International Journal of STD & AIDS
2021, Vol. 32(13) 1204–1211
DOI: 10.1177/09564624211030368
journals.sagepub.com/home/std

Sexually transmitted infections among HIV serodiscordant partners: A secondary analysis of HIV Prevention Trial Network 052

Maganizo B Chagomerana[1,2], Mina C Hosseinipour[1,2], Jose Henrique Pilotto[3], Sharlaa Badal-Faesen[4], Mulinda Nyirenda[5], Emily Shava[6], Sheela V Godbole[7], Victor Akelo[8], Suwat Chariyalertsak[9,10], Ravindre Panchia[11] and Myron Cohen[2]

Abstract

Sexually transmitted infections (STIs) remain a public health concern because of their interaction(s) with HIV. In the HPTN 052 study, STIs were evaluated in both HIV-positive index cases and their HIV-negative partners at enrollment and at yearly follow-up visits. Our definition for STI was based on any infection with *Chlamydia trachomatis, Neisseria gonorrhoeae*, syphilis, or *Trichomonas vaginalis*. We used log-binomial regression models to identify factors associated with prevalent STIs. Generalized estimating equation models with the Poisson distribution were used to compare STI incidence between HIV-positive index cases and HIV-negative partners. 8.1% of the participants had STIs at enrollment. The prevalence of STIs (8.9 vs. 7.2) was higher in HIV-positive index cases than HIV-negative partners. Being female (prevalence ratio (PR) = 1.61; 95% CI: 1.20–2.16) or unmarried (PR = 1.92; 95% CI: 1.17–3.14) was associated with prevalent STIs. Compared to HIV-negative male partners, HIV-positive female index cases had a higher risk of STI acquisition (incidence rate ratio (IRR) = 2.25; 95% CI: 1.70–2.97). While we are implementing HIV prevention interventions for HIV-negative people, we should also intensify targeted STI prevention interventions, especially among HIV-positive women.

Keywords

Antiretroviral therapy, heterosexual, syphilis (*Treponema pallidum*), gonorrhea (*Neisseria gonorrhoeae*), chlamydia (*Chlamydia trachomatis*)

Date received: 26 February 2021; accepted: 14 June 2021

Introduction

Sexually transmitted infections (STIs) are widespread worldwide and remain a public health concern. In 2016, new infections of chlamydia, gonorrhea, syphilis, and trichomoniasis accounted for an estimated 376.4 million new STIs among sexually active men and women aged 15–49 years globally (WHO).[1] Besides the immediate clinical syndrome, STIs can lead to devastating consequences in sexual and reproductive health. STIs during pregnancy can lead to adverse birth outcomes including fetal loss through miscarriage or stillbirth, low birth weight, prematurity, congenital infections, and neonatal deaths.[2–4] Some STIs, like gonorrhea and chlamydia, can lead to infertility among women.[5]

Sexually transmitted infections increase both HIV transmission and acquisition.[6] Depending on the infection,

[1] UNC Project-Malawi, Lilongwe, Malawi
[2] Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
[3] Hospital Geral de Nova Iguacu and Laboratorio de AIDS e Imunologia Molecular-IOC/Fiocruz, Rio de Janeiro, Brazil
[4] Clinical HIV Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[5] Johns Hopkins Project, University of Malawi College of Medicine, Blantyre, Malawi
[6] Botswana Harvard Aids Institute Partnership, Gaborone, Botswana
[7] CMR-National AIDS Research Institute, Pune, India
[8] Kenya Medical Research Institute (KEMRI), Nairobi, Kenya
[9] Research Institute for Health Sciences, Chiang Mai University, Chiang Mai, Thailand
[10] Faculty of Public Health, Chiang Mai University, Suthep, Thailand
[11] Perinatal HIV Research Unit, University of the Witwatersrand, Soweto HPTN CRS, Soweto, South Africa

Corresponding author:
Maganizo B Chagomerana, Data and Manuscript Unit, UNC Project-Malawi, Private Bag A-104, Lilongwe, Malawi.
Email: mchagomerana@unclilongwe.org

STIs can disrupt the integrity of the genital mucosa, induce genital inflammation, or cause genital ulceration.[7] Infection with STIs among HIV-positive persons reduces $CD4^+$ level and increases HIV RNA in blood plasma and genital fluids,[8,9] thus increasing the potential of transmitting HIV to their sexual partners. In HIV-negative individuals, STIs increase genital inflammation that recruits HIV target cells, enhancing HIV acquisition during sex.[7] Because of this, STIs may undermine efforts to prevent both HIV transmission and acquisition.

