 1, and 3 months. TV screening using wet mount microscopy and confirmed by TV InPouch culture Amount of cell free HIV-1 RNA in the vaginal fluids was determined by the Amplicor HIV-1 Monitor ultrasensitive assay.	To examine if effective TV treatment reduces the presence of vaginal HIV-1 RNA	Most women (81.3%) were black and the mean age was 37.5 (SD 8.7). At baseline, 46.0% had plasma HIV-1 RNA >10,000 copies/mL, 26.4% had CD4<200, 54.7% were taking ART, and only 26.0% had detectable HIV-1 RNA in their vaginal fluids. **TV-positive women who were effectively treated for TV were less likely to shed HIV vaginally** at 3-months post-treatment compared to baseline (RR 0.34, CI:0.12– 0.92); there was no change for TV-negative women.	Samples could have been collected at different phases of menstrual cycle, which can also influence HIV shedding	B

Kissinger (2010)[114]	Nonblinded multicenter RCT N=270	English-speaking, HIV-infected (≥18 years) women undergoing routine gynecological care at selected public HIV outpatient clinics in the southern United States between May 1, 2006 and July 17, 2009 with a positive TV culture were eligible.	To determine if metronidazole (MTZ) 2gx1 is as effective as the alternative 7-day, 500 mg, twice-a-day dose for treatment of TV in HIV-infected women TV tested at baseline, TOC (test of cure 6-12 days after medication completion), and at 3 months		135 women in each treatment arm. 92% were African-American with mean age 40 years. 65% were on antiretroviral therapy and 30% had a CD4 count ≤200. TV prevalence at baseline: 16.9% At TOC, N=255, 12.5% were TV+ (8.5% in 7-day arm vs 16.8% in single-dose arm, RR 0.50, CI:0.25-1.00; P=0.045) At 3 months, N=152, 17.8% were TV+ (11.0% in the 7-day arm vs 24.1% in the single-dose arm, RR 0.46, CI:0.21-0.98, P=0.03).	76% of participants reported partner treatment with no significant difference between the 2 study arms. Test method?	A

Moodley (2003)[115]	Cross-sectional study N=692	Women presenting to primary health clinic in Kwa Zulu-Natal with GU sx.	Interview and exam. TV diagnosis by culture (Diamonds) Syndromic rx with cipro 250mg po x 1, metronidazole 2g x 1 and doxy 200mg qd z 7. Return to clinic 8-10 days later for questions and repeat exam	Clinical (resolution of signs and symptoms) and microbiologic cure	Mean age 24, previous history of discharge/dysuria in 46%. Vaginal discharge present in 91% of participants. 75% positive for any STD. **29% had TV** , 33% of HIV+ women and 25% of HIV- women (p=0.02) 80% women returned for follow-up and 70% allowed another exam. 65% women with TV clinically cured and 88% microbiologically cured. **No difference in cure rate by HIV status (90% HIV+ and 82% HIV- cured; p=0.3)**	Microbiologic TOC lower in women returning who were now asymptomatic (65%) vs women returning who were symptomatic (83%)	B

7. Management of TV in Women with BV

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Martin (2013)[116]	Laboratory study	Vaginal samples from 30 TV-infected women were matched by Nugent score to those from 30 TV-uninfected women	The vaginal microbiota was assessed using 454 pyrosequencing analysis of polymerase chain reaction-amplified 16S ribosomal RNA gene sequences	Principal coordinates analysis of the pyrosequencing data showed divergence of the vaginal microbiota in TV-infected and TV-uninfected patients among women with normal and those with intermediate Nugent scores but not among women with BV	Cluster analysis revealed 2 unique groups of TV-infected women. One had high abundance of Mycoplasma hominis and other had high abundance of an unknown Mycoplasma species. Women in the former group had clinical evidence of enhanced vaginal inflammation. TV may alter the vaginal microbiota in a manner that is favorable to its survival and/or transmissibility. An unknown Mycoplasma species plays a role in some of these transformations. In other cases, these changes may result in a heightened host inflammatory response.		

Gatski (2011)[117]	Secondary analysis of data from a clinical trial N=244	HIV+/TV+ women randomized to either single dose or multidose metronidazole treatment: 2 g once versus 500 mg BID x 7 days	Repeat TV infection rates were compared for women with a baseline TV/BV coinfection versus baseline TV infection only, and stratified by treatment arm. BV was classified using Nugent scores from baseline Gram stains. Women were recultured for TV at 6-12 days after treatment (TOC) and again at 3 months	Influence of BV on the response to TV treatment among HIV+ women.	92% black, mean age 40, 66.8% with BV. Women with BV were more likely to report douching and ≥1 recent sex partners. HIV+ women with baseline TV/BV coinfection were more likely to be TV-positive at TOC than women with baseline TV infection only (RR 2.42, CI: 0.96-6.07, p=0.05). When stratified by treatment arm, the association was only found in the single-dose arm (p=0.02) and not in the multidose arm (p=0.92). This interaction did not persist at 3 months.	Gram stains not collected at TOC or 3-month visits so unknown whether BV resolved	A
Schwebke (2007)[118]	RCT N=107 randomized (53 intervention/54 control)	Women presenting to Alabama STD clinic with asymptomatic BV defined by Nugent criteria and lack of vaginal sx. Women with STD (except HSV-2) at baseline excluded.	Block randomization to metronidazole gel qhs x 5day followed by twice weekly x 6mo versus observation. Followed monthly x 6mo then q3mo x 1yr. Screened for NG (NAATS), CT (NAATS), TV (InPouchTV), HSV-2 (serology) each visit	Vaginal flora defined by gs Time to first STI	Mean age 25.1y, all AA, no baseline differences by study arm, no difference in f/u. Women assigned to gel experienced sign. Vaginal flora better in gel group first 6mo of study though not all data points reached statistical sign. Longer time to any STI compared to observation group (median 138d vs 94d; p=0.02). STI rate sign lower in gel group (1.58py;1.29-1.87) compared to observation group (2.29py;1.95-2.63) Sign differences only for 6mo while on metro gel and driven by lower CT rates in gel group. TV rates not significantly different by RX group. No diff. after 7mo.	Unable to obtain full sample size due to resource constraints.	IB

Hillier (1992)[119]	Cohort N=7918	Pregnant women at 23 to 26 weeks' gestation	Women with normal flora were least likely to have elevated vaginal pH, amine odor, milky discharge, or colonization by Gardnerella, Bacteroides, or genital mycoplasmas. TV was most associated with intermediate flora.	Characteristics and persistence of vaginal flora. Vaginal smears were categorized as normal (predominant lactobacilli), intermediate (reduced lactobacilli), or positive for BV	At follow-up, 81% of the women with normal flora had remained normal. Of the women with intermediate flora, 32% acquired BV and 30% shifted to normal flora. Only 12% of the women with BV had shifted to normal flora. Trichomoniasis may indicate a disruption of vaginal flora with fewer lactobacilli than the normal vaginal environment, yet more lactobacilli than are present in BV.		B

8. Management of Men with NGU

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Sena (2012)[120]	Secondary analysis of data from trial below (Schwebke 2011) N=293	Heterosexual men age 17–45 attending U.S. STD clinics with symptomatic NGU	Nucleic acid amplification tests detected CT, MG, and TV at baseline and at 1 and 4 weeks after NGU therapy (doxy or azithro) with or without tinidazole	Persistence after treatment for CT, MGen, TV	Baseline prevalences: CT 44%, Mgen 31%, TV 13%. 98% African-American. We detected persistent CT in 12% and MGen in 44% of participants at 4 weeks after therapy. Persistent CT was detected in 23% of participants after azithromycin treatment vs 5% after doxycycline treatment (P = .011); persistent MG was detected in 68% of participants after doxycycline vs 33% after azithromycin (P = .001). **All but 1 TV infection cleared after tinidazole.**	Defined persistent infections based on a positive NAAT at 1 week after therapy if the participant did not return thereafter.	A

Schwebke (2011)[121]	Randomized, controlled, double-blinded phase IIB trial of men with NGU N=305	Heterosexual men age 16–45 with NGU who attended STD clinics in Birmingham, Alabama; New Orleans, Louisiana; Durham, North Carolina; and Baltimore, Maryland	Participants were randomized to receive either doxycycline 100mg PO BID x 7d (plus or minus tinidazole 2g PO x1), or azithromycin 1g PO x 1 (plus or minus tinidazole 2g PO x1) and were observed for up to 45 days.	We sought to determine whether the addition of tinidazole, an anti-trichomonal agent, to the treatment regimen for NGU would result in higher cure rates than those achieved with treatment with doxycycline or azithromycin alone. A secondary aim was to compare the efficacy of doxycycline therapy and with that of azithromycin therapy.	Baseline prevalences among men with NGU: CT 43%, Mgen 31%, TV 13%, no identified pathogens 29%. 98% African-American. Clinical cure rates at the first follow-up visit were 74.5% (111 of 149 patients) for doxycycline-containing regimens and 68.6% (107 of 156 patients) for azithromycin-containing regimens. By the final visit, cure rates were 49% (73 of 149 patients) for doxycycline-containing regimens and 43.6% (68 of 156 patients) for azithromycin-containing regimens. No significant differences in clinical response rates among the treatment arms. **Addition of tinidazole to the treatment regimen did not result in higher cure rates but effectively eradicated TV.** However, the chlamydia clearance rate was 94.8% (55 of 58 patients) for the doxycycline arm and 77.4% (41 of 53 patients) for the azithromycin arm (P 5 .011), and the M. genitalium clearance rate was 30.8% (12 of 39 patients) for the doxycycline arm and 66.7% (30 of 45 patients) for the azithromycin arm (P 5 .002).	In this study, tinidazole did not enhance the clinical cure rates of conventional therapy for NGU. This finding may be attributable to the lower-than-anticipated prevalence of trichomonas among study participants and the high rate of spontaneous regression of trichomonas in the absence of tinidazole.	A

Wetmore (2011)[122]	Cohort enrolled in an NGU treatment trial N=370	Men at an STD clinic in Seattle, WA 2007-2009 with visible urethral discharge and/or microscopic evidence of urethral inflammation by Gram-stain (≥5 PMNs/HPF)	Urethral swabs and urine specimens, NAATs for GC, CT, MG, TV, and UU	Etiology of NGU	Pathogens were detected in only 50.7% of the 367 eligible cases: - CT in 22.3% - MG in 12.5% **- TV in 2.5% (100% black, 89% ever in jail)** - UU in 24.0% - Multiple pathogens 9.5% - Idiopathic 45.8% Pathogen detection was associated with young age, black race, risky sexual behaviors, cloudy or purulent discharge, and visible discharge plus ≥5 PMNs/HPF.		B
Nyirenda (2009)[123] (poster)	Cross-sectional N=2845	Males with urethritis presenting between 2006-2008 to the Kamuzu Central Hospital STI Unit in Malawi. Persistent symptoms included dysuria and/or discharge within 5-30 days of the initial diagnosis of urethral discharge.	Prior to 2007, the standard treatment for urethritis in Malawi was single dose Gentamycin 240mg IM and Doxycycline 100mg BID x 7. A study in this setting demonstrated a TV prevalence of 20% in males with persistent symptoms of urethritis. In 2007 the national treatment guidelines changed to add metronidazole 2 grams stat to the standard treatment of urethritis.	We looked at the number and percentage of patients returning with persistent urethritis symptoms amongst patients treated with gentamicin+doxycline versus those treated with gentamicin+doxycline+metronidazole.	1395 (49%) were treated with gentamicin+doxycline; 1152 (40.5%) were treated with gentamicin+doxycline+metronidazole. Overall return rate for those treated with gentamicin+doxycycline was 19.1%, versus those treated with gentamicin+doxycline+metronidazole at 14.2% (p=0.001). Continued symptoms were also higher among those treated with gentamicin+doxycline compared to those treated with gentamicin+doxycline+metronidazole (7.8% vs. 5.0%, p=0.005). The addition of metronidazole to treat patients with urethritis reduced the overall return rate by about 25% and appears to reduce persistent symptoms by about one-third.	No information on partners	B

