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Modeling the impact of *Trichomonas vaginalis* infection on HIV transmission in HIV-infected individuals in medical care

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Abstract

Background—To assess factors associated with having a *Trichomonas vaginalis* (TV) infection among persons receiving care for HIV and estimate the number of transmitted HIV infections attributable to TV.

Methods—HIV clinic patients were recruited from two secondary prevention studies, screened by urine nucleic-acid amplification tests for sexually transmitted infections (STIs) and interviewed about risk factors (baseline, 6 and 12 months). We conducted mathematical modeling of the results to estimate the number of transmitted HIV infections attributable to TV among a cohort of HIV-infected patients receiving medical care in North Carolina.

Results—TV was prevalent in 7.4%, and incident in 2% – 3% of subjects at follow-up. Individuals with HIV RNA less than 400 copies/ml (OR 0.32, 95% CI: 0.14 – 0.73) and at least 13 years of education (OR 0.24, 95% CI: 0.08 – 0.70) were less likely to have TV. 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

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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 co-infected with TV.

Conclusions—The data suggest the need for improved diagnosis of TV infection and suggest that HIV-infected women in medical care may be appropriate targets for enhanced testing and treatment.

Keywords

HIV; Secondary prevention; Trichomonas infections; Sexually transmitted diseases

INTRODUCTION

The southeastern (SE) region of the USA carries an excess burden of the 55,000 HIV diagnoses and the nearly 19 million sexually transmitted infections (STIs) occurring annually^{1, 2}. In 2007, 46% of new AIDS diagnoses were in the SE USA; 40% of the people living with AIDS; and of the 14000 individuals who died of AIDS in 2007, 50% lived in the SE³. Trichomoniasis is the most common curable STI among young, sexually active women worldwide and an estimated 174 million new cases of TV occur globally each year⁴ and highly prevalent in African-Americans, a population carrying the burden of HIV in the SE USA.⁵ In the US, 3.1% of the adult population is estimated to be infected with TV⁶, however detailed epidemiology is limited as TV is not a reportable infection.

Studies now suggest that trichomoniasis, caused by the protozoan parasite, *Trichomonas vaginalis* (TV), also plays an important but under-appreciated role in increasing the sexual acquisition and transmission of HIV^{7–13}. The mechanisms by which TV may increase HIV acquisition include: 1) elicitation of an inflammatory response of vaginal, exocervix and urethral epithelia with recruitment of CD4 lymphocytes, macrophages and micro-hemorrhages, potentially compromising the mechanical barrier; 2) association with increased HIV viral load in genital secretions; 3) degradation of secretory leukocyte protease inhibitors; and 4) enhanced susceptibility to bacterial vaginosis or colonization with other abnormal vaginal flora, which in turn increases the risk of HIV acquisition¹².

Sexual partners exchange TV readily. One cross-sectional study found 71% of male partners of infected women were infected when assessed at a single time point and several other populations report a high prevalence of TV^{14, 15}. Therefore it has been hypothesized that TV infection plays a significant role in HIV transmission at a global or national or level even if the effect on an individual's risk is small⁴.

TV remains a highly prevalent STI among HIV-infected patients even when patients are in care for years¹⁶. The effect of TV on HIV transmission from HIV co-infected people is less well defined. HIV acquisition was unchanged in the presence of TV infection in some studies while in others, it was increased by 1.2 to 4.8-fold among cohorts of African and African-American women infected with TV^{8–11}. HIV shedding in semen was 19-times higher among 5 men with TV-associated urethritis and four times higher in women with TV compared with TV uninfected men and women with HIV^{17, 18}. Three studies have looked at the effect of TV infection on HIV transmission and the effect size ranged from no effect to an increased odds of 1.84^{10, 19, 20}. One study used presence or absence of discharge to detect STIs including TV (no effect found). Gray and colleagues reported an effect size of 1.5 but combined TV with other vaginal infections. Only Quinn et al. reported the effect (1.8) of TV independently by controlling for other STIs in multivariate analyses.