Since STI incidence is a marker of unsafe or risky sexual behavior[10] and STIs have the potential to facilitate HIV transmission, it is important to understand the prevalence and incidence of STIs among couples. In this analysis, we estimate the prevalence and assess demographic and sexual behavior factors associated with prevalent STIs at enrollment among serodiscordant couples who were enrolled in the HPTN 052 study. We also estimate and compare the rate of STI acquisition between HIV-positive index cases and their HIV-negative sexual partners.

Materials and methods

Study setting and population

We used data from HIV Prevention Trial Network (HPTN) 052 study, a Phase III, two-arm, randomized, controlled, multi-center trial among 1763 HIV serodiscordant couples; 1763 HIV-positive index cases and 1793 HIV-negative partners.[11,12] The HPTN 052 study evaluated the effect of early versus delayed combination antiretroviral therapy on the prevention of HIV-1 transmission to uninfected partners for patients with HIV-1 infection who had CD4 counts between 350 and 550 cells/mm^3 and who were in a stable sexual relationship with a partner who was not infected. More HIV-negative partners were enrolled than HIV-positive index cases because additional partners were allowed to be added throughout the study to replace partners who discontinued their participation in the study before reaching a primary study end-point. The study was conducted in Rio de Janeiro, Brazil; Gaborone, Botswana; Pune and Chennai, India; Kisumu, Kenya; Blantyre and Lilongwe, Malawi; Johannesburg and Soweto, South Africa; Chiang Mai, Thailand; Boston, USA; and Harare, Zimbabwe. Participants were enrolled from June 2007 through May 2010, followed up until May 2015.

Ethical consideration

The parent study was approved by the institutional review board or ethics committee at each study site and by the institutional review board at the US Centers for Disease Control and Prevention (CDC) for the CDC-affiliated site in Kenya.

STI diagnosis

Both HIV-positive index cases and HIV-negative partners were tested for STIs at enrollment and during yearly follow-up visits. If the HIV-negative partner seroconverted, both the HIV-positive index case and their partner were examined for genital ulcer diseases. As part of clinical care, clinicians would also diagnose and treat STIs at any time during the study as clinically indicated. The infections that were evaluated in both HIV-positive index cases and HIV-negative partners included *Chlamydia trachomatis, Neisseria gonorrhoeae*, *Treponema pallidum* (syphilis), and *Trichomonas vaginalis*. Whenever a genital ulcer was found during examination, the clinician took a genital swab.

Rapid plasma reagin test (BD Macro-Vue™ RPR by Becton Dickinson) was used as the screening test for *T. pallidum* followed by a confirmatory test using *T. pallidum* particle agglutination (TP-PA) test. Urine was collected for *Neisseria gonorrhea* and *Chlamydia trachomatis* testing using BD ProbeTecTM analyzer with Probe Tech CT/NG Amplified DNA Assay reagents manufactured by Becton Dickinson. Vaginal swabs were collected to prepare saline wet mount slides for *T. vaginalis* detection. The swabs for genital ulcers collected at the sites were shipped to HPTN Central Laboratory for etiology determination using multiplex PCR, which has been described in detail elsewhere.[13–16] All STIs diagnosed at enrollment and during the study were treated adequately as per country and WHO guidelines.

In this secondary analysis, our definition for STI was therefore based on any infection with *Chlamydia trachomatis, N. gonorrhoeae*, *T. pallidum*, or *T. vaginalis*.

Variable definitions and classification

The two outcomes of interest were STI prevalence at enrollment and STI incidence during follow-up. We defined STI prevalence as a positive diagnosis of any of the STIs at enrollment. STI incidence was defined as a new positive diagnosis of any of the STIs (except syphilis) during the follow-up period. We estimated prevalence and incidence in an individual (HIV-positive index case or HIV-negative partner), and within a couple (any STI in either HIV-positive index case or HIV-negative partner). We excluded syphilis test results in our estimation of incidence because of the difficulty in differentiating new infections from prevalent or past infections without frequent titers.

The following baseline demographic and sexual behavior factors were considered for assessment as risk factors for prevalent STIs: gender (female and male), age in years (18–25, 26–40, and >40), marital status (married or living with a partner and unmarried), level of education (never attended school, primary school, secondary school, and post-secondary school), circumcision status for men (circumcised and not circumcised), number of sexual acts in the

past week (0, 1–2, 3–4, and >4), and number of condoms used in the past week (0, 1–2, 3–4, and >4).

Statistical analyses

All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC). We summarized baseline demographic and sexual behavior characteristics using medians and interquartile ranges (continuous variables) and frequencies or percentages (categorical variables). STI prevalence and the corresponding 95% confidence interval (CI) were based on the proportion of persons with any STI at enrollment. We estimated STI prevalence for individual infections as well as for all infections (overall prevalence), as defined above. Log-binomial regression was used to identify factors associated with prevalent STIs in both unadjusted and adjusted models. In the multivariable log-binomial regression model, we included only those predictors that yielded a p-value ≤0.20 in univariable analyses.