Schwebke (2003)[124]	Cross sectional study N=300	Heterosexual men attending STD clinic in Alabama 6/01-12/01. Exclusion: urination w/in 1 hr/abx w/in 14days.	2 urethral swabs for Gram stain and TV testing. Next, 20ml or first fraction urine processed for GC/CT LCR and TV PCR (primers TV3/7).	GC/CT/NGU/ TV prevalence. Clinical spectrum of TV in men. Association of TV and NGU	Prevalence CT 20%; GC 18%; **TV 17%.** Coinfection GC/CT 13%; GC/TV 9%; CT/TV 11%. GC and CT significantly more common in men w/ sx of urethritis. TV 20% in men w/ sx and 15% in men w/o (p=0.2). If limited to single pathogen, no significant difference in CT in sx or asx. Isolated TV more prevalent in asx men then w/ sx (51% vs. 23%; p=0.009.) No association of urethritis on Gram stain and TV. Men w/ NGU isolated CT 21%, isolated TV 15%. Including multipathogen infections, CT 25% and TV 20% of NGU cases.	Not stipulated if blinding between lab result. No demographic or risk factor data explored for TV. No assessment of age on prevalence.	B
Srugo (2003)[125]	Cross-sectional study N=238	Men at STD clinic in Israel with sx/findings of urethritis. Exclusion : abx w/in 2 wks or urination w/i 2hrs	Urethral sample after prostate massage: GC Gram stain/cx, ureaplasma cx, mycoplasma cx, TV wet prep, and HSV antigen detection. FVU for CT PCR. Serum HSV gG	Prevalence evaluation for etiologies of NGU	Median age 34y. Etiology for urethritis sx found in 71/238 (30%). 3 had GC. CT 35/68 (51.5%), U.U. 31/68 (45.6%), M. hominis 9/68 (13.2%) & **TV 1/68 (1.5%).** Using antigen detection, HSV found 7/68 (10.3%); none had a history of genital lesions. 3 were seropositive HSV-1, 2 for HSV-2, & 2 were seronegative for both. None were HIV+	Very limited evaluation of TV may have resulted in underestimation of role of TV. Multiple swabs may have limited yield of dx evaluation.	B
Wendel (2003)[126]	Cross sectional study N=355	Consecutive men attending an STD clinic in Baltimore. 3-7/2000	Urethral swab for Gram stain and GC cx. First fraction urine: sediment of 15ml for TV cx, 7ml for CT PCR and remainder for TVPCR	Prevalence of TV, performance of urine TV PCR, characteristics of TV in men	GC+ (19%) (95%CI, 15-24) CT+ 11% (95% CI, 8-14) **TV+ 47/355 (13%)** (95%CI, 10-17); 13 (28%) by TV cx; 44 (94%) by TV PCR. Older age was associated with TV+ cx (p=0.03) but TV by cx or PCR not associated with age. **In men with TV infection, only 67% had sx, 44% had NGU**. In men over 28y, TV (13%) higher prevalence than CT (4%)	Urine volume used for TV PCR not standardized. Retrospective blinded TV PCR testing. Cohort 99% black may not be representative of other populations or settings	B

Morency (2001)[127]	Cross-sectional N=510 (410 sx men and 100 controls)	Men with sx urethritis at STD clinic in Bangui (7/96-1/97.) Control group w/o genital complaints	Men with sx: Urethral Gram stain & GC cx, PCR for GC/CT/MG/UU/TV. In controls, no Gram stain and urethral GC cx	Prevalence of pathogens and association with NGU	**Prevalence in controls vs. men with urethritis**: GC 9% vs. 67%, CT 6% vs. 14%, **TV 7% vs. 16%,** MG 15% vs. 21%, UU 48% vs. 35%. GC, CT, and TV were all significantly more frequent in cases (TV OR 2.55) but not after multivariate assessment of TV infection in men w/o GC. In men w/ GC, 34% coinfected w/ CT and 15 w/ TV. 11% w/ urethritis were neg for all 4 pathogens. 18% w/ NGU had TV.	No data on HIV. No data was provided on the effect of age on multivariate model of TV and urethritis.	B
Pepin (2001)[128]	Multi-center cross-sectional study N=659 cases and 339 controls	Men with sx of urethritis from West Africa attending outpatient clinics	Urethral swab for PCR GC/CT/TV/MG/UU. (TV & MG PCR semi nested)		GC, CT, TV (univariate OR 2.7; p<0.001) all significantly more common in cases then controls. UU not associated w/ urethritis. In cases, prevalence GC 62% (408), CT 13.4% (88), **TV 13.8%** (91), MG 10% (66), UU 26.3% (173). In cases w/ urethritis w/o GC/CT, prevalence TV 15.3% (32), MG 17.7% (37), UU 29.7% (62). In controls, prevalence GC 4.7% (16), CT 4.1% (14), TV 5.6%(19), MG 8.8% (30), UU 28.0% (95). Of GC cases 11.3% CT coinfected and 13.7% TV coinfected. Prevalence TV varied 10x between countries p<0.001. TV cases: 100% visible d/c, 80% dysuria, 48% d/c for ≥14d.	Monitored for inhibition, large sample size. No HIV status information.	B
Chandeying (2000)[129]	Cross-sectional study N=142	Men attending an STD clinics in Thailand w/ sx of urethritis	Urethral loop for Methylene blue PMN/GC smear & GC cx. FVU for LE test, GC/CT/TV PCR. 2nd urine sample for haziness, urethral threads w/ acetic acid	Sensitivity/specificity nonspecific testing modalities	9 men unable to provide sufficient urine. 4 w/ degradation of specimen. Mean & median age 30y. Prevalence GC 42/129 (33%), CT 30/129 (23.3%), TV 2/129 (1.6%). Sensitivity & specificity of LE test 58.5% and 78.1% and for 2-glass urine test 56.9% and 82.8%.	TV PCR protocol not validated in male urine. Volume of urine not specified.	B

9. TV Diagnostic Methods

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIASES	SUBJECTIVE QUALITY RATING
Dize (2013)[130]	Cross-sectional N=634	Matching penile-meatal swabs and urines were collected at home after online recruitment to the internet study; via http://www.iwantthekit.org.	Both swab and urine were placed into individual Aptima transport media tubes and mailed to the laboratory for testing. All specimens were tested for CT and NG using the GenProbe Aptima Combo2 Assay and for TV using GenProbe Aptima Analyte Specific Reagents with TV oligonucleotides.	**Sensitivity of self-collected male penile-meatal swabs and urine for the detection of CT, NG and TV.**	CT: 86 (13.6%) men were positive TV: 56 (9.3%) men were positive NG: 9 (1.4%) men were positive For CT, penile-meatal swab sensitivity was 81/86 (94.2%), and urine sensitivity was 66/86 (76.7%). For NG, penile-meatal swab sensitivity was 9/9 (100%) and urine sensitivity was 8/9 (88.9%). For TV, penile-meatal swab sensitivity was 45/56 (80.4%) and urine sensitivity was 22/56 (39.3%).	Self-collected	B
Schwebke (2011)[131]	Prospective multicenter U.S. clinical trial N=1,025	Asymptomatic and symptomatic women	Vaginal swab, endocervical swab, ThinPrep PreservCyt, and urine specimens were collected. Subject infection status was determined by wet-mount microscopy and culture. Aptima T. vaginalis assay performance was determined for each specimen type by comparison to subject infection status.	**Performance of the automated Aptima T. vaginalis assay for detecting TV in women**	Of 933 subjects analyzed, 59.9% were symptomatic. Aptima T. vaginalis clinical sensitivity and specificity were, respectively, 100% and 99.0% for vaginal swabs, 100% and 99.4% for endocervical swabs, 100% and 99.6% in ThinPrep samples, and 95.2% and 98.9% in urine specimens. Aptima T. vaginalis performance levels were similar in asymptomatic and symptomatic subjects, and in adolescent and adult women.	Performance of the Aptima T. vaginalis assay was lower in self-collected urine samples; however, the difference in assay sensitivity between vaginal or cervical (100%) and urine samples (95.2%) was not statistically significant.	B

Hollman (2010)[132]	Cohort N=144	Consecutive clinical sample of sexually active females, aged 13-21.	Subjects completed a questionnaire on sexual history and current vaginal symptoms, and provided two self- or physiciancollected vaginal swabs and urine. A wet preparation test was performed with one swab and the APTIMA Trichomonas vaginalis (ATV) assay (Gen-Probe, Inc.) was performed with the other and with urine.	Feasibility of screening high-risk adolescent females using APTIMA NAAT	Mean age 18 years; 55% Hispanic, 35% black. **A three-fold higher prevalence of trichomoniasis (6.3%) was detected by ATV than by wet preparation (2.1%)** with **100% concordance between vaginal swab and urine**. No vaginal symptom distinguished those with trichomoniasis. Subjects with trichomoniasis were more likely than those without to be black (P<0.01), and to report past gonorrhea (P<0.01) and past PID (P<0.001).	Did not distinguish between self-collected versus patient-collected vaginal swabs	B
Huppert (2010)[133]	Cohort N=209	Sexually experienced women aged 14–22 years	Women self-collected a vaginal swab for a POC test (OSOM TV Trichomonas Rapid Test) Using a speculum, the clinician obtained vaginal swabs that were tested for TV using OSOM, wet mount, culture and TMA using standard and alternative primers. Self and clinician results were compared with true positives, defined as either culture-positive or TMA-positive with both sets of primers.	Accuracy of self-performed OSOM with clinician-performed tests for TV in adolescent women.	Mean age 17.8 years; 87% black. 74% reported vaginal itching or discharge, 51 (24%) had trichomoniasis. Over 99% correctly performed and interpreted her self-test for TV. Self and clinician OSOM tests were highly correlated (95.7% agreement, κ=0.87). Compared with true positives, the sensitivity of the self-OSOM test was 78% (CI 65% to 89%), similar to that of the clinician-OSOM test (84%, CI 71% to 93%) and culture (82%, CI 69% to 92%), and significantly better than wet mount (39%, CI 26% to 54%). The specificity of the self-POC test was 99% (CI 96% to 100%), similar to that of the clinician-POC test (100%, CI 98% to 100%). The sensitivity of the self-POC test was not affected by vaginal symptoms or other variables.	Therefore, for asymptomatic women for whom a speculum and full pelvic examination are not indicated, a self-obtained vaginal swab may be the specimen of choice to detect trichomoniasis	B