HIV transmission is a complex event that depends on many inter-related behaviors, including the presence or absence of STIs. Knowledge of population level HIV transmission

can be enhanced less expensively by using individual level data in mathematical modeling. We examined clinical, demographic and behavioral characteristics associated with TV infection and used this information to conduct mathematical modeling to estimate the number of transmitted HIV infections attributable to TV among a cohort of HIV-infected patients receiving medical care in North Carolina.

MATERIALS AND METHODS

Study site and participants

The STI sub-study was part of two HIV prevention studies: 1) Prevention with Positives Special Project of National Significance (SPNS)²¹ (May 7, 2004, to May 31, 2006) and 2) CDC Positive STEPS (CDC)²² (May 19, 2004, to October 13, 2004) conducted at the University of North Carolina – Chapel Hill with Institutional Review Board approval. The UNC Healthcare Infectious Diseases clinic is a public academic medical clinic and was the site of the studies. SPNS eligibility requirements were: 18 years of age, planning to receive care at the clinic for one year, English-speaking, treated at the clinic at least once previously, and currently sexually active or injecting drugs. This study compared provider based prevention counseling to the combination of specialist delivered MI prevention sessions in addition to the provider-delivered prevention standard of care. The CDC study eligibility required the subject to have been diagnosed HIV-positive for 6 months or more prior to enrollment in addition to the same criteria use for SPNS enrollment. The CDC study evaluated the implementation of provided-delivered prevention counseling in a quasi-experimental pre-post intervention design²³. Subjects who completed the CDC study were allowed to enroll in the SPNS study after a 3-month washout period.

Audio-Computer Assisted Self-Interview (ACASI) programs at baseline and two (2) 6-month follow-up time points were used in both studies to record socioeconomic, psychosocial, clinical, and sex behavioral characteristics^{21, 22}. The CDC study collected sexual behavior (number of sex acts, vaginal and anal sex acts, use of condoms and HIV status of partners) over the prior 3 months and the SPNS study collected the same sexual behavior over the prior 6 months. In other respects the data were similar. Chart abstraction was performed for information on zip codes, CD4, HIV RNA, and STI lab tests, medical visits, and antiretroviral therapy (ART) use. Interview data collected during participation in the CDC study was used when subjects had participated in both studies. Urine samples were provided at baseline and follow-up (6 months and 13 months). Zip codes were used to approximate rural-urban commuting areas (RUCA), a census-tract based classification of a residence's rural urban status.²⁴ Categories used: Urban: RUCA 1–3; Large town: RUCA 4–6; Small town: RUCA 7–9; Rural: RUCA 10.

Conversion of 3-month sexual behavior data

The only key difference between data collected in the two studies was that the referent time period for sexual behavior was 3 months for the CDC study and 6 months for the SPNS study. The dually enrolled subjects had both 3 month and 6 month sexual behavior data to use for validation of our method of converting 3 to 6 month data. To estimate CDC participants' 6-month sexual behavior, the number of sex acts in 3 months was multiplied by two. To estimate the number of sex partners, main partnerships were assumed to remain constant (1 main partner in 3 months is still 1 main partner in 6 months) but casual partners were assumed to increase across time (2 casual partners in 3 months but 4 casual partners in 6 months)²⁵. Participants were considered to have one main partner if they were married, in a committed relationship, in a domestic partnership *or* lived with a sex partner or spouse. This main partner was subtracted from the total number of sex partners to determine the number of casual partners. Partner numbers for participants *with* $\{(n^{6mo}) = 1 + 2(n^{3mo} - 1)\}$

or *without* $\{(n^{6mo}) = 2(n^{3mo})\}$ a main partner were estimated for 6 months. This equation was validated by comparing its results with actual data from 76 participants who enrolled in both studies; the equation was found to slightly underestimate 6-month partner number (estimating 0.91 partners for each actual partner) but did not alter the predicted partner number for any individual.