We also used log-binomial regression models to examine the association between: (1) prevalent STIs and participants' HIV status (HIV-positive index cases vs. HIV-negative partners); (2) prevalent STIs at enrollment among HIV-positive index cases and HIV transmission; (3) prevalent STIs at enrollment among HIV-negative partners and HIV acquisition; and (4) diagnosis of any new STI during study follow-up within couples (any STI in either HIV-positive index case or HIV-negative partner) and HIV acquisition among HIV-negative partners.

Sexually transmitted infection incidence was calculated as the number of new infections per 100 person-years. We used generalized estimating equations (GEEs) with an exchangeable correlation matrix and Poisson distribution with log link function to compare the rate of STI acquisition between HIV-positive index cases and their HIV-negative partners. In the adjusted GEE model, we included predictors that yielded a score statistic with p-value ≤0.20 when included in a model with only participant index status stratified by gender as the main exposure.

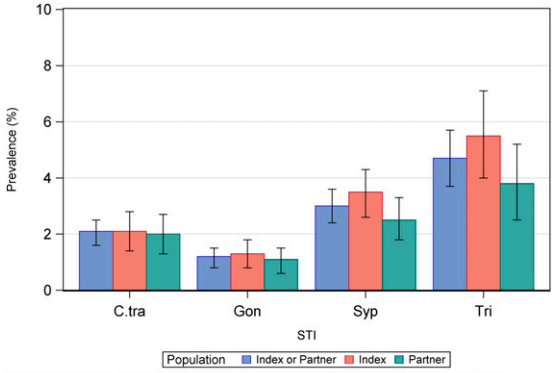
As a priori, we stratified our comparisons of prevalence and incidence between HIV-positive index cases and HIV-negative partners by gender because of the inherent differences in risk of STI acquisition between men and women and potential differences in the clinical presentation that might influence STI diagnosis.[17]

Results

Of the 3526 participants enrolled in the study, 3448 (97.8%) had information on STI test results at baseline. Two hundred and seventy-eight participants were diagnosed with at least one STI at enrollment (266 with 1 STI, 10 with 2 STIs, and 2 with 3 STIs), and the overall STI prevalence was 8.1%; 95% CI: 7.2–9.0. The prevalence was higher in HIV-positive index cases (8.9%) than HIV-negative partners (7.2%), although the results were not statistically significant (PR = 1.24; 95% CI: 0.99–1.55, p = 0.067). A similar trend in prevalence difference between HIV-positive index cases and HIV-negative partners was also observed for each infection (Figure 1).

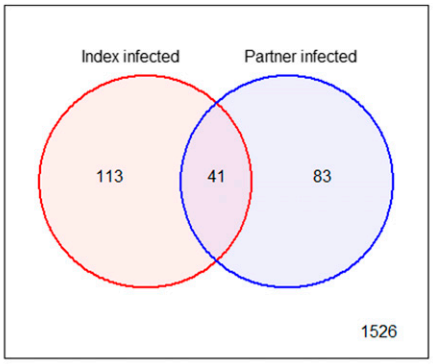
At least one member in 237 couples of the 1763 couples enrolled in the study was diagnosed with an STI at enrollment, couple STI prevalence = 13.4%; 95% CI: 11.8–15.0. Both members in 41 couples of the 237 couples were diagnosed with at least one STI infection (Figure 2). The common STIs diagnosed within couples were *T. pallidum* (5.9% [104/1763]) and *T. vaginalis* (4.7% [77/1640]) (Figure 3).

Among both HIV-positive index cases and HIV-negative partners, the prevalence of STI was higher in unmarried persons than married persons (aPR = 1.92; 95% CI: 1.17–3.14) (Table 1). There was also a significant increase in STI prevalence among women compared to men (aPR = 1.61;



C.tra: Chlamydia trachomatis; Gon: Neisseria gonorrhoeae; Syp: Treponema pallidum; Tri:Trichomonas vaginalis

Figure 1. Sexually transmitted infection prevalence among individuals at enrollment and corresponding 95% confidence limits.



STIs:*Chlamydia trachomatis, Neisseria gonorrhoeae, Treponema pallidum,* or *Trichomonas vaginalis*

Figure 2. Distribution of Sexually transmitted infections among couples at enrollment.