Nye (2009)[134]	Cross-sectional N=296 women and 298 men	Adult men and women age ≥18 attending the Jefferson County Health Department STD clinic in Alabama in 2006 Excluded if took antibiotics within 2 weeks, urinated within 1 hour, or could not provide all specimens	Performance of ATV TMA was compared with wet mount microscopy, culture, and polymerase chain reaction (PCR). Results were analyzed using 3 interpretative algorithms.	**Performance characteristics of APTIMA Trichomonas vaginalis (ATV) transcription-mediated amplification (TMA**) for diagnosis of T vaginalis (TV) infection from female vaginal swab, endocervical swab, and urine specimens and from male urethral swab and urine specimens.	For women, vaginal swab ATV TMA was significantly more sensitive than wet mount or culture. In male subjects, urethral swab ATV TMA was significantly more sensitive than culture or PCR. Slightly but not significantly lower sensitivity for female urine samples (87.5%) than for vaginal and endocervical swab samples (96.6% and 89.8%, respectively) by use of the Aptima T. vaginalis assay in conjunction with a molecular test-resolved algorithm.	Mostly African-American (>89%)	B

Lowe (2009)[135]	prospective clinical comparative study N=535	Active duty United States military women presenting with vulovaginal symptoms.	Clinical diagnoses were made by research staff using a standardized protocol of history, physical examination including pelvic examination, determination of vaginal pH, vaginal fluid amines test, and wet-prep microscopy. Vaginal fluid samples were obtained for DNA analysis. The research clinicians were blinded to the DNA results.	accuracy of the clinical diagnosis of the three most common causes of acute vulvovaginal symptoms (bacterial vaginosis, candidiasis vaginitis, and trichomoniasis vaginalis) using a traditional, standardized clinical diagnostic protocol compared to a DNA probe laboratory standard.	Participants presented for abnormal discharge (50%), itching/irritation (33%), malodor (10%), burning (4%), or others such as vulvar pain and vaginal discomfort. According to laboratory standard, there were 225 cases (42%) of bacterial vaginosis, 76 cases (14%) of candidiasis, 8 cases (1.5%) of TV, 87 cases of mixed infections (16%), and 139 negative cases (26%). Clinical diagnosis for TV had a sensitivity of 84.6% and a specificity of 99.6% when compared to the DNA probe standard.	Small subgroup size for TV	B

Pattullo (2009)[136]	Cross-sectional study N=376	Females 14-21 with and without GU symptoms; no metronidazole x 2weeks Popln mostly AA (82%) with multiple STI risk	Pelvic exam and 4 direct vaginal swabs (**wet mount, culture, OSOM TV and Aptima GenProbe NAAT**) If wet mount negative, 2 secondary TV performed **culture** (on residual wet mount saline) and **OSOM TV** (on original wet mount swab). Wet mount read for motile trich, WBCs, clue cells and yeast forms. Clinical data recorded.	Defined sensitivity of different tests and algorithms. True TV+ = any of 4 primary test positive (initial 4 swabs). Compared sensitivity of secondary tests (culture and OSOM TV) to the true positive TV. Evaluated effect of time to test on sensitivity.	Data available for 345/376. 307 wet mount negative. True positive TV prev 18.8%. Prevalence 8.8% in wet mount negative group. 100% concordance between primary rapid test and secondary rapid test. Secondary culture picked up 12 of 15 primary culture positives. Trend for decreased secondary culture + after 50 min but increased rapid test + after 50 min (3.8% secondary rapid test + </=50 min and 19% + after 50min; p=0.001). **Wet prep alone se 58.5%, (95% CI 45.6-70.6);** Culture alone se 76.9% (95% CI 64.8-86.5); Rapid test alone se 84.6% (95% CI 73.5-92.4); Wet mount for all, if negative rapid test se 86.2% (95% CI 75.3-93.4); Wet mount for all, if neg and multiple partners do rapid test se 73.9 (95% CI 61.5-84); Wet mount for all, if neg do culture se 78.5% (95% CI 66.5-87.7); Wet mount for all, if neg do rapid, if neg do culture se 92.3% (95% CI 82.9-97.4); **Wet mount for all, if neg do NAAT se 100% (95% CI 94.5-100)**	Costs not calculated for different algorithms, ?specificity	B

Rabe (2009)[137] (poster)	Cross-sectional study N=242	Women age 18 to 52 were enrolled.	Seven vaginal swabs were sequentially collected for: (1) BVBlue, (2) OSOM Rapid TV, (3) pH, (4) wet mount for clue cells and TV, and KOH for amine odor, (5) TV culture, (6) Gen-Probe® Aptima® NAAT TV, (7) Nugent score. The OSOM testing personnel were blinded to the results of other tests.	Compare the OSOM TV and BVBlue point-of-care tests to the most commonly used diagnostic tests for TV and BV in symptomatic and asymptomatic women.	Sensitivity and specificity for TV, compared to culture for TV: APTIMA TV: All women (N=242): 100%/95% Symptomatic women (n=120): 100%/96% Asymptomatic women (n=122): 100%/95% OSOM TV: All women (N=242): 96%/99% Symptomatic women (n=120): 100%/100% Asymptomatic women (n=122): 89%/98% Wet mount: All women (N=242): 41%/99% Symptomatic women (n=120): 39%/99% Asymptomatic women (n=122): 44%/100%		B

Campbell (2008)[138]	Cross-sectional N=1,009	Diagnostic laboratory (>100 samples/d) selected simultaneously collected genital specimens from symptomatic women whose provider submitted vaginal swab for vaginal pathogens and endocervical swab for CT and NG.	**Vaginal swab** (Copan liquid Amies medium) tested for TV by **OSOM TV and wet prep**. Swabs >36hr old rejected. Genprobe APTIMA Combo2 for GC and CT. Discrepant results between wet prep and OSOM resolved with GenProbe APTIMA TV test (TMA). Resource utilization costs captured.	Performance characteristics of OSOM compared to composite standard defined as positive TV APTIMA plus either positive OSOM TV or wet prep	Mean age 31.7; 2% TV positive (19/1,009). 3.9% CT +. 0.4% NG +. OSOM se 94.7%, sp 100%, PPV 100%, NPV 99.9%, efficiency 99.9%. Based on 1700 tests/mo, **increase in overall resource costs with institution of OSOM (total monthly cost increase $6,732.06 and increase in total annual cost $80,784.72) but decrease of monthly labor costs by 46.2%** (0.21 FTE) – Canadian dollars	Performance characteristics for wet prep not given.	B

Rivers (2008)[139]	Cross-sectional with randomization of sample storage conditions N=100	Alabama STD clinic, post-pubescent and >/= 16, not pregnant, no metronidazole or tinidazole x 2 wk 89% AA, median age 24	All participants had direct **vaginal swab inoculated into InPouch TV** and kept at 37C (gold standard). **Specimens for transport in universal transport medium (UTM) and eSwab transport medium** taken from all women and randomly inoculated with Room temp (RT) specimens and stored at RT inclu. Transport vs inoculated with 37C specimens and stored/transported at 37C. In lab, all specimens inoculated in InPouch TV and incubated at 37C and read for 5 days.	Performance characteristics of UTM and eSwab InPouch TV cx vs bedside inoculation In Pouch TV cx	TV prevalence = 34/100 (34%). Median time between collection and culture = 5hr. 4 outliers excluded. No differences in RT vs 37C specimen handling conditions. UTM se 91.2 (95% CI 77-97); sp 97.0 (89.6-99.2); PPV 93.9 (80.4-98.3); NPV 95.5 (87.6-98.5). eSwab se 85.3 (69.9-93.6); sp 98.5 (91.9-99.7); PPV 96.7 (83.3-99.4); NPV 92.9 (84.3-96.9)		B

Huppert (2007)[140]	Cross-sectional (Convenience sample) N=330	Females 14-21 presenting to teen health center or ED with GU symptoms or risk of STI (unprotected sex, >/=2 partners, STI contact), who have not had metro. X 2 wk	Interview and pelvic exam with **4 vaginal swabs (wet prep, OSOM TV rapid Ag, InPouch TV cx media, TV ASR Aptima Combo2)**, endocervical swabs for CT and NG.	Sensitivity and specificity of 4 diagnostic methods using 3 statistical approaches (2 reference standards (traditional std defined as +wet prep +/- cx and composite reference std defined + as any TV test+ and neg as all TV tests -) and latent class analysis)	330 women complete data, mean age 17.7, 84% AA, 63% symptomatic, TV prevalence 9.4% (wet prep)-18.5% (any TV test). AA race and concurrent CT and/or NG significant predictors of TV. Test performance: Traditional std: Wet prep se: 64.6%; sp NA; cx se 95.8%, sp NA; OSOM se 89.6%, sp 97.5%; TMA se 97.9%, sp 95.3% Composite std: Wet prep se: 50.8%; sp NA; cx se 75.4%, sp NA; OSOM se 82.0%, sp NA; TMA se 98.4%, sp NA Latent class analysis: Wet prep se: 56.0%; sp 100; cx se 83.0%, sp 100; OSOM se 90.3%, sp 100%; TMA se 98.2%, sp 98.0% Application of tests to asymp. Females resulted in reduced sensitivity for WP (57.4% to 38.1%) and OSOM (92.5% to 61.9%) Se remained same for cx and TMA. TMA best for asympt.	Assumed 100% sp for WP and cx (traditional std), assumed 100% sp for each test for composite std. and assumed conditional independence of tests for latent class analysis.	B

Van Der Pol (2006)[141]	Cross-sectional study	Males and females attending Midwestern STD clinic who provided consent for future use of samples to study novel diagnostic assays	TV PCR adapted to CT/NG NAAT: evaluated performance of TVA, TVK and beta-tubulin primer sets to wet prep and TV culture using vaginal swabs, endocervical swabs, urine (male and female). For male urine TVK and B-tub studied and TVA primer resolved discrepancies. Comparison of female specimen types and storage performed with TVK primer set, as well as evaluation of stability of vaginal swabs.	**Test performance of commercially available CT/NG NAAT (PCR) adapted to detect TV** Infection defined as: + wet prep or cx or two separate PCR results +	TVA primers detected as few as 5 trichomonads and TVK primer detected 1 trichomonad TVA and TVK primers amplified TV when CT (up to 900 IFU) and NG (up to 960 CFU) organisms present Vaginal swabs (N=174F): 22.4% infected, WP 61.5% se (46.2-76.8), TVA 48.7% se (33.0-64.4) TVK 79.5% se (66.8-92.2). No difference in sp between 2 primer sets (TVA 100% vs TVK 97.8%) Male urine (N=503M): 5% infected, cx 56% se (36.5-75.5), TVK 96% se (88.3-100), beta-tubulin 92% se (81.4-100). Sp for TVK and beta-tub equal (99.2 and 99.4% respectively). Female urine and endocervical swabs (archived up to 5y; N=463). Cervical se 96.8% (93.2-100), sp 99.2 (98.3-100); urine se 94.7 (90.2-99.2), sp 98.9 (97.9-100) No difference in se and sp for vaginal and endocervical swabs and no difference in se and sp between endocervical swabs and female urine. Storage temp (4C vs ambient) did not affect se or sp of vaginal swabs. No statistically sign difference in se and sp between 3 vs 7 days of storage.	Dichotomy of specimen types collected for various studies over various time points led to different specimen combinations/storage conditions available for any one individual. Retrospective analysis made it impossible to confirm wet mount QC (read at clinic site). 17.9% of cases had +WP and negative PCR results.	B