Laboratory detection and treatment of STIs

Nucleic acid amplification tests (NAATs) for the detection of *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and TV were performed on first-catch urine samples collected at baseline and each of two (2) 6 month follow-up times. For CT/NG testing, we used Gen-Probe APTIMA Combo 2 according to the manufacturer's instructions. For TV testing, we used real-time PCR (September 28, 2004 to August 15, 2006)²⁶ or Gen-Probe TV Analyte Specific Reagents (ASR, after August 15th 2006)²⁷. Published sensitivities and specificities of the TV assays are as follows: 90.1% and 100%, respectively, for detection of TV in urine by real-time PCR.²⁶; 98.2% and 98.0%, respectively, for detection of TV in vaginal swabs by this ASR²⁷; and 95.2% and 98.9%, respectively, for detection of TV in urine by FDA-approved NAAT analogous to the ASR assay²⁸.

Statistical analyses

Predictors of TV Diagnosis—Prevalence and incidence estimates were determined from the baseline and the follow-up (6m and 13m) STI results, respectively. Participants were considered as TV-infected if TV was detected at any time point. Bivariate analyses determined the associations of hypothesized predictor variables²² with TV diagnosis using chi square χ^2 and Wilcoxon rank sum tests. Variables for multivariable logistic regression (performed with and without gender) were selected based on the bivariate analysis and importance in the literature, while avoiding collinear elements.

Estimation of HIV transmission attributable to TV—Analyses to estimate the HIV transmission attributable to the STI study participants and the effect of TV infection on transmission were conducted by estimating the potential number of new HIV infections in 6 months. To create a mathematical model, we adapted an equation used previously^{21, 29} that calculates, based on self-reported risk behavior and other factors, for each study participant, the probability, P_i , that he or she would transmit HIV to a sexual partner. The probability of HIV transmission depends upon the number and type of sex acts in 6 months (superscripts a, b, c, d, n, [unprotected]; A, B, C, D, N), [protected], condom effectiveness (β), probability that an unknown partner is HIV infected (λ), HIV viral load (μ) and TV infection (TV). The number of unprotected sex acts in 6 months is represented by lower case superscripts a, b, c, d and n (a: insertive vaginal, b: receptive vaginal, c: insertive anal and d: receptive anal and n: total acts). Protected acts are denoted by the corresponding upper case superscript (A, B, C, D, N). Condom efficacy (β) (when used) was estimated as 90% for the base estimate and 80–100% for sensitivity analyses. The probability that a partner of unknown sero-status is actually HIV infected (λ) is also included in the model. The addition of TV infection effect (TV) and the actual HIV viral load in blood plasma (μ) (instead of a 50% reduction in risk if anti-retrovirals were being used) were adaptations to the previously published model.

The effect of TV on HIV transmission is unknown. A meta-analysis of risk estimated the TV effect on HIV acquisition as 1.5 in 2001 and ranged from 0 to 4.8 in subsequent studies of African and African American women¹¹. The effect on HIV transmission was determined independently in one study, reported as 1.8¹⁰. Consequently, the effect of TV on per-act transmission probability was determined by multiplying α by the effects of TV infection (1.8). The TV effect was estimated as 1.0 (no effect) to 2.0 in a sensitivity analysis.

The λ parameter denotes the probability that the partner was already infected with HIV and λ was set as 1 for HIV-positive partners, 0 for HIV-negative partners, 8.47% for HIV unknown status male partners of men³⁰; 0.72% for HIV unknown status male partners of women and 0.22% for HIV unknown status female partners of men³¹. The range for the sensitivity analysis for the probability of prior infection was estimated as 50% (1/2) of the prevalence reported, to 200% (2-fold) the predicted prevalence.