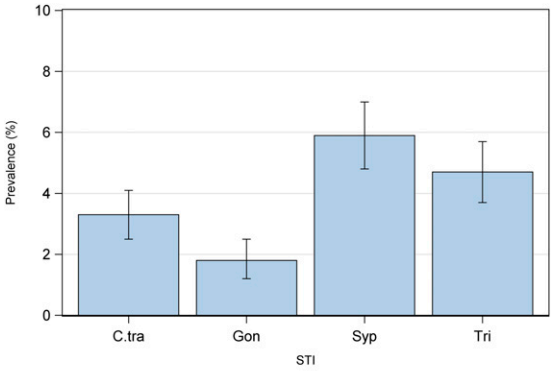


Figure 3. Couple sexually transmitted infection prevalence at enrollment and corresponding 95% confidence limits.

95% CI: 1.20–2.16). Condom use in the past week was indicatively associated with reduced STI prevalence compared to no condom use in the past week; aPR = 0.54; 95% CI: 0.33–0.89 for 1–2 condoms, aPR = 0.49; 95% CI: 0.28–0.84 for 3–4 condoms, and aPR=0.77; 95% CI: 0.42–1.43 for >4 condoms. We did not find a clear trend in the prevalence of STIs with participants' highest level of education.

Sexually transmitted infections prevalence was relatively higher in both HIV-positive female index cases and HIV-negative female partners than their male counterparts, 8.1% vs. 6.4% and 11.9% vs. 6.0%, respectively (Table 2). After adjusting for age, marital status, education, and condom use, sexually transmitted infections prevalence among HIV-positive female index cases was 2.15 times (95% CI: 1.43–3.22) the prevalence among HIV-negative male partners. Compared to HIV-negative male partners, the STI prevalence was slightly higher among HIV-negative female partners (aPR = 1.49; 95% CI: 0.95–2.33) and HIV-positive male index cases (aPR = 1.31; 95% CI: 0.83–2.06).

During the study follow-up, there were 556 new STI diagnoses. The rate of new STI infections was higher in HIV-positive index cases (346 new infections among 1699 HIV-positive index cases over 9532.15 person-years) than HIV-negative partners (210 new infections among 1650 HIV-negative partners over 8166.79 person-years), incidence rate ratio (IRR) = 1.40; 95% CI: 1.16–1.68. When stratified by gender, the STI incidence rate among HIV-positive female index cases was 2.3 times (95% CI: 1.70–2.97) the incidence rate among HIV-negative male partners, adjusted for age and education (Table 3). The rate of acquiring STI was lower among HIV-positive male index cases (adjusted IRR = 0.50; 95% CI: 0.33–0.75) compared to the rate of acquisition among HIV-negative male partners. There was no difference in rates of STI acquisition between HIV-negative female partners and HIV-negative male partners.

At least one member in 382 couples of the 1715 couples was diagnosed with an STI over 9543.25 couple-years of follow-up corresponding to an overall STI incidence of 4.0 infections per 100 couple-years. Both members in 48 couples had at least one STI infection during follow-up (Figure 4). The incidence for each STI within couples ranged from 1.66 infections per 100 couple-years to 2.53 infections per 100 couple-years (Table 4).

Seventy-eight HIV infections were observed among partners during the study follow-up. Nine (11.5%) of the partners who acquired HIV and 115 (6.8%) of the partners who did not acquire HIV were diagnosed with at least one STI at enrollment. Among HIV-positive index cases, 11 (14.1%) of the partners to individuals who acquired HIV and 143 (8.5%) of the partners to individuals who did not acquire HIV were diagnosed with at least one STI during enrollment. Partners who acquired HIV were more likely to have been diagnosed with an STI during enrollment compared to partners who did not acquire HIV; PR = 1.69; 95% CI: 0.89–3.20, though results were not statistically significant. Similarly, HIV-positive index cases to partners who acquired HIV during the study were more likely to have been diagnosed with an STI during enrollment than HIV-positive index cases to partners who did not acquire HIV; PR = 1.65; 95% CI: 0.93–2.91. Of the 78 partners who were diagnosed with HIV, 32 partners (41.0%) were from couples that experienced at least one episode of STI during follow-up. HIV-negative partners among couples that experienced at least one episode of STI during follow-up had 2.4 times (95% CI: 1.56–3.73) the risk of acquiring HIV compared to their counterparts among couples that never experienced an STI during follow-up.

Discussion

STIs were prevalent among HIV serodiscordant couples enrolled in the HPTN 052 study. The prevalence among unmarried participants was almost twice that of participants who were married or living with partner. During study follow-up, new STI diagnoses were common in both HIV-positive index cases and HIV-negative partners. However, the rate of acquiring new STIs was highest in HIV-positive female index cases. The presence of STIs among HIV serodiscordant couples highlights the importance of continued STI screening and counseling among HIV serodiscordant couples and individuals seeking HIV testing services.