Hardick (2006)[142]	Cross-sectional N=615	Male and female STD clinic attendees	BTUB FRET PCR and GenProbe TMA for TV compared using **290 male urine samples and 321 self-obtained vaginal swabs**	**Performance of TMA** Infxn status=2 positive results by 2 different tests (including **WP**) Discordant samples adjudicated with PCR utilizing TVK3 and TVK4.	Resolved Performance of TMA: Female: se 98.2% , sp 98.1%, PPV 91.8%, NPV 99.6%; Male: se 100%, sp 100%, PPV 100%, NPV 100%. Final prevalence: in males = 4.5%, in females = 17.8%		B
Huppert (2005)[143]	Multicenter cross-sectional Study N=449	Women ≥18y presenting w/ signs and sx vaginitis, TV exposure, ≥ 2 sex partners w/i 30d or f/u for TV w/i 30 d.	Immunochromatographic assay for TV (OSOM, Genzyme diagnostics) on vaginal swabs and remaining saline/swab wet prep solution. Wet prep and TV cx	**Performance of OSOM** on vaginal swab or remaining wet prep solution in comparison to composite reference **standard of wet prep(+) or TV cx (+)**	Prevalence TV 23.4% (105/449) by CRS. OSOM vaginal-swab: sensitivity 83.3%, specificity 98.8% Wet prep: sensitivity 71.4%, specificity 100% OSOM significantly better than wet prep (P = 0.004) Detected TV in samples requiring 48-72 h to become cx(+)	Up to 20min to wet prep reading. Potential for false positives in low prevalence settings. No TV PCR to assess TV cx (-) OSOM (+) samples	B

Adu-Sarkodie (2004)[144]	Cross-sectional N=618	Women attending an antenatal clinic in Ghana	Self administered vaginal swabs were screened for TV using the Kalon TV latex agglutination test	Subjects w/ (+) TV latex agglutination, and following 2 consec. women testing (-) had 2 further vaginal swabs. Not matched by sx. Swabs were tested wet prep and InPouch cx. Tests read independently and blinded	Latex agglutination sensitivity 98.8% (95.9-99.9) specificity 92.1% (89.2-94.5) PPV 83% (77.2-87.9) Wet prep sensitivity 81.5% (74.9-87) Cx sensitivity 98.2% (95-99.6) Estimated cost $1.56 and time to test completion <3 min	35 samples only + by latex test no PCR to validate. Calculated PPV limits use of test in low prevalence setting. No evaluation of effect coinfections. Unclear if difference between self-obtained swabs vs. provider obtained	B
Brown (2004)[145]	Cross-sectional two center study N=425	Women attending outpatient clinics. Exclusion criteria included abx or antifungal rx in 1 week or douching w/i 24hrs.	1 swab for wet prep microscopic evaluation for TV, clue cells, hyphae and amine test w/ KOH. Another vaginal swab for Affirm VP III Microbial Identification Test (BD, Sparks, MD, USA). Nucleic acid Hybridization test. Affirm swab in Ambient temperature transport system (ATTS) and processed w/i 1hr if at RT and w/i 4hrs if refrigerated.	**Assess performance Affirm VP III v microscopy**	Affirm: Gardnerella 190/425 (45%) Candida 45/425 (11%) TV 30/425 (7%) Microscopy: Clue cells 58/425 (14%) Hyphae 31/425 (7%) TV 23/425 (5%) Significantly higher detection for Gardnerella then clue cells (p=0.001) And candida by affirm (p=0.04)	Test processing time <1 hr. An extended specimen transport option (Affirm VP III ATTS) extends specimen stability to 72hrs at ambient temperature.	B

Kaydos-Daniels (2004)[146]	Substudy w/ patients from clinical trial of metronidazole for sx urethritis or longitudinal Study of HIV and TV who were eligible and ≥18 yo and would return for f/u for 5wks n=1361	**Me**n attending STD and dermatology clinics of Lilongwe Central Hospital, Malawi, between 27 January 2000 and 28 June 2001.	standardized questionnaire and exam. 1. HIV and syphilis testing. 2. Urethral swabs for TV cx (InPouch) and Gram stain. 3. 20–30 ml FVU for TV cx F/u: Men from derm clinic who were HIV(+) w/o other STDs and men from either clinic who were TV+ at baseline. 3 urogenital specimens. Urethral swabs were obtained for Gram stain and TV cx. FVU and semen obtained for TV cx,. Men dx w/ TV rx w/ metronidazole 2g PO and f/u in 1–2 wks	Evaluation of sensitivity of **TV cx from different specimens**	Sensitivities of urine specimen and urethral swab cx =, each correctly dx 95 TV cases. **Comparing urine to urethral swab, 1/3 TV+ by urine cx only, 1/3 urethral swab cx only, and remainder + by both cx**. Sensitivities urethral swab and urine cx 66.3% (95% CI, 57.6–73.8%) and 66.4% (95% CI, 56.6–73.8%), respectively. Comparing urine, urethral swab, and semen, sensitivity urethral swab cx 62.2% (95% CI, 53.6–69.8%), urine cx 61.6% (95% CI, 53.0–69.3%), and semen cx 66.7%(95% CI, 49.6–79.7%). 11 cases (25.6%) detected by semen cx only. Among TV+ on at least 2 occasions, type of specimen(s) that tested (+) changed at least once for 59.5%.	Samples were always collected urethral swab then urine then semen which may have affected the sensitivity estimates. No comment of blinding of microscopists to other specimen results. Patients providing semen samples tended to be older. Some cultures were only evaluated on day 2 and 5.	B
Landers (2004)[147]	Prospective cohort study N=598	Non pregnant women 18-45yo w/ ≥1 untreated genital complaint	Questionnaire on current and past med and soc hx: menses, STDs, and genital infections. Speculum exam: MPC vaginal d/c, KOH test. wet mount, 10%KOH slide prep, pH, vaginal Gram stain, TV cx, yeast cx, endocervical Gram stain , GC cx, CT PCR, and Pap test.	Comparison of sensitivity and specificity of hx/physical/point of care diagnostics to Gold standard dx.	Culture dx of TV in 72 patients (12%) 60% black, 32% white **Wet Prep:** **Sensitivity 62%** **Specificity 97%** **PPV 75%**	Surprisingly low PPV of wet prep. Data on cx techniques not provided. Wet prep handling and skill of microscopists not addressed.	B

Kingston (2003)[148]	Prospective Cohort N=65	Positive wet preparations from women attending STD clinic July 2000 to April 2001	**Wet prep** prepared by collecting d/c from posterior vaginal fornix and mixed w/ normal saline. Slide was examined immediately then reread q 10 min for **motile organisms**	Time to negative wet preparation	**13/65 (20%) samples were negative at 10minutes after the initial reading**, 23/65 (35%) were negative at 30 minutes, 51/65 (78%) were negative at 2 hrs.	Amount saline for wet prep may be variable. Unclear if blinded slide reading or if >1 reader. Lighting and temp may alter wet prep survival time	B
Lara-Torre (2003)[149]	Cross-sectional study N=203	Women seen in urban health center 6/01 to 10/01	Liquid-based pap smear, InPouch TV cx with reading dailyx5d, and in women with vaginal d/c a wet prep	**Assess performance of liquid-based pap in TV dx (vs standard wet prep)**	TV cx was positive in 44 (21.6%) Sensitivity, specificity, PPV, NPV: Wet prep(n=63) 50%, 93%,, 77%, 80% Pap smear (n=203) 61.4%, 99.4%, 96.4%, 90.8%. Pap sensitivity in n=90 sx patients was 73% and Pap sensitivity in n=113 asx patients was 44%.	No data on blinding of readers. No calculation of sensitivity of samples only evaluated by wet prep and Pap to compare against each other. Likely high prevalence cohort	B
Lobo (2003)[150]	Cohort	Women attending a gynecology clinic in Brazil w/o abx for 15 days. N=1008	2 Cervicovaginal swabs obtained. 1 used for Pap smear. Other divided for modified wet prep, cx and PCR with 2 sets of TV primers. 1 PCR product subject to restriction enzyme digestion to confirm product (primers TV1/2 & OP1/2)	Comparison of sensitivity and specificity of Pap smear to TV PCR Positive defined as PCR (+) by both primer sets.	TV PCR (+) 61/1008 Cx sensitivity 79% specificity 100% Pap sensitivity 61% specificity 98%. PPV 62% Modified wet prep sensitivity 66% specificity 100%	Nonstandard techniques for cx and wet prep. .	B
Mohamed (2001)[151]	Substudy community based study N=675	Women w/ & w/o access to female condoms at 2 study sites	Self-obtained vaginal swabs for TV cx and urine pellet directly inoculated for TV cx (InPouch TV). TV cx read daily for 5d. Blinded reading of cx.	TV cx swab vs. urine	Vaginal swab TV+ in 121 (18%); Urine TV+ 23 (3.4%). Sensitivity of urine in comparison to vaginal swab cx (17%) & specificity (99.6%)	Not reported as first void. Unclear if urine was first fraction and urine volume not specified	B

Lawing (2000)[152]		Women attending an STD clinic for a new complaint	Screened for TV by wet-preparation (wet-prep) microscopy and culture and for the presence of TV DNA by specific PCR of vaginal and urine specimens		The overall prevalence of TV in the population was 28% (53 of 190). The sensitivity and specificity of PCR using vaginal samples were 89 and 97%, respectively. Seventy-four percent (38 of 51) of women who had a vaginal wet prep or vaginal culture positive for trichomonads had microscopic and/or culture evidence of the organisms in the urine. Two women were positive for trichomonads by wet prep or culture only in the urine. The sensitivity and specificity of PCR using urine specimens were 64 and 100%, respectively. These results indicate that the exclusive use of urine-based detection of T. vaginalis is not appropriate in women. PCR-based detection of T. vaginalis using vaginal specimens may provide an alternative to culture.		B
DeMeo (1996)[153]	Multicenter cross-sectional study N=615	Women attending family planning clinics with sx and signs of vaginitis. Exclusion if abx/antifungals ≤7d or douching in ≤24hrs. U.S.	TV cx in Diamonds media evaluated dailyx7d, wet prep and Affirm VP test (MicroProbe Corp.) True positive: TV culture+ or we prep and DNA probe+.	Performance Affirm VP	Sensitivity and specificity: Cx 93/95 (98%, 95%CI 93-99.7%), 520/520 (100%, 99-100%) Wet prep 76/95 (80%, 70.5-88%), 518/520 (99.6%, 98.6-99.9%) Affirm 32min incub 85/95 (89.5%, 81.5-94.8%), 519/520 (99.8%, 98.9-100%) Affirm 55min 86/95 (90.5%, 82.8-95.6%), 519/520 (99.8%, 98.9-100%)	Only sx patient population was tested. No data on status of blinding of readers to results.	B

Briselden (1994)[154]	Cohort N=176	Consecutive women attending a sexually transmitted disease clinic for genital complaints	Vaginal swabs	Evaluation of a commercial system (Affirm VP Microbial Identification Test) for detection of vaginal pathogens	The TV probe was positive for 12 of 12 specimens positive by wet mount and 12 of 15 specimens positive by culture. There were no false positives and three false negatives for the Affirm VP test compared with culture and/or wet mount for TV.		
Williams (2008)[155] (poster)	Prospective study N=379	Women enrolled in adolescent sexual behavior study in Indiana	PCR for CT, GC and TV 82 women with CT 42 women with TV 38 women with GC	Mean time in weeks to first negative test for CT, GC and TV	Mean time to first negative result: CT – 1.7 +/- 0.15 weeks GC – 1.4 +/- 0.20 weeks **TV – 1.4 +/- 0.10 weeks** >92% negative 2 weeks after tx for GC & TV >86% negative 2 weeks after tx for CT	No details about treatment of patients or partners	B