The associated per act transmission probabilities (α) were indicated as α_a , α_b , α_c , and α_d (0.0006 for unprotected receptive anal and vaginal intercourse, 0.001 for unprotected insertive vaginal intercourse, and 0.02 for unprotected insertive anal intercourse)²¹. The terms “receptive and insertive” refer to the role of the study subject in the sex act. The standard per act transmission probabilities (α) (see below) were estimated from participants who were not on anti-retroviral therapy and typically have a HIV RNA level of 4.5 log₁₀ copies/ml.^{10, 32}

The μ parameter represented the predicted change in transmissibility based on the participants’ actual viral load (the majority while on antiretroviral therapy) compared with an untreated population average $\mu/(\text{actual log}_{10} \text{ HIV RNA} - \text{log}_{10} 4.5)$ and was estimated as 2.45⁹. Most (75%) of the participants were on antiretroviral therapy and viral loads were lower than the base level of 4.5 log₁₀ copies/ml. The fold change effect per log viral load (μ) reduced the impact of the viral load on transmissibility if the subject’s viral load was less than the untreated average. In this case, a higher fold-change effect (3.26) will produce a lower estimate of transmission had a greater reduction in the effect of the viral load compared with smaller fold-change effect size (1.86).

The following equation represents the transmission probability. $P_i = (1 - \lambda) \{ 1 - (1 - (1 - \mu)\alpha_{aTV})^{a/n} (1 - (1 - \mu)\alpha_{bTV})^{b/n} (1 - (1 - \mu)\alpha_{cTV})^{c/n} (1 - (1 - \mu)\alpha_{dTV})^{d/n} (1 - (1 - \mu)\alpha_{aTV})^{A/n} (1 - (1 - \mu)\alpha_b(1 - \beta)_{TV})^{B/n} (1 - (1 - \mu)\alpha_c(1 - \beta)_{TV})^{C/n} (1 - (1 - \mu)\alpha_d(1 - \beta)_{TV})^{D/n} \}$. Using the probability (P_i) and the number of partners, the number of new HIV infections from each study participant was predicted as the sum of new infections predicted for each of four partner types (HIV-negative male, HIV-unknown status male, HIV-negative female, HIV-unknown status female).

RESULTS

Participants

Participants in two prevention with positive studies (CDC = 186, SPNS = 234), were offered participation in an STI screening sub-study. Of the 186 CDC subjects, 140 agreed to participate in the sub-study. Of the 234 SPNS subjects, 223 agreed to participate but 76 of these individuals had previously participated in the CDC sub-study leaving 147 new subjects enrolled from the SPNS study and a total of 287 unique STI sub-study subjects. One participant failed to complete the ACASI. Four urine samples contained inhibitors of amplification, leaving a total of 541 usable urine samples from 285 active participants.

The 285 participants included in the STI sub-study sample did not differ from those in the total SPNS/CDC study sample in age, sex, or race/ethnicity (all $p > 0.05$). The mean age was 42 years; 63% were men, 66% were African American, 28% were white, 61% had 12 years of education or less, 56% had an annual income of <\$10,000 and 61% were unemployed. The study population (37% female, 66% AA, 28% white non-Hispanic, 6% other race/ethnicity; 31% MSM exposure, 48% heterosexual exposure to HIV, and 63% aged over 40) was similar to the HIV population in North Carolina (28% women, 66% AA, 27% white non-Hispanic, 7% other, 33% MSM, 25% heterosexual exposure to HIV, and 53% aged over 40) except that women and older ages were over represented in the sub-study. The

difference between the 48% heterosexuals in the sub-study and 25% heterosexuals in NC is due to a large category of “no reported risk” in the NC data.

STI Prevalence and Incidence

A total of 541 urine samples were collected from 285 patients and analyzed for NG, CT, and TV (Figure 1). TV was detected in 34 urine samples from 28 individuals (5 heterosexual men, 0 MSM and 23 women). TV was detected at baseline in 7.4% ($n = 21/285$). New TV (incident) infections were found in 3% of patients at the first (6m) and 2% at the second (13m) follow-up (5/174 and 2/86). Also TV was present at follow-up secondary to failure to receive treatment ($n=2$) and relapse or re-infection ($n=4$). CT (3/285 at baseline; 2/174 at 1st follow-up; 0/86 at 2nd follow-up) and NG (2/285 at baseline; none at either follow-up) were rarely detected, and 3 of these 7 patients were co-infected with TV. All patients with TV, NG or CT were treated. NG and CT infections were reported the NC Division of Public Health.