In this era of ART, there have been concerns that STI and HIV–STI coinfection could undermine the effect of ART in HIV prevention. ART greatly minimizes the level of viral load in blood, semen, or vaginal fluids resulting in reduced HIV transmission during sexual intercourse.[18,19] In case of HIV–STI coinfection, STI can induce local genital inflammation resulting in increased HIV shedding and subsequent increased infectious.[7–9] When this happens, the effect of ART in reducing HIV/RNA shedding in the genital tract is compromised. However, blood viral suppression

Table 1. Association between demographic and sexual behavior factors and sexually transmitted infection prevalence at enrollment.

	STI			
	Yes (*N*=278), *N* (%)	No (*N*=3170), *N* (%)	Unadjusted PR (95% CI)	Adjusted PR (95% CI)
Demographics				
Gender				
Male	110 (6.2)	1670 (93.8)	1.0	1.0
Female	168 (10.1)	1500 (89.9)	1.63 (1.29–2.05)	1.61 (1.20–2.16)
Age				
18–25	66 (10.8)	547 (89.2)	1.0	1.0
26–40	160 (7.6)	1946 (92.4)	0.71 (0.54–0.93)	0.78 (0.57–1.08)
>40	52 (7.1)	677 (92.9)	0.66 (0.47–0.94)	0.62 (0.39–0.99)
Marital status				
Married/living with partner	253 (7.8)	2999 (92.2)	1.0	1.0
Unmarried	25 (12.8)	171 (87.2)	1.64 (1.12–2.41)	1.92 (1.17–3.14)
Education				
No schooling	30 (8.7)	317 (91.3)	1.0	1.0
Primary school	13 (10.3)	1203 (89.7)	1.19 (0.82–1.73)	1.67 (0.97–2.86)
Secondary school	91 (6.4)	1342 (93.6)	0.73 (0.49–1.09)	1.01 (0.57–1.77)
Post-secondary school	19 (5.8)	308 (94.2)	0.67 (0.39–1.17)	0.78 (0.35–1.74)
Sexual behavior				
Circumcised				
No	92 (6.2)	1396 (93.8)	1.0	—
Yes	12 (5.1)	225 (94.9)	0.82 (0.46–1.47)	—
Total sex acts in the past week				
No sex	3 (37.5)	5 (62.5)	5.02 (2.02–12.47)	—
1–2	125 (7.5)	1547 (92.5)	1.0	—
3–4	39 (6.2)	587 (93.8)	0.83 (0.59–1.18)	—
>4	24 (11.4)	187 (88.6)	1.52 (1.01–2.30)	—
Total condom use in the past week				
No condoms[1]	16 (13.6)	102 (86.4)	1.0	1.0
1–2	118 (7.2)	152 (92.8)	0.53 (0.33–0.87)	0.54 (0.33–0.89)
3–4	38 (6.5)	543 (93.5)	0.48 (0.28–0.84)	0.49 (0.28–0.84)
>4	19 (10.6)	161 (89.4)	0.78 (0.42–1.45)	0.77 (0.42–1.43)

[1]Among male participants.

STI: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Treponema pallidum*, or *Trichomonas vaginalis*. 77 participants missing STI diagnosis at enrollment, sexual behavior details missing for 931 participants.

Note: STI: Sexually transmitted infections.

persists in the presence of an STI infection. Among gay men on ART in Thailand, ART effectively suppressed HIV RNA at months 12 and 24 after initiating ART although the rates of STIs remained high during the study.[20] STIs do not increase infectiousness of HIV-positive index cases, as demonstrated in HPTN 052 and more recently in studies of MSM.[21,22] Given the potency and effectiveness of ART in reducing viral load and preventing HIV transmission, any relative contribution of STIs to HIV acquisition appears difficult to quantify for those on ART.

Our results that new sexually transmitted infections were common among HIV-positive index cases are consistent with findings from other studies, and this can persist in the era of ART albeit, at a slightly lower rate. In South Africa, the rate of treatment-seeking for new STIs was estimated to be 9.57 per 100 person-years in the period prior to initiating ART and 5.5 per 100 person-years in the period once on ART.[23] Among patients who had been on ART for over 4 years and followed up to 3.5 years in Uganda, the incidence of STIs was approximately three per 1000 person-years.[24]

The reduced prevalence of STIs among people who reported using condoms in the past week is not surprising. Condoms have long been known to reduce transmission and acquisition of STIs, including HIV. When used consistently and correctly, condoms can reduce HIV transmission among HIV serodiscordant couples and the risk of acquiring STIs.[25–27] In a mathematical modeling study of trends in HIV incidence in South Africa, a 39% decline in HIV incidence was attributed to condom use.[28]

Most of the STIs we have included in this analysis have distinct etiologies. Therefore, risk factors including age, gender, and education can vary substantially among these

Table 2. Comparison of STI prevalence between HIV-positive index cases and HIV-negative partners.