10. TV Sequelae — TV-HIV Interactions

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJ. QUALITY RATING
Hughes (2012)[156]	Prospective study (Partners in Prevention HSV/HIVTransmission Study) N=3297	African HIV–serodiscordant couples	Serologic testing for HSV-2 and NAAT testing for STIs were done at study enrollment. We assessed HIV transmissions for linkage within the study partnership, based on HIV-1 sequencing	HIV transmission among serodiscordant couples, given the number of sex acts with their study partner.	Results. Of 3297 couples experiencing 86 linked HIV-1 transmissions, the unadjusted per-act risks of MTF transmission was 0.0019 (CI: .0010–.0037) and FTM transmission was 0.0010 (CI: .00060–.0017). Each log10 increase in plasma HIV-1 RNA increased the per-act risk of transmission by 2.9-fold (CI: 2.2–3.8). **In multivariate analysis, TV infection of the HIV-infected partner was not significantly associated with HIV transmission. However, TV infection of the HIV-uninfected female partner was associated with an increased risk of the per-act probability of her acquiring HIV (OR 2.57, CI: 1.42–4.65 .002)** Self-reported condom use reduced the per-act risk by 78% (RR 0.22, CI: .11–.42). Modifiable risk factors for HIV-1 transmission were plasma HIV-1 RNA level and condom use, and, in HIV-1–uninfected partners, herpes simplex virus 2 infection, genital ulcers, Trichomonas vaginalis, vaginitis or cervicitis, and male circumcision.	Men in this study were not tested for TV. Because only couples that had not previously transmitted HIV-1 were enrolled in the study, if transmission risk varies significantly between couples, the highest-risk individuals would be expected to transmit early and never enter the cohort; such a ‘‘survivorship bias’’ could lead to an underestimate of infectivity.	B

Anderson (2012)[157]	Prospective cohort study N=557 screenedand 60 (10.8%) were TV+	TV+ HIV-infected women age 18-50 not taking antiretrovirals, who presented for routine HIV care in South Africa Excluded: recent PEP or antibiotics, active genital ulcers, systemic illness, and CT/GC+	Directly Observed Therapy (DOT) with 2g oral metronidazole. Screened for TV using self-collected vaginal swabs with a rapid point-of-care immunochroma tographic antigen test. Paired cervical wicks and plasma were collected for viral load measurement. A follow-up visit was scheduled 1 month after therapy, and partner letters were provided.	Evaluate whether TV treatment reduces genital HIV shedding	Of 46 women evaluated at follow-up, 37 (80.4%) were cured of TV. **Genital tract viral load decreased significantly**, by 0.5 log10 (P _ 0.01). The mean genital tract viral load (log10) decreased from 4.66 (<3.52– 6.46) to 4.18 (<3.52– 6.48) (P < 0.01) after therapy. Plasma viral load was not significantly different after therapy (P=0.93)	Could not assess HIV transmission risk since not allowed to assess partners or provide them with therapy. Potential for reinfections.	

Quinlivan (2012)[158]	Math model	HIV-infected patients at an HIV clinic in North Carolina	Participants were recruited from 2 secondary prevention HIV studies, screened by urine NAAT for STIs and interviewed by ACASI about risk factors (baseline, 6, and 12 months).	Estimated number of transmitted HIV infections attributable to TV	TV was prevalent in 7.4%, and incident in 2% to 3% of subjects at follow-up. Mathematical modeling predicted that 0.062 HIV transmission events occur per 100 HIV-infected women in the absence of TV infection and 0.076 HIV infections per 100 HIV- and TV-infected women (estimate range: 0.070–0.079), indicating that **23% of the HIV transmission events from HIV-infected women may be attributable to TV infection** when 22% of women are coinfected with TV.	Model based on estimates. Did not include an adjustment for changes in sex behavior over time or more than 1 main partner. 1-site study.	B
Mavedzenge (2010)[159]	Propsective cohort (from RCT data) N=4948	Sexually active HIV-negative nonpregnant women age 18-49 at 3 trial sites in Harare, Zimbabwe, and Durban and Johannesburg in 2003-2005	Randomized to receive either a diaphragm, lubricant gel and condoms, or condoms only. Followed up quarterly for 12-24 months. At each visit, women received product adherence and risk-reduction counselling, treatment of curable STIs, condoms, and resupply of Replens gel (for intervention arm)..	Risk of HIV acquisition among women recently infected with TV, and also, risk of TV among women infected with HIV	10% of women experiencing at least one incident case of TV and there were 309 HIV seroconversions. After controlling for potential confounders, TV+ women were more likely to test positive for HIV at the following visit (aHR=2.05; CI:1.05–4.02). Similarly, HIV+ women were more likely to test positive for TV at the following visit (aHR=2.1; CI:1.35–3.32).	While other STIs were significant risk factors for HIV acquisition, TV remained independently associated with HIV risk All women were asked to use condoms at every sex act.	B

Paz-Bailey (2010)[160]	Cross-sectional N=387	HIV-positive men were recruited at primary health care clinics in South Africa as part of a randomized trial of episodic acyclovir among men with GUD.	Participants were serologically screened for HIV infection, syphilis, and herpes simplex virus type 2 infection and for urethritis and ulcer etiology by polymerase chain reaction. Plasma and genital ulcer HIV-1 loads and CD4 cell counts were quantified. TV in urine samples was done using realtime multiplex PCR.	Correlates of HIV lesional shedding among men with genital ulcer disease (GUD)	Median plasma HIV-1 load and CD4 cell count were 87,200 copies/mL and 282 cells/mm3. Overall, 173 (45.6%) had detectable HIV-1 RNA in ulcers. **Men with TV infection had higher ulcer viral loads on average than did those without TV but the difference was not significant (mean difference, 0.62; CI: 0.07–1.2).** After multivariable analysis, higher plasma HIV-1 load (OR 2.5; CI, 1.7–3.5), larger lesions (OR 2.5; CI 1.5–4.1), purulent ulcers (OR 2.2; CI, 1.1–4.2), multiple ulcers (OR 3.6; CI:1.6–8.4), and herpes seropositivity (OR, 3.4; 95% CI, 1.7–7.0) were associated with increased odds of HIV-1 lesional shedding.	Cross-sectional, cannot determine causality	B

Gumbo (2010)[161]	Observational cohort study N=479	HIV-infected pregnant women in a PMTCT program in three primary maternal and child health clinics in Zimbabwe in 2002-2003	Mother-infant pairs followed from delivery through 15 months with infant HIV testing. Wet mount preparations of maternal specimens at the time of delivery were used for diagnosis of TV, Candida albicans and BV	To identify the risk factors of HIV vertical transmission in pregnant women	281 infants had a known definitive HIV result by 15 months of age, and 31.7% of the infants become HIV infected. In univariate analysis, significant risk factors in the mother at enrollment were presence of vaginal discharge, genital itchiness, genital ulcers, dysuria, breast or vaginal infections (T. vaginalis, B. vaginosis and C. albicans). In multivariate analysis, vaginal infections (RR 1.72, CI: 1.03–2.88) and symptomatic breast swelling/pus (RR 4.36, CI: 2.89–6.58) were the only significant predictors of HIV vertical transmission.	Wet mount used for TV diagnosis, could bias toward the null. Authors call for screening for vaginal infections and examining pregnant women for mastitis to identify women at risk of HIV vertical transmission for prevention	B

Van der Pol (2008)[162]	Nested Case-Control Study N=218 cases and 419 controls (1:2 = 1:1 match)	Women enrolled in longitudinal cohort study of hormonal contraception and HIV acquisition in Uganda and Zimbabwe.	Women with incident HIV infection (63 Uganda; 155 Zimbabwe) classified as cases; Controls matched on study site, age, composite STI variable (CT, NG, BV) and length of f/u. For cases samples analyzed were from seroconversion visit and visit preceding seroconversion. For controls, samples analyzed based on f/u closest to f/u for visits for cases. Composite behavioral risk variable used and primary sex partner risk composite score used. TV status based on microscopy from parent study and PCR analysis of case and control samples.	Association between TV and incident HIV infection	Median age 24 for cases and controls. Median 84 days between last visit HIV- and incident HIV visit. Median 83 day f/u for controls. Multivariable analysis: **TV associated with incident HIV (aOR 2.74, CI:1.25-6.00).** This risk was higher when analyses limited to lower risk setting (family planning participants) with adjOR 3.3;95%CI 1.36-7.85). Relationships even stronger if limit analyses to wet-prep positives only (i.e. eliminate those positive only through PCR). Other significant risk factors: HSV-2 positivity (aOR 4.03, CI:2.39-6.78); recruitment from high risk setting (aOR 3.41;CI:1.21-9.60); participant behavior risk (aOR 3.39, CI:1.12-10.32); primary sex partner risk (aOR 1.72, CI:1.08-2.73). Living with sex partner protective (aOR 0.44, CI:0.23-0.84). .	Possible selection bias due to study design.	B/IIA

Miller (2008)[12]	Cross-sectional study N=228	Black women from Brooklyn,NY age 18 (or 16 or 17 if emancipated minors), used cocaine, heroin, crack or daily pot and no plans to move	Survey administered and women tested for HIV-1, HSV-2, trichomoniasis (PCR), CT, NG, syphilis (1/2).	Prevalence of STIs and Index of infection (extent of co-infection)	All AA, mean age 34, 38/228 = HIV+; 180/228 (79%) HSV-2+; 2/228 (<1%) syphilis +; 84/228 (37%) trich+; 25/228 (11%) CT+; 5/228 (2%) NG+. **HIV+ women more likely infected with Trichomonas (52.6%),** HSV-2 (94.7%), and more likely to be infected with multiple STIs. HIV+ women more than 2x as likely to report current sex work (p=0.05)	Cross-sectional. Does not address biological synergism that may occur with multiple STIs	B
McClelland (2007)[163]	Prospective Study N=1335	Open cohort study of FSW attending municipal clinic in Mombasa, Kenya	Standardized interview, physical exam and laboratory testing for HIV/STIs at enrollment and monthly. Women with signs/sx STI syndromically managed at visit and asked to return in 1 wk for f/u test results. TV diagnosed via wet prep. HIV-women with at least 1 f/u included in analyses.	Test hypothesis that TV increases risk of HIV-1 acquisition in study popln	Median age 26, Mean duration of prostitution 1yr. At enrollment, 6% TV+, 37% BV+, 5% NG+806 incident TV infxn (23.6/100py) and 265 HIV seroconversions (7.7/100py). Infection with Trichomonas vaginalis increases the risk of HIV-1 acquisition: Multivariate model with **aOR 1.52 (CI:1.04-2.24, p=0.03) for the association of TV with HIV seroconversion**. Model controlled for baseline education level, parity, alcohol use, workplace, vaginal washing practices, other STIs, contraceptive method, age, duration prostitution, # partners/week, condom use, freq sex.		IIB

Brogly (2007)[164]	Subanalysis of data from prospective study N=638 in analysis	HIV+ girls, perinatally infected, >/=13yo, who participated in protocol 219C From 75 pediatric ID clinics in 24 states and districts in US	At f/u visit every 3mo, demographic, clinical and lab data collected. Pelvic exams performed q3yr beginning age 15 or onset of sexual debut. Changed to annual pelvic/pap in 2002. Screening for STI not routine though diagnostics tests sent for symptomatic girls	Cumulative incidence and incidence rate per 1000py of first pregnancy, CT, NG, TV, syphilis, condyloma	174/638 sexually active (27.3%). AA (55.5%), Hispanic (28.5%), W (14.6%) CI (sex active) Pregnancy 24.2% Condyloma 8.2 (3.7-12.7) **TV 6.9 (2.4-11.5)** CT 5.5 (2.0-9.1) NG 3.9 (0.8-7.0) Syphilis 1.6 (0.0-3.7)	STI rates underestimated as screening was not being performed, testing was performed only on girls with symptoms. It was not specified in the study the diagnostic modality used for TV testing.	IIC