Bivariate Analyses

Men were less likely to have TV infection compared to women (Table 1; OR 0.10). Non-whites were less likely to have TV infection compared to those who were white (OR 0.28). Participants with higher levels of education or employment were less likely to have TV (OR 0.24; OR 0.24, respectively). Participants with HIV RNA copy numbers >400 copies/ml were less likely to have TV infection (OR 0.32). TV infection did vary by type of sexual act and was strongly associated with all vaginal sex acts (protected and unprotected). Privately insured participants were less likely to have TV than un-insured or publicly insured patients (0% vs. 11%). Those living in urban settings had less TV infections than those living in other settings (7% vs. 13%); and those receiving anti-retroviral medications versus those who were not (8% vs. 13%), but these differences did not reach statistical significance. Number of sexual partners (>1 vs. 1), alcohol use, and cocaine use were selected because of associations with risks for STI exposure and unprotected sex behaviors but were not associated with TV. TV was not associated with CD4 count, time living with HIV, time in HIV care, overall health status, distance to clinic (data not shown).

HIV Transmission Risk

TV only contributed to the transmission risk for women, as TV was not detected in men who have sex with men (MSM) and men who have sex with women (MSW) infected with TV only reported HIV+ partners (Table 3). Using a TV effect size of 1.8, the mathematical model predicted that 0.062 HIV infections would occur per 100 female HIV participants in the absence of TV infection and 0.076 HIV infections will occur if TV infection was prevalent in 22% of the HIV-infected women. HIV infection estimates were 0.062, 0.070 and 0.079 per 100 persons if TV effect sizes 1.0, 1.5 or 2.0 were used, estimating 0%, 14%, or 28% additional HIV infections. In the base estimate, one-fifth of HIV transmission events (22.5%) from HIV-infected women participants will be caused by TV infection if TV remains prevalent in one of five women.

The model for all subjects was not sensitive to the estimated effect of TV infection or the prevalence of HIV in unknown-status partners reported from the NHANES study (using $\frac{1}{2}$ to 2-fold)^{30, 31}. However, the model was sensitive to the efficacy of condoms (0.14 – 0.39 per 100 persons using 80% – 100% efficacy, $\pm 47\%$ change) on the estimate of HIV infections. The model was also sensitive to the effect size (1.85 to 3.26) of each $\log_{10}$ change in HIV RNA (-13 , $+25\%$ of the base estimate). Predicted transmission events ranged from 0.23 per 100 persons with the highest effect size of HIV RNA log change (3.26/(actual HIV RNA – $\log_{10}4.5$)) to 0.33 for the lowest effect size for HIV RNA change (1.85/(actual HIV RNA – $\log_{10}4.5$)). Most of the HIV RNA values were less than the untreated

population average of $\log_{10}4.5$, so a higher effect size produced a larger reduction in transmission risk.

DISCUSSION

In this study of HIV infected patients in care, we used individual level data to inform an attributable risk model to describe the effect TV infection may have on HIV transmissibility. Our model estimates that this range is from 0% to 28% and the base model estimate is that 22% of projected HIV transmissions from women are attributable to TV infections and up to 2% of all HIV transmission in the USA may be related to TV infection. The estimates of transmission risk in a previous study are approximately 2 to 4-fold higher of that reported here²¹. Two differences in the studies may explain this. First, the number of MSM recruited was very different (50% vs. 33% in our study). Second, the inclusion of HIV RNA values varied. In the prior study, the transmission risk was estimated as the standard risk if a person was receiving antiretroviral therapy, otherwise the transmission risk per act was not adjusted for the viral load. In our study we adjusted the standard per act transmission risk based on the actual difference between the subject's HIV RNA value and the usual untreated population HIV RNA of 38,000 copies/ml. The model showed that estimates of new HIV infections were very sensitive to estimates of transmission probabilities associated with viral load. These results support the recently proposed use of antiretroviral therapy as a component of an HIV epidemic control strategy^{33, 34}.