		STI			
	Gender	Yes, *N* (%)	No, *N* (%)	Unadjusted PR (95% CI)	Adjusted PR[I] (95% CI)
Partner	Male	57 (6.4)	840 (93.6)	1.0	1.0
	Female	67 (8.1)	756 (91.9)	1.28 (0.91–1.80)	1.49 (0.95–2.33)
Index	Male	53 (6.0)	830 (94.0)	0.94 (0.66–1.36)	1.31 (0.83–2.06)
	Female	101 (11.9)	744 (88.1)	1.88 (1.38–2.57)	2.15 (1.43–3.22)

STI: *Chlamydia trachomatis, Neisseria gonorrhoeae, Treponema pallidum,* or *Trichomonas vaginalis.*
Note: STI: Sexually transmitted infections.
[I]Adjusted for age, marital status, education, and condom use.

Table 3. Comparison of STI incidence between HIV-positive index cases and HIV-negative partners.

	Gender	No. of infections	Follow-up time	Incidence rate/100 person-years	Unadjusted IRR (95% CI)	Adjusted IRR[I] (95% CI)
Partner	Male	89	3977.07	2.24	1.0	1.0
	Female	121	4189.72	2.88	1.27 (0.91–1.76)	1.11 (0.79–1.57)
Index	Male	54	4831.17	1.12	0.49 (0.34–0.73)	0.50 (0.33–0.75)
	Female	292	4700.98	6.21	2.69 (2.08–3.49)	2.25 (1.70–2.97)

STI, *Chlamydia trachomatis, Neisseria gonorrhoeae,* or *Trichomonas vaginalis.*
Note: STI: Sexually transmitted infections.
[I]Adjusted for age and education.

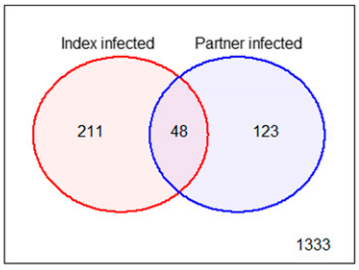


Figure 4. Distribution of sexually transmitted infection incidence among couples during study follow-up.

STIs. However, due to the low prevalence of some infections in this study, we could not look at the prevalence of each infection separately. While our decision to lump several STIs together may be reasonable for examining overall prevalence or incidence, this is less informative for assessing potential risk factors for infections. Bundling all STIs together may have obscured some associations which we would have observed had we looked at each STI separately.

Under this clinical trial setting, several factors may have resulted in either underestimation or overestimation of both STI prevalence and incidence. For example, couples in this study received high degrees of counseling and condom promotion that may have reduced their risk of acquiring STIs, compared to the general population. Herpes simplex virus type 2 (HSV-2) was not evaluated during this study. Herpes simplex virus type 2 is highly prevalent in sub-Saharan Africa, with disproportionally high infections among women aged over 25 years.[29] Since HSV-2 associated genital ulcers are common in Africa,[30,31] HSV-2 is highly associated with increased risk of HIV acquisition.[32,33] We also excluded syphilis in our incidence estimations due to difficulties in differentiating new infections from prevalent or past infections without frequent titers. Much as these three scenarios above may have underestimated our estimates for prevalence or incidence, we do not expect this to be differential to affect our estimates for prevalence ratio and incidence rate ratios. All participants received the same degree of counseling and condom promotion, none received HSV-2 evaluation, and all syphilis results during follow-up were excluded during incidence analyses.

Except for a few infections in participants who presented with symptoms indicative of STI outside the scheduled study visits, most of the infections included in our estimation of STI incidence were diagnosed during scheduled annual visits. Some STIs are asymptomatic, and many persist for less than a year even if untreated. For example, some *Chlamydia trachomatis* infections resolve spontaneously within a year.[34] As a result, the STI incidence we have observed in this study may be an underestimate of the true STI incidence in this population. However, we do not expect this underestimation to be differential between index cases

Table 4. STI incidence among couples during follow-up period.

	Number of couples tested	Number of new infections	Couple follow-up time (years)	Incidence rate/100 person-years
Chlamydia trachomatis	1715	204	9543.25	2.14
Gonorrhea	1715	158	9543.25	1.66
Trichomonas vaginalis	1640	233	9198.80	2.53
STI	1715	556	9543.25	5.83

STI, *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, or *Trichomonas vaginalis*.
Note: STI: Sexually transmitted infections.

and their HIV-negative partners or between men and women.