Chesson (2004)[165]	Math model		Model of HIV transmission Stages of sexual partnerships: first when exposed to a TV+ partner (and possibly HIV) but have not yet acquired TV, and 2nd after acquired TV and are potentially exposed to HIV in the same or other sex relationship(s).	Assumed 35% TV+ have sx, get rx & abstain. Assumed 180d of asx TV and 0.186 unprotected sex acts/day. Base case value of 5 for cofactor effect of TV on HIV infectivity. TV estim. to increase HIV suscept. 1.8- 3.0x.	Under base case assumptions, an **estimated 746 new HIV cases in U.S. women attributable to TV each year**. If 3.7 million U.S. women with TV, ~1734/yr would be expected to acquire HIV. Without TV, only 988 would be expected to acquire HIV. Lifetime medical care costs of the 746 TV-attributable HIV infections = ~$167 million	Most important input is cofactor effect of TV on HIV transmission and acquisition. Cofactor effect estimate based on OR reported in studies that examined HIV acquisition over a series of sexual encounters. Assumed that women with asymptomatic TV would be at increased susceptibility to HIV. They do not incorporate any estimate of STD co-infections	B

Magnus (2003)[166]	Retrospective cohort study N=1,578	HIV Outpatient Program database. HIV+ women age>13y, with at least 1y data available Louisiana 1990-2000	Screened q 6mo by wet prep/CT antigen or ELISA/ GC cx or urine/ syphilis/exam for HPV. TV+ rx w/ metronidazole 2g or 500mg bid x 7d. Partners referred for rx.	TV infection and risk factors in HIV+ women	**13.1% TV+,** 5.3% CT and 4.9% GC. 30% of 1578 women had TV $\geq$1x. 37% had at least 1 subsequent (+) test. **Women <22 yrs, black, w/ other STD, and substance users had significantly higher incidences of initial TV+.** Subsequent (+) TV test significantly higher in women w/ any other STD. Immune status, ART use, PI use not assoc. w/ TV +	No TV cx. Large cohort with frequent evaluations and monitoring. Unable to differentiate recurrent from persistent TV. Possible selection bias given all patients long term enrollment	B
Cu-Uvin (2002)[167]	Multi-center longitudinal cohort study N=871 HIV+ and N=439 HIV(-)	Women with HIV and women at high risk of HIV acquisition recruited form 4/93 to 1/95. women with AIDS-defining illness were excluded	Every 6mo patients evaluated with interview, exam, blood, urine and genital tract specimen collection. TV assessed by wet prep and TV culture from visit 4-12.	Analysis of data from first 12 visits.	**Imputed TV prevalence: HIV+=29% vs HIV-=23%.** Majority of patients were black. Patients with CD4<200 were less likely to have baseline TV (p=0.03).On multivariate analysis, baseline TV associated with IDU, crack use, ETOH, candidiasis and BV. Black race, recent crack use, cigarette use, and BV were associated with TV+ in time trend. No significant difference in incidence, persistence or recurrence of TV in HIV+ or HIV(-) women. In HIV+ women, no difference based on CD4 count	Imputed baseline TV rates by wet prep results and subsequent data on Wet prep sensitivity by site. No reliable data on treatment for TV between visits. Therefore unable to differentiate persistent from recurrent infection.	B

11. TV Sequelae — Perinatal Transmission

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
Mann (2010)[168]	Retrospective observational study of administrative data (linked Medicaid billing data for pregnant women and their children) N=108,346	Pregnant women with singleton pregnancies and their children born 1996-2002 in South Carolina, with follow-up data through 2008. Controlled for race, maternal age, infant's sex, maternal tobacco and alcohol use, and maternal education.	ICD-9 codes in South Carolina Medicaid data were used to identify maternal infections. Gestational age was obtained from birth certificates.	To investigate **the association between diagnosed maternal sexually transmitted infections (STIs) and very preterm or late preterm birth.**	TV, GC, or CT/NGU diagnosed in 4,208 women. Preterm birth occurred in 9% of pregnancies. Women diagnosed with TV in the first 7 months of pregnancy were more likely to deliver very preterm infants at ≤33 weeks (HR=1.22, CI:1.02-1.46). Women diagnosed with TV in the first 8 months of pregnancy were more likely to deliver late preterm infants at 33-36 weeks (HR=1.59, CI:1.18-2.14)	Diagnoses determined by use of ICD-9 diagnostic billing codes Study design cannot address causality or underlying mechanism	B

Cotch (1997)[169]	Prospective cohort (Vaginal Infections and Prematurity Study) N=13,816 women (5,241 black, 4,226 Hispanic, and 4,349 white)	Pregnant women at mid-gestation at University-affiliated hospitals and antepartum clinics in 5 U.S. cities were enrolled, tested for TV, and followed up until delivery.	TV testing by vaginal swab culture, followed by observation Only 432 women in this cohort received metronidazole during pregnancy, and only 176 of those were TV+. Treatment not randomized.	Association between TV infection and preterm delivery(PTD) /low birth weight(LBW) PTD=delivery <37 weeks (also analyzed very preterm at <34 weeks with similar results) LBW=<2500 g at birth	TV prevalence at enrollmnt: 12.6% (Black: 22.8%, Hispanic: 6.6%, White: 6.1%). After multivariate analysis, **TV at mid-gestation was significantly associated with low birth weight (aOR 1.3; CI:1.1-1.5), preterm delivery (aOR 1.3; CI:1.1-1.4), and preterm delivery of a low birth weight infant (aOR 1.4; CI:1.1-1.6).** In bivariate analysis (but not multivariate), infected women were also significantly more likely to have postpartum endometritis (6.9% v 4.7%, p<0.001), stillbirth (1.2% v 0.7%, p=0.02), or neonatal death (1.6% v 0.8%, p=0.005). Estimated increased risk of adverse pregnancy outcome: 30% to 40%.	Multivariate analysis considered covariates including institution, race, age, mariatal status, education, smoking, income, gravidity, weight, previous adverse pregnancy outcome, and infections including Candida, NG, BV, and metronidazole use	B

Trintis (2010)[170]	Case report N=1	A 29-1/7-week premature female neonate, weighing 1210 g, born vaginally to a 19yo mother, after preterm labor and preterm premature rupture of membranes and maternal chorioamnionitis. Mom had symptoms and was diagnosed with TV 16d prior to delivery, treated with 2g metronidazole POx1.	On DOL#1, intubated for respiratory distress, treated presumptvely for sepsis with amp/gent. TV diagnosed on DOL#5 by microscopy during routine U/A of bag urine. Treated TV with 2 doses of metronidazole (15mg/kg, then 7.5 mg/kg), weaned to room air by DOL#6.	On DOL#14, represented for apnea; UCx: E. coli/E.faecalis, BCx: S. epi, CSFcx: neg. Microscopy negative for TV but received empiric vanc/cefotax/ metronidazole x5-8 days..	Resolved and sicharged home in good health on DOL#46.	Infant of high-risk mothers Microscopic examination may be insensitive diagnostic method for TV.	C

Carter (2008)[171]	Case report	2 week old girl presented with lethargy and respiratory decline in setting of concomitant HSV.	NP wash at time of intubation with trichomonads 16-22um in length and no other pathogen	Trichomonal DNA extracted and PCR using specific primers for small subunit rRNA genes for Trichomonas sp. Performed and archived TV and T.}| tenax sequences. Sequence most compatible with TV.	Treated with metronidazole and extubated. Death attributed to HSV.	Rare	C
Mann (2011)[172]	Retrospective observational study of administrative data (linked Medicaid billing data for pregnant women and their children) N=84,721	Linked records for pregnant women with singleton pregnancies and their children born 1996-2002 in South Carolina, with follow-up data through 2008.	Maternal GU infections and pre-eclampsia were identified on the basis of diagnoses made during pregnancy, and cases of ADHD were identified on the basis of diagnoses made in the child's Medicaid file.	Assess relationship between maternal genitourinary (GU) infection during pregnancy and ADHD in the child.	**Maternal genitourinary infection was associated with significantly increased odds of having a child with ADHD (OR = 1.29, 95% CI = 1.23-1.35).** Trichomoniasis, CT/NGU, UTI, and candidiasis were associated with increased risk of ADHD, whereas GC was not.	Diagnoses determined by use of ICD-9 diagnostic billing codes Underlying mechanism of association unclear; cannot establish causality	B

Mann (2009)[173]	Retrospective observational study of administrative data (linked for pregnant women and their children) N=134,596	Medicaid-insured singleton births in South Carolina, 1996-2002. Excluded: Children with a known cause of mental retardation and pregnancies with diagnosed UTI, CT, GC, or vulvovaginal candidiasis.	Linked maternal, infant, and child records obtained from Medicaid billing records, birth certificates, and administrative data from the South Carolina Department of Education (DOE) and the Department of Disabilities and Special Needs (DDSN).	To examine the association between maternal trichomoniasis during pregnancy and intellectual disability (ID) in their children.	Controlling for potential confounders, **women with trichomoniasis were significantly more likely to have a child with Intellectual Disability (HR 1.28, CI: 1.12–1.46).** The association was stronger for moderate to severe ID documented by the school system or DDSN (HR 1.84; CI: 1.35–2.51). Second-trimester trichomoniasis was associated with more than a three-fold increase in the odds a child was identified as trainable mentally handicapped or profoundly mentally handicapped in the public school system, or was receiving ID services from DDSN. There was no significant difference in the risk of ID in children of women with treated versus untreated trichomoniasis.	Diagnoses determined by use of ICD-9 diagnostic billing codes Underlying mechanism of association unclear; cannot establish causality	B

12. TV Sequelae — Others

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
Stark (2009)[174]	Nested case-control (Physicians Health Study) N=673	Men diagnosed with prostate cancer up to 18 years after blood collection (1982 – 2000) and who had available plasma samples. 1:1 controls matched by age, smoking, and follow-up time.	Plasma was assayed for antibodies against T vaginalis and men were followed prospectively	The relationship between TV+ antibodies with incident prostate cancers	**TV seropositivity was significantly associated with increased risks of extraprostatic prostate cancer (OR 2.17, CI: 1.08-4.37), and cancer that would ultimately progress to bony metastases or prostate cancer-specific death (OR 2.69, CI: 1.37-5.28).**	Time between TV infection and blood collection was not known.	B
Sutcliffe (2009)[175]	Nested case-control within a prospective cohort (Prostate Cancer Prevention Trial) N=616	Cases were men ≥55yo diagnosed with prostate cancer on any biopsy after visit 2 or on their end-of-study biopsy. 1:1 controls matched on age, treatment arm, and family history of prostate cancer. Participants had a PSA concentration >3 ng/mL and a normal DRE at enrollment	Men were screened annually for prostate cancer, and if not diagnosed during the trial, were offered an end-of-study prostate biopsy. Serum from visit 2 was tested for anti-TV IgG antibodies by ELISA	Association between TV antibodies and prostate cancer	Low TV seropositivity: 21.5% of cases and 24.8% of controls High TV seropositivity: 15.2% of cases and 15.0% of controls Compared to seronegative men, the **odds ratio of prostate cancer for men with low seropositivity was 0.83 (CI: 0.63–1.09),** and the odds ratio of prostate cancer for men with high seropositivity was 0.97 (95% CI: 0.70–1.34). Null association persisted after adjustment for potential confounders, investigation of several different prostate cancer endpoints, and stratification by finasteride, factors hypothesized to influence prostatic infection/inflammation, markers of underlying susceptibility for prostate cancer, and race.	Very early stage of prostate cancer: nearly half of prostate cancer cases (46.9%) were diagnosed by end-of-study biopsy, indicating that their prostate cancer was not detectable by prostate cancer screening or symptoms.	B