The prevalence of TV infection was far greater than either gonorrheal or chlamydial infections. This is quite consistent with other studies of TV prevalence in HIV infected women¹⁵ where TV infection is reported in 22% HIV + women when culture or PCR are used as the detection methods. This difference is likely to be due to the relative sensitivity of screening for NG and CT compared with traditional methods of screening for TV. Screening for TV has been a manual assay previously and therefore not as readily used for screening due to the labor involved and the low sensitivity of microscopy. The prevalence is only 11% if of wet mounts are used as the detection method. It is also possible that co-infection with HIV allows a more persistent infection with TV but not NG or CT, explaining the increased prevalence. NAAT screening for TV was easily implemented and allowed an unrecognized infection present in more than 10% of the study population to be identified and treated.

TV infection was associated with high HIV viral loads. HIV RNA was higher in TV-infected participants when examined by either the proportion of participants with less than 400 copies/ml or by mean HIV copies/ml. The association between high viral loads and TV infection suggests that TV occurs more often in women who are receiving less than adequate care whether they are new to care or only marginally engaged in care. Improved entry and retention in care will prevent complications of both TV and HIV infection and avoid the human and economic costs associated with small, but significant numbers of HIV infections. Other previously described variables associated with TV infection were vaginal intercourse low socioeconomic status (low educational attainment, unemployment, lack of private insurance), and non-white race. Poverty has been consistently associated with TV infection with a 3-fold increase in TV when income was <1.85 of the federal poverty level⁶. An association of TV with educational status has been previously reported, but the 5-fold increased risk with low education reported in the present study is much greater⁶. The association between low educational attainment and TV suggests that inadequate health literacy may be an important element in the pathway to TV-infection^{21, 22}. In data presented here, a 3-fold difference in TV prevalence was seen between whites and non-whites. However, in multivariable analysis, race remained associated with TV infection but not statistically, perhaps due to sample size or a lack of the racial association within a cohort of HIV- infected people.

The limitations of this study include the self-reported nature of some of the data on which risk estimates are based, however ACASI technology was used to minimize this. The study was conducted at one site, which may limit the applicability to other populations. However, the study site draws patients from a wide geographic area within NC. Demographics of the STI sub-study are similar to the demographics of the population of newly HIV diagnosed persons in North Carolina; therefore, the study findings may be applicable to HIV-infected individuals receiving medical care in North Carolina. Our TV effect estimate of 1.8 is based on HIV acquisition and limited HIV transmission studies. Although these estimates are based on limited data and our analyses would be strengthened by more robust data, there are no other direct data. Moreover, our sensitivity analyses took into account changes in these assumptions. Third, a conversion method was needed to the estimations we used to convert three month data to six-month data did not include adjustment for changes in sex behavior over time or an adjustment the possibility of more than one main partner. However in the subset of patients who were enrolled in both studies, the calculation was able to predict the number of partners subjects reported in 6 months by using data from the 3-month data collection. Fourth, models are based on estimates and not observations. A full discussion of the strengths and weaknesses of HIV transmission risk models are beyond the scope of this paper but have been recently discussed³⁵. Finally, the findings, we report here are only based on NAAT testing of urine specimens, other detection methods and use of vaginal specimens instead are likely to influence the findings.

An incidence of TV infection of 2% –3% for HIV-infected women, as reported here, suggests that more than 5000 new TV infections are occurring in the 290,000 HIV infected US women annually and potentially contributing to HIV transmission events. Medical care settings provide the opportunity to address both behavioral and biologic aspects of HIV transmission. Biological factors, such as TV, that enhance HIV transmission may be addressed with STI and HIV medical treatments. TV diagnostic assays are appropriate when clinical history and exam support use of GC and CT testing. However, due to the often-asymptomatic nature of TV, the limited use of nucleic acid amplification assays, the insensitivity of cytology, and requirement for a pelvic examination for collection, TV is frequently overlooked. Examination of the synergistic effects of medical care, education and counseling, combined with STI treatment and antiretroviral use, should provide more insights into effective HIV epidemic control.