Our analysis has shown that incident STIs were relatively common in HIV discordant couples despite high degrees of counseling and condom promotion in a clinical trial setting. This finding signals the burden of STIs both in HIV serodiscordant and seroconcordant couples. While ART eliminates the contribution of STIs to HIV transmission,[21,22] they have major adverse health consequences. While the data used for this analysis are more than five years old, in the interim the incidence and prevalence of STIs has increased worldwide.[1,35] It is possible that improvements in prevention and treatment of HIV have increased sexual risk-taking behavior.[36] The results of this study emphasize the degree of difficulty in controlling the spread of STIs, even under conditions of careful measurement and ongoing counseling.

Conclusions

STIs are common among HIV serodiscordant couples. HIV-positive female index cases are more likely to acquire STIs from their HIV-negative partners or other partners. While we are implementing HIV prevention interventions for HIV-negative people, we should also intensify targeted STI prevention interventions, especially among HIV-positive women.

Acknowledgements

We thank the HPTN 052 study team and participants for providing the samples and data used in this study. We also thank the laboratory and clinical staff and counselors at study sites and the staff at the HPTN Laboratory Center for their help with sample management and testing.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The primary author's work on this manuscript was supported through the HPTN Scholars Program, funded by NIAID and NIMH, and NIH Fogarty training grant, D43 TW010060. The HPTN 052 trial also received funding through U01-AI018136. Study drugs used in HPTN 052 were donated by Abbott Laboratories, Boehringer-Ingelheim Pharmaceuticals, Inc., Bristol-Myers Squibb, Gilead Sciences, Inc., GlaxoSmithKline/ViiV Healthcare, and Merck & Co., Inc.

ORCID iDs

Maganizo B. Chagomerana https://orcid.org/0000-0003-4231-4553
Emily Shava https://orcid.org/0000-0001-9288-7881

References

1. Rowley J, Vander Hoorn S, Korenromp E, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. *Bulletin of the World Health Organization*. 2019; 97: 548–62p.
2. Reekie J, Donovan B, Guy R, et al. Risk of Ectopic Pregnancy and Tubal Infertility Following Gonorrhoea and Chlamydia Infections. *Clinical Infectious Diseases*. 2019; 69: 1621–3.
3. Mullick S, Watson-Jones D, Beksinska M, et al. Sexually transmitted infections in pregnancy: prevalence, impact on pregnancy outcomes, and approach to treatment in developing countries. *Sex Transm Infect* 2005; 81: 294–302.
4. Warr AJ, Pintye J, Kinuthia J, et al. Sexually transmitted infections during pregnancy and subsequent risk of stillbirth and infant mortality in Kenya: a prospective study. *Sex Transm Infect* 2019; 95: 60–66.
5. Reekie J, Roberts C, Preen D, et al. Chlamydia trachomatis and the risk of spontaneous preterm birth, babies who are born small for gestational age, and stillbirth: a population-based cohort study. *Lancet Infect Dis* 2018; 18: 452–460.
6. Galvin SR and Cohen MS. The role of sexually transmitted diseases in HIV transmission. *Nat Rev Microbiol* 2004; 2: 33–42.
7. Mayer KH and Venkatesh KK. Interactions of HIV, other sexually transmitted diseases, and genital tract inflammation facilitating local pathogen transmission and acquisition. *Am J Reprod Immunol* 2011; 65: 308–316. New York, NY, 1989.
8. Anderson BL, Wang CC, Delong AK, et al. Genital tract leukocytes and shedding of genital HIV type 1 RNA. *Clin Infect Dis* 2008; 47: 1216–1221.