Sutcliffe (2006)[176]	Nested case-control (Health Professionals Follow-up Study) N=691	Prostate cancer cases were men diagnosed with prostate cancer between the date of blood draw (1993-1995) and 2000. 1:1 age-matched controls men with ≥1 PSA.	Serologic evidence of a history of trichomonosis was assessed by a recombinant Trichomonas vaginalis A-actinin IgG ELISA.	Association between TV and incident prostate cancer	**13% percent of prostate cancer cases and 9% of controls were seropositive for trichomonosis (aOR, 1.43; CI:1.00-2.03).** Association slightly stronger but not significant for high-grade prostate cancer (aOR 1.76, CI:0.97-3.18), and strongest among men who used aspirin infrequently over the course of their lives (OR 2.05; CI: 1.05-4.02).	Association persisted after additional adjustment for such factors as a history of other STIs (CT, NG, HPV, syphilis)	B
Allsworth (2009)[177]	Nationally representative survey N=3,648 (weighted)	Women age 14-49 in the civilian, non-institutionalized U.S. population National Health and Nutrition Examination Survey(NHANES) combining the 2001–2004	Crude and adjusted relative risks were estimated using logistic regression for rare STIs (< 10%; CT, syphilis and HIV) and Poisson regression for common STIs (HSV-1 and HSV-2).	**Association between TV and 6 other STIs**: CT, GC, HSV-1, HSV-2, syphilis and HIV	Prevalence of TV: 3.2% with over 80% of cases asymptomatic. All 6 STIs were more common among women with a positive test for TV. After adjusting for race/ethnicity, age and recent sexual partners. Only HSV-1 (RR=1.20, CI 1.09-1.34) and HSV-2 (RR=1.51, CI 2.32-3.23) were significantly associated with TV.	Rare outcomes might not be adequately represented in this sampling	A
Ozdemir (2010)[178]	Case series N=80	Infertile men at a hospital age 19-60 in East Anatolia, Turkey in 2009	Fresh semen tested for TV using wet mount microscopy, Giemsa staining, culture and PCR methods.	TV and male factor infertility	**In semen of infertile men, we found 2.5% positivity for TV** using PCR. Both PCR-positive patients were symptomatic. Giemsa staining and culture tests were positive in 1 patient (1.25%). Wet mount microscopy was ineffective.	No controls	C
Benchimol (2008)[179]	In vitro study	Interactions between TV and sperm cells from uninfected men.	Light microscopy, video microscopy, scanning, and transmission electron microscopy	**TV interference with sperm counts and motility**	Microscopy studies first revealed a tropism, then a close proximity followed by a tight adhesion between these TV cells and sperm cells. Sperm cells in contact with the parasites rapidly became immotile. TV parasites could be seen to phagocytose and digest the sperm.	TV has not been studied in vivo as a potential cause of male factor infertility	C

Cherpes (2006)[180]	Cross-sectional (secondary analysis) N=736	Nonpregnant women age 15-30 with purulent cervical discharge, untreated GC or CT, symptomatic BV, or sexual contact with a male diagnosed with GC, CT, or NGU, at STD or gyn clinics in Pittsburgh, 1998-2000. Excluded PID.	At enrollment: endometrial biopsy, vaginal fluid for Gran stain for BV and TV culture, endocervical specimens for GC culture and CT PCR, HSV-2 serology. 12 weeks later, hysterosalpingogram to detect fallopian tube obstruction	**Association between STIs with endometritis and/or fallopian tube obstruction.**	**Women with TV at enrollment were more likely to have acute endometritis. (19/82=23%, p=0.001).** Also associated were BV, HSV, CT, or NG at enrollment. Women coinfected with HSV-2 and TV, GC, NG, or BV were more likely to be diagnosed with acute endometritis than were women infected with one of these pathogens alone. HSV-2 prevalence was 42.6% (308 of 725). Among women with available HSV-2 serology and hysterosalpingogram results, HSV-2 was the only genital tract pathogen infection associated with fallopian tube obstruction (OR 1.7; CI: 1.0–2.8; P=0.04).	Could not control for sexual activity	B
Moodley (2002)[181]	Cross-sectional study N=696 (577 with vag d/c and 199 clinical PID)	Women attending an STD clinic in Kwamsane, South Africa, during 1999-2000	Assessment of STDs and TV culture by Diamond's media and HIV serology. PID clinical diagnosis by 1.low abd pain, 2. low abd tenderness, 3. CMT	**Relationship between TV and PID**	56% had HIV and 29% had TV. Patients with trichomoniasis had a significantly higher risk of PID than did women without trichomoniasis (p=.03). Association between TV and PID disappeared among HIV- patients (RR 0.8; p=0.4). However, association between TV and PID increased significantly among HIV+ women w/ TV (RR 1.9; p=.002)	Clinical dx PID may have resulted in misclassification. TV assessment by culture only may have resulted in misclassification.	B

Sherman (1987)[182]	Retrospective case-control N=321	Women age 20-39 with tubal infertility in King County, WA during 1979-1981. Controls were married women who gave birth during the same time period.	Multivariate analysis controlling for use of an intrauterine device, cigarette smoking, number of prior pregnancies, and number of sexual partners	Association of past genital herpes, genital warts, gonorrhea, or trichomoniasis with subsequent tubal infertility	The adjusted relative risk of tubal infertility in women reporting gonorrhea after their last pregnancy, was 2.9, CI:1.4-5.9. The **relative risk of tubal infertility was also significantly higher among women reporting trichomoniasis (aRR 1.7, CI: 1.1-2.6)** or genital warts (aRR 2.3, CI:1.3-4.1).	Self-reported disease history	C

13. TV Screening

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
Roth (2011)[183]	Two cross-sectional studies N=222 women at an STD clinic N=471 women at a correctional facility	High-risk women at a public STD clinic, and a correctional facility in Indiana	A) Rate of positivity detected using standard wet prep microscopy versus PCR on residual specimens B) Comparing universal v targeted screening of symptomatic women using PCR on vaginal specimens	Frequency of missed diagnosis of TV when using current routine practices for TV screening in high-risk female populations	A) In the first study, a 5-fold increased incidence of TV infection was detected when PCR was performed instead of wet mount microscopy in a sample of 222 women screened at a sexually transmitted disease clinic. B) The second study detected a 5-fold increase in cases among a sample of 471 incarcerated women when universal screening was implemented.	All incarcerated women participated in the study, so results are true prevalence in study B.	B
Gatski (2010)[184]		HIV-infected women			Probable persistent, undetected TV infections have been observed among HIV-infected women retested 3 and 6 months after initial evaluation.		B

Peterman (2009)[185]	N=1236	A study of reproductive-age women at U.S. STD clinics in 3 cities	Periodically tested for TV by culture and treated with standard therapy		119 (10%) were positive for TV at baseline, 16.5% were positive at 3 months, 18.5% were positive at 6 months, 12.5% were positive at 9 months, and 6.9% were positive at 12 months. Among women who were TV-infected at baseline, 16.5% had another positive TV culture during the study, indicating potential treatment failure versus reinfection from an untreated sex partner. Further analysis indicated that of the 21 new infections, 13 occurred in women who had been treated previously for TV infections, and 11 of these 13 (85%) had an intervening negative test result before having another positive result when no sexual exposure was reported; furthermore, the risk of new infection with TV was nearly identical for women who did (4.2%) and did not (3.9%) report having sex during the most recent 3-months.		B

Helms (2008)[186]	Cross-sectional analysis N=1462	Female participants in RESPECT-2 (STD clinics in Denver, Long Beach and Newark. Eligible clients presented to clinic for full diagnostic eval for STI, were HIV- at enrolment, reported vaginal/anal sex/3mo and were 15-39yo f/u at 3,6,9,12 mo post-enrollment	TV cx used InPouch TV or Diamonds media. New infxn defined as +lab result preceded by negative result for same pathogen or infxn detected >14 d after provision of Ab for the pathogen in question.	Predictors of prevalent and incident TV infection.	TV prevalence 13%. Log regression: significant predictors included older age (compared with 15-19yo) – Ad OR increases with age (3.73 (1.86-7.46) for 35-39. Black race Ad OR 3.03 (1.9-4.83) compared to other races. Concurrent CT Ad OR 2.37 (1.44-3.9). 3955 f/u visits with incidence 4.6% per 3mo interval over 1yr f/u. Predictors of incident infxn: age Ad OR 2.26 (1.14-4.48 for 35-39), black race (Ad OR 3.31 (2.04-5.37), concurrent CT Ad OR 2.37 (1.08-5.20), multiple partners (>/=2)/3mo ad OR 1.71 (1.13-2.60) and trich infxn in previous interval (ad OR 3.12 (1.93-5.03).	New infxn defined as +lab result preceded by negative result for same pathogen or infxn detected >14 d after provision of Ab for the pathogen in question. ?reinfection vs persistence (2nd definition) Not sure if partners treated	A

Peterman (2006)[187]	Secondary analysis of data from RCT N=2419 individuals with 8129 f/u intervals.	3 urban STD clinics; Eligible clients presented to clinic for full diagnostic eval for STI, were HIV- at enrolment, reported vaginal/anal sex/3mo and were 15-39yo	Patients counseled, examined, tested at 0, 3, 6, 9 and 12 mo. Tested for CT, NG, TV (cx InPouch TV or Diamonds) Analysis limited to those who returned for testing and could be classified as infected or uninfected; MSM excluded	New infection, risk factors for infxn	Among 1256 women, 319 (25.8%) with at least 1 new infection – 147 (11.9%) CT, 78 (6.3%) NG, 158 (12.8%) TV. Of 1183 men, 174 (14.7%) with at least 1 new infxn – 111 (9.4%) CT, 84 (7.1%) TV. New TV infxn more likely in women with previous TV or NG infxn compared to those with no baseline STD or CT at baseline. Black race and older age (26-39) predictor of recurrent TV. Young, black or Hispanic patients more likely to have new infx with CT, NG or TV. For participants with baseline STD, slightly more likely to have new STD at 3 and 6 mo visit compared to 9 and 12 mo though risk remained high throughout. 43.3% of recurrent TV infxn asymptomatic	Lack of generalizability to other settings. New infxn defined as +lab result preceded by negative result for same pathogen or infxn detected >14 d after provision of Ab for the pathogen in question. ?reinfection vs persistence (2nd definition)	A