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SUMMARY

HIV infected patients with an undetectable HIV RNA and >12 years of education were less likely to have *Trichomonas vaginalis* (TV) infection; theoretical modeling of HIV transmission suggested that 22% of female-to-male events may be attributable to TV when the prevalence of TV in HIV-infected women is one in five.

Figure 1. STI Screening. Urine was screened using nucleic acid amplification tests to detect *Trichomonas vaginalis*, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. BL= baseline; F/u = follow-up.

TABLE 1

Characteristics of Patients With and Without *Trichomonas vaginalis* Infection

	<u><i>T. vaginalis</i> (+)</u>	<u>OR</u>	<u>95% CI</u>	<u>Probability</u>
	<u>N/All in Category (%)</u>			<u>[chi]²</u>
Age				
Age [ltequ] 40 y	15/180 (14)	REF		
Age [mt] 40 y	13/105 (7)	0.47	0.21–1.02	0.0533
Gender				
Women	23/106 (22)	REF		
Men	5/179 (3)	0.10	0.04–0.28	[lt]0.0001
Race/ethnicity				
AA, Hispanic, other	25/205 (12)	REF		
White, non-Hispanics	3/80 (4)	0.28	0.08–0.96	0.0314
HIV exposure				
Heterosexual	22/138 (16)	REF		
MSM + MSM/IDU	0/87 (0)	NA	—	NA
IDU + other	6/60 (10)	0.59	0.22–1.53	0.0005 ^a
Education				
12 y or less	24/175 (14)	REF		
13 y or more	4/110 (4)	0.24	0.08–0.70	0.0054
Income				
[lt]\$10,000	18/143 (13)	REF		
\$10–20,000	4/56 (7)	0.53	0.17–1.65	0.0121 ¹
[mt]\$20,000	0/58 (0)	NA	—	NA
Employment				
Unemployed	24/175 (14)	REF		
All others	4/110 (4)	0.24	0.08–0.70	0.0054
Insurance				
Public or none	26/213 (11)	REF		
Private insurance	0/37 (0)	N.A.	NA	NA
Rurality				
Rural	2/26 (8)	REF		
Small town	11/72 (15)	2.16	0.45–10.49	
Large town	5/44 (11)	1.54	0.28–8.56	
Urban	10/143 (7)	0.90	0.19–4.38	0.2656
Current ART				
No	10/71 (14)	REF		
Yes	17/211 (8)	0.53	0.23–1.23	0.1354
HIV RNA ^b				
HIV RNA [mt] 400	19/122 (16)	REF		
HIV RNA [ltequ]400	9/162 (6)	0.32	0.14–0.73	0.0051
CD4 count ^c				

	<u><i>T. vaginalis</i> (+)</u>	<u>OR</u>	<u>95% CI</u>	<u>Probability</u>
	<u>N/All in Category (%)</u>			<u>[chi]²</u>
CD4 count [mt]350	18/166 (11)	REF		
CD4 count [lt]350	10/115 (9)	0.78	0.35–1.76	0.5552
Sexual group				
Women	23/106 (22)	REF		
MSM + MSM/W	0/93 (0)	NA	NA	NA
MSW	5/86 (6)	0.22	0.08–0.61	[lt]0.0001 ^a
Relationship				
No main partner	20/166 (12)	REF		
<ems>Main partner	8/119 (7)	0.53	0.22–1.24	0.1363
Partners				
2 or more	7/72 (10)	REF		
0 or 1	19/199 (10)	0.99	0.39–2.44	0.9656
Alcohol binges				
Any binges	9/86 (9)	REF		
No binges	17/183 (9)	0.99	0.43–2.31	0.9814
Cocaine use				
Any use	7/49 (14)	REF		
No use	20/229 (9)	0.57	0.23–1.44	0.2336

Note 2. a = Monte Carlo method; b = copies/mL; c = cells/mm³; d = years. B = binge alcohol use is more than 4 drinks/d; c = crack or powder cocaine; d = acts/6 mo; e = sexual behaviors = means acts/6 m.