9. Duffus WA, Mermin J, Bunnell R, et al. Chronic herpes simplex virus type-2 infection and HIV viral load. *Int J STD AIDS* 2005; 16: 733–735.
10. Naidoo S, Wand H, Abbai NS, et al. High prevalence and incidence of sexually transmitted infections among women living in Kwazulu-Natal, South Africa. *AIDS Res Ther* 2014; 11: 31.
11. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365: 493–505.
12. Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med* 2016; 375: 830–839.
13. Aumakhan B, Gaydos CA, Quinn TC, et al. Clinical reactivations of herpes simplex virus type 2 infection and human immunodeficiency virus disease progression markers. *PloS one* 2010; 5: e9973.
14. Aumakhan B, Hardick A, Quinn TC, et al. Genital herpes evaluation by quantitative TaqMan PCR: correlating single detection and quantity of HSV-2 DNA in cervicovaginal lavage fluids with cross-sectional and longitudinal clinical data. *Virol J* 2010; 7: 328.
15. Aumakhan B, Gange SJ, Beyrer C, et al. Quantitative and qualitative correlates of cervicovaginal herpes simplex virus type 2 shedding among HIV-infected women in the Women's Interagency HIV Study. *Int J STD AIDS* 2011; 22: 273–277.
16. Mehta SD, Pradhan AK, Green SJ, et al. Microbial diversity of genital ulcers of HSV-2 seropositive women. *Sci Rep* 2017; 7: 15475.
17. Panchanadeswaran S, Johnson SC, Mayer KH, et al. Gender differences in the prevalence of sexually transmitted infections and genital symptoms in an urban setting in southern India. *Sex Transm Infect* 2006; 82: 491–495.
18. Phillips AN, Staszewski S, Weber R, et al. HIV viral load response to antiretroviral therapy according to the baseline CD4 cell count and viral load. *Jama* 2001; 286: 2560–2567.
19. Graham SM, Holte SE, Peshu NM, et al. Initiation of antiretroviral therapy leads to a rapid decline in cervical and vaginal HIV-1 shedding. *AIDS (London, England)* 2007; 21: 501–507.
20. Phanuphak N, Pattanachaiwit S, Pankam T, et al. Sexually transmitted infections and HIV RNA levels in blood and anogenital compartments among Thai men who have sex with men before and after antiretroviral therapy: implication for Treatment as Prevention programme. *J Int AIDS Soc* 2018; 21: e25186.
21. Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *Jama* 2016; 316: 171–181.
22. Rodger AJ, Cambiano V, Bruun T, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. *Lancet* 2019; 393: 2428–2438.
23. Lurie MN, Kirwa K, Daniels J, et al. High burden of STIs among HIV-infected adults prior to initiation of ART in South Africa: a retrospective cohort study. *Sex Transm Infect* 2014; 90: 615–619.
24. Okoboi S, Castelnuovo B, Moore DM, et al. Incidence rate of sexually transmitted infections among HIV infected patients on long-term ART in an urban and a rural clinic in Uganda. *BMC public health* 2019; 19: 87.
25. Hanenberg RS, Rojanapithayakorn W, Kunasol P, et al. Impact of Thailand's HIV-control programme as indicated by the decline of sexually transmitted diseases. *Lancet* 1994; 344: 243–245.
26. Ghys PD, Diallo MO, Ettiègne-Traoré V, et al. Increase in condom use and decline in HIV and sexually transmitted diseases among female sex workers in Abidjan, Côte d'Ivoire, 1991-1998. *Aids* 2002; 16: 251–258.
27. Levine WC, Revollo R, Kaune V, et al. Decline in sexually transmitted disease prevalence in female Bolivian sex workers. *Aids* 1998; 12: 1899–1906.
28. Johnson LF, Hallett TB, Rehle TM, et al. The effect of changes in condom usage and antiretroviral treatment coverage on human immunodeficiency virus incidence in South Africa: a model-based analysis. *J R Soc Interf* 2012; 9: 1544.
29. Smith JS and Robinson NJ. Age-specific prevalence of infection with herpes simplex virus types 2 and 1: a global review. *J Infect Dis* 2002; 186(Suppl 1): S3–S28.
30. O'Farrell N. Increasing prevalence of genital herpes in developing countries: implications for heterosexual HIV transmission and STI control programmes. *Sex Transm Infect* 1999; 75: 377–384.
31. Phipps W, Nakku-Joloba E, Krantz EM, et al. Genital herpes simplex virus type 2 shedding among adults with and without HIV infection in Uganda. *J Infect Dis* 2016; 213: 439–447.
32. Weiss HA, Buvé A, Robinson NJ, et al. The epidemiology of HSV-2 infection and its association with HIV infection in four urban African populations. *Aids* 2001; 15(Suppl 4): S97–S108.
33. Wald A and Link K. Risk of human immunodeficiency virus infection in herpes simplex virus type 2-seropositive persons: a meta-analysis. *J Infect Dis* 2002; 185: 45–52.
34. Geisler WM, Lensing SY, Press CG, et al. Spontaneous resolution of genital Chlamydia trachomatis infection in women and protection from reinfection. *J Infect Dis* 2013; 207: 1850–1856.
35. WHO-International Agency for Research on Cancer. *Cancer Today: Population Fact Sheets*. https://gco.iarc.fr/today/fact-sheets-populations accessed April 20, 2021.
36. Traeger MW, Cornelisse VJ, Asselin J, et al. Association of HIV preexposure prophylaxis with incidence of sexually transmitted infections among individuals at high risk of HIV infection. *Jama* 2019; 321: 1380–1390.