Van Der Pol (2005)[188]	Substudy within longitudinal study of mid-adolescent women N=268	Women receiving care at 1 of 3 primary health clinics in IN. Eligible if 14-17yo, English-speaking,, not pregnant	Up to 10 clinical interviews and exams (enrollment and quarterly). Vaginal swabs obtained during clinical exam. Also, data and weekly vaginal swab collection x 12wk waves during 27 mo study period (up to 5 12wk cycles). TV rx'd with 2gm metro. Women found TV + during weekly diary period (not at clinical exam), were treated at next clinical exam (could go out to 11 wks prior to rx) Swabs sent for NG, CT and TV PCR	Prevalence, incidence and clearance of TV	Avg age 15.4y, 89% black, TV at enrollment 6%. (NG 4.1% and CT 10.1%) 245 patients with at least 1 quarterly visit. (5.3% of which had TV at enrollment), 23% (57/245) had at least 1 infection at f/u (cumulative prevalence) and 31.6% (18/57) with an infection at some point during study had multiple infections during study. 18.4% with at least one incident infection during study. For 42 infection episodes, documentation of treatment and follow-up weekly testing available. 39/42 (93%) cleared DNA by 2 wk. 1 remained + additional 8wk post-rx and 2 remained + 12 wk post-rx (until rx again)		B

Swygard (2004)[189]	Cross-sectional study N=2,194	2 urban STD clinics. Women presenting for care who were >/=18yo, spoke English, no metro use/4wk First visit only	Routine hx and PE Routine testing routine: vaginal swab for wet prep, endocerv swabs for gram stain, culture for GC and LCR/EIA for CT, Swab for TV culture (InPouchTV)	Predictors of TV in wet mount-women	Majority (79%) black and between 18-29. Most (61%) presented for symptom eval. 6.4% with GC and 11.2% CT 285 (13%) WP+ for TV of which 236/285 (82.8%) with + cx. 1909 WP-, 99(5.2%) TV cx+ TV prev. 17.5% using combined WP/cs std. Sign predictors of TV among WP- women: black race (AOR 9.1; 95%CI 2.8-29.5); Contact to TV (AOR 7.1;95%ci1.3-37.7); any drug use (AOR 2.3;95%CI 1.4-4.1). If use all 3 predictors, se 0%, sp 100% (test 0 women); If use one of 3 predictor to direct cx testing, se 97.8%; sp 20.4% (test 1,369 women); If test for TV cx if drug use AND contact to TV OR black race, se 96.7% and sp. 24.5% (test 1,302 women). WP+ women more likely to have signs and sx than WP-women but not statis sign in model	STD clinic setting, limited generalizability No cost-benefit analysis	B

14. Prevention of Trichomoniasis

CITATION	STUDY DESIGN	STUDY POP. TYPE/SETTING	EXPOSURE/ INTERVENTION	OUTCOME MEASURES	REPORTED FINDINGS	DESIGN ANALYSIS QUALITY/BIAS	SUBJECTIVE QUALITY RATING
Garcia (2012)[190]	Community-randomized trial (Peru PREVEN) of interventions to control STIs Baseline STI screening of N=15,261 young adults in 24 Peruvian cities. Followup with 6556 women and 6374 men.	Baseline STI screening in Aug-Nov 2002, in random household samples of young adults (age 18–29) and FSWs in Peruvian cities with >50,000 inhabitants. 20 geographically separate Geographically separate cities were matched into pairs, with half randomly assigned to intervention and the other to standard of care. Follow-up surveys of random samples were done after 2 years and 3 years.	4-modality intervention: I) strengthened STI syndromic management by pharmacy workers and clinicians; II) mobile-team outreach to FSWs for STI screening and pathogen-specifi c treatment; III) periodic presumptive treatment of FSWs for trichomoniasis q8weeks; IV) condom promotion for FSWs and the general population. Individuals in control cities received standard care.	Effect of a multicomponent community intervention (including periodic presumptive treatment of female sex workers for TV) on curable STIs. Composite primary endpoint was infection of young adults with CT, TV, NG, or syphilis.	In the 2006 follow-up survey, data for the composite primary outcome were available for 12,930 young adults. **TV prevalence was significantly reduced in intervention cities compared with control cities.** Reduction was significant among young women (RR 0.66, CI:0.48–0.92) and female sex workers (RR 0.49, CI:0.32–0.75) but not young men (RR 0.82, RR 0.36–1.89). For other STIs together, prevalence in young adults was reduced but not significantly in intervention cities compared with control cities (RR 0·84, CI:0·69–1·02). HIV prevalence was reduced in intervention cities but not significantly (RR 0.65, CI 0.32–1.30).	All analyses were done by intention to treat. HIV prevalences were low in all cities.	A-

Crosby (2012)[191]	Prospective cohort N=929	STD clinic patients in 3 cities in the northeastern U.S. followed for 6 months during 2007-2011	Urine STI nucleic acid amplification testing was performed at baseline, 3 months and 6 months for CT, NG, and TV using Taq-Man PCR-ELISA Participants received daily prompts from a handheld device by to report on condom use for each penile-vaginal sexual intercourse event.	Evaluate the protective value of consistent and correct use of latex condoms against the acquisition of CT, NG, and TV	**Individuals who used condoms both correctly and consistently were estimated to have 59% lower odds of acquiring an STI (eOR=0.41; CI:0.19-0.90), compared to those who did not.** Consistent and correct use of condoms reduced the estimated odds of an infection by almost 60%, with no significant differences in effectiveness by age group, gender or STI history.	Not powered to analyse condom effectiveness separately for CT, GC, and TV. Estimate of 0.41 should be considered conservative since study participants could have been aware of the infection status of their sex partners.	B
Balkus (2011)[192]	Randomized trial (secondary analysis of data from a prospective cohort) N=310	Female sex workers, HIV-1 seronegative, aged 18–45 years, and nonpregnant, in Mombasa, Kenya, between May 2003-December 2006	Participants were randomized to receive 2 g of metronidazole plus 150 mg of fluconazole or identical placebo monthly as DOT. Syndromically treated women with vaginal discharge or itching with a single 2g dose of oral metronidazole plus clotrimazole 200mg vaginal suppositories nightly for 3 nights.	To evaluate whether **periodic presumptive treatment reduces vaginal infections**	The incidence of a healthy vaginal environment (normal flora confirmed by Gram stain with no candidiasis or trichomoniasis) was 608 cases per 100 person-years in the intervention arm and 454 cases per 100 person-years in the placebo arm (HR 1.36; CI:1.17–1.58). Sustained vaginal health (healthy vaginal environment for R3 consecutive visits) was also more frequent in the intervention arm (HR, 1.69; 95% CI, 1.23–2.33). PPT is effective at establishing and sustaining a healthy vaginal environment.	Could not evaluate impact on reducing HIV transmission Could not assess potential increases in antimicrobial resistant TV	A

Gray (2009)[193]	Randomized trial N=825 wives of circumcised men and 783 wives of controls (delayed circumcision)	Wives of HIV-negative men in Rakai, Uganda.	Genital symptoms, bacterial vaginosis (BV), and trichomonas were assessed in HIV-negative wives of married participants. TV detected from cultures of vaginal swabs using the InPouch culture method	The effects of male circumcision on female partners' genital tract symptoms and vaginal infections	At 1 year follow-up, the **risk of TV was reduced in the partners of circumcised men (aPRR 0.52; CI, 0.05-0.98**), as were the risks of any BV (aPRR 0.60; CI: 0.38-0.94) and genital ulceration (aPRR 0.78; CI:0.63-0.97), but there were no differences in vaginal discharge or dysuria.	BV was more common among the control than the intervention arm women at enrollment	A
Sobngwi-Tambekou (2009)[194]	Randomised controlled trial N=1767	Men aged 18–24 participating in a circumcision trial in Orange Farm, South Africa	Urine analyzed by PCR for CT, GC, and TV	Effect of male circumcision on prevalent GC, CT, and TV	In an intention-to-treat analysis comparing intervention and control groups, prevalence of NG was 10.0% v 10.3% (OR 0.97; p=0.84), CT was 2.1% versus 3.6% (OR 0.58; p=0.065) and TV was 1.7% versus 3.1% (OR 0.54; p=0.062). TV association was also borderline when controlling for age, ethnic group, number of lifetime partners, marital status, condom use and HIV status (aOR 0.48; p=0.069). **In the as-treated analysis, TV was significantly lower among circumcised men (OR 0.49, p=0.030**; aOR 0.41, p=0.030).	Demonstrates effect of male circumcision on TV prevalence and not incidence	A
Mehta (2009)[195]	Randomized trial N=2655	Men aged 18–24 participating in a circumcision trial in Kisumu, Kenya	First incident nonulcerative STI during 2 years of follow-up	Background. We examined the effect of male circumcision on the acquisition of 3 nonulcerative STIs: CT, GC, and TV	342 incident infections occurred, combined incidence 7.3 (CI: 6.49–8.13) cases per 100 person-years CT: 4.6 per 100 person-years GC: 3.5 per 100 person-years TV: 1.3 per 100 person-years Incidence did not differ by circumcision status	Low TV prevalence may be due to use of TV testing by InPouch only, no PCR	A-

Tsai (2009)[196]	Prospective cohort (REACH Project of the Adolescent Medicine HIV/AIDS Research Network) N=411	All adolescent females age 12-19 at baseline, both HIV-infected and HIV-uninfected, at 16 locations in 13 US cities 1996-1999.	Followed high-risk female adolescents over a median 3-year period, both by time from study entry/first STI-free visit until an incident STI for participants who never, intermittently, and always douched (per ACASI) and also by reported douching at a given STI-free visit and incidence of STI at the next visit, using adjusted Cox proportional hazards models to calculate hazard ratios.	Association between douching and STI incidence (of TV, CT, GC, and/or HSV-2). TV diagnosis by wet mount, culture (In Pouch), and/or cytology	About 2/3 had HIV. **Time to STI was shorter for adolescents who always (HR 2.1; CI:1.2-3.4) and intermittently (HR 1.5; CI:1.0-2.2) douched, compared with never-douchers**. An adjusted hazard for STI was 1.8 times larger for always-douchers (CI:1.1-3.1) and 1.4 times larger for intermittent douchers (CI:0.9-2.0), compared with never-douchers. When classifying by follow-up after an STI-free visit, always-douchers had a shorter STI-free time than never-douchers (aHR 2.1; CI:1.5-3.1).	By adjusting for STI at current visit, analysis might underestimate overall effect of douching on STI	B

Wawer (1999)[197]	Randomised, controlled, single-masked, community-based trial N=6602 in intervention group, and 6124 controls	HIV-uninfected persons in Rakai District, Uganda Ten community clusters were randomly assigned to intervention or control groups. All consenting residents aged 15–59 years were enrolled; visited in the home every 10 months; interviewed; and asked to provide biological samples for assessment of HIV-1 infection and STDs	Intensive STD control, via homebased mass antibiotic treatment: azithromycin, ciprofloxacin, metronidazole in the intervention group, vitamins/anthelmintic drug in the control group. Intention-to-treat analyses used multivariate, paired, cluster-adjusted rate ratios.	Background The study tested the hypothesis that community-level control of sexually transmitted disease (STD) would result in lower incidence of HIV-1 infection in comparison with control communities.	At 20-month follow-up, the prevalences of syphilis (RR 0·80, CI 0.71–0.89) and **trichomoniasis (182/1968 {9·3%} vs 261/1815 {14·4%}; RR 0.59 (0.38–0.91) were significantly lower in the intervention group** than in the control group. In pregnant women, the follow-up prevalences of trichomoniasis, bacterial vaginosis, gonorrhoea, and chlamydia infection were significantly lower in the intervention group than in the control group. Baseline HIV prevalence: 15·9%. The incidence of HIV-1 infection was 1·5 per 100 person-years in both groups (rate ratio 0·97, CI: 0·81–1·16). No effect of the intervention on incidence of HIV-1 infection was observed in pregnant women or in stratified analyses.	Mass treatment in Rakai with metronidazole reduced TV incidence but didn't seem to prevent HIV infections	A-

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