ART indicates antiretroviral therapy; CI, confidence interval; IDU, injection drug use; MSM, men with male partners; MSM/W, men with male and female sexual partners; MSW, men with female sexual partners; NA, not applicable; T, *Trichomonas*; UAVI, unprotected anal or vaginal sex; UVI, unprotected vaginal sex.

TABLE 2*Trichomonas vaginalis* (TV) Infection and Sexual Behaviors

	TV([minus])	TV(+)	Wilcoxon Rank Sum
Sex partners			
No. partners in 6 mo, mean	2.44	1.52	—
Sex behaviors (sex acts in 6 mo, mean)			
Anal or vaginal sex	19.15	53.42	—
Vaginal sex	13.79	53.04	0.0009
Anal or vaginal sex, unprotected	9.57	42.50	0.0909
Vaginal sex, unprotected	6.99	42.27	0.0012
All (n)	257	28	

TABLE 3
Estimated Number of New HIV Infections Transmitted per 100 Persons and Sensitivity Analysis of Factors Impacting Transmission

TV [*]	Effectiveness of Condom Use [§]				Risk Estimate for Change in HIV RNA [¶]		Prevalence of HIV [‡]	
	Base [‡]				80%	100%	2 × Est.	1/2 Est.
No TV	1.5 Risk	1.8 Risk	2.0 Risk	2.0 Risk	3.26	1.85	2 × Est.	1/2 Est.
All								
Mean	0.261	0.264	0.266	0.267	0.14	0.39	0.231	0.333
% change	Ref. 1	2	2	2	[minus]47	47	[minus]13	25
MSW								
Mean	0.133	0.133	0.133	0.133	0.068	0.197	0.1025	0.1916
% change	Ref. 0	0	0	0	[minus]49	48	[minus]23	44
MSM/MSMW								
Mean	0.6045	0.6045	0.6045	0.6045	0.2927	0.9124	0.5455	0.7154
% change	Ref. 0	0	0	0	[minus]52	51	[minus]10	18
WOMEN								
Mean	0.0617	0.0704	0.0756	0.079	0.0639	0.0872	0.0572	0.1109
% change	Ref. 14	23	28	28	[minus]15	15	[minus]24	47

^{*}TV infection range of risk estimates = 1.0 fold (no TV-associated risk), 1.8 fold (base), 1.5 fold, 2.0 fold.

[‡]Base prediction: TV infection is associated with a 1.8-fold increased risk of transmission; condom efficacy is 90%; HIV RNA risk = 2.45-fold change in risk/(actual HIV RNA log10 [minus] HIV RNA log10(4.5)); HIV prevalence is 8.74% male partners of men, 0.72% male partners of women, 0.22% female partners of men.

[§]Condom efficacy: base assumption = 90%; range = 80% to 100%.

[¶]HIV RNA risk = 2.45-fold change in risk/(actual HIV RNA log10 [minus] HIV RNA log10(4.5)) (base); range, 1.85[times] risk, 3.26[times] risk. Note: Most viral loads in study subjects were less than 38,000 (the average viral load in populations used to determine per act transmission probabilities) and higher risk estimate/log HIV RNA change indicates a larger reduction in transmission risk if HIV RNA is [lt]38,000 (log10 4.5).

[¶]Prevalence of HIV in unknown status partners: Base assumptions = 8.47% male partners of men; 0.72% male partners of women; 0.22% female partners of men; range= ½ estimated prevalence to 2 times the estimated prevalence.

TV indicates *Trichomonas vaginalis*; MSW, men with female sexual partners; MSM, men with male sexual partners; MSMW, men with male and female sexual partners.