Published in final edited form as:
Sex Transm Infect. 2014 December ; 90(8): 615–619. doi:10.1136/sextrans-2013-051446.

High Burden of STIs among HIV-Infected Adults Prior to Initiation of ART in South Africa: A Retrospective Cohort Study

Mark N. LURIE, PhD[1], **Kipruto KIRWA**[1,2], **Johann DANIELS**[3], **Marcel BERTELER**[3], **Seth C KALICHMAN**[4], and **Catherine MATHEWS**[5]

Mark N. LURIE: Mark_Lurie@Brown.edu

[1]Assistant Professor of Epidemiology, Brown University School of Public Health, Providence, RI USA, (401) 863-7593

[2]Department of Epidemiology and Nutrition, Moi University School of Public Health, Eldoret, Kenya

[3]Health Information and Technology, City Health, City of Cape Town, South Africa

[4]Department of Psychology, University of Connecticut, Storrs CT, USA

[5]Health Systems Research Unit, South African Medical Research Council; and the School of Public Health and Family Medicine, University of Cape Town, South Africa

Abstract

Objectives—To assess the burden of STIs among HIV-positive South Africans in the period prior to ART initiation compared to the period once on ART.

Methods—We linked the clinic records of 1,465 patients currently on ART to the electronic database which records all visits to City clinics. We used a mixed effects Poisson model to assess the relative rates of occurrence of treatment seeking for an STI in the periods prior to initiation of ART and while on ART.

Results—We accumulated 4,214 person-years of follow-up, divided nearly equally between the pre-ART and on ART periods. The rate of treatment seeking for new STIs was 5.50 (95% CI 5.43–5.78) per 100 person-years, and individuals had on average a seven-fold higher rate of seeking treatment for STIs in the period prior to initiating ART (9.57 per 100 person-years) compared to the period once on ART (5.5 per 100 person-years) (adjusted rate ratio [RR] 7.01, 95% CI 4.64–10.59). Being male (RR 1.73, 95% CI 1.18–2.55) or younger (<age 25) (RR 2.67, 95% CI 1.53–4.65) was associated with higher incidence of clinic visits for STI treatment, while

Contribution Statement
The paper was conceived by ML, SK, and CM. ML supervised the data extraction, analysis and manuscript write-up. KK took the lead in data analysis, performed under the supervision of ML. SK, CM, MB and JD all read and provided detail comments on data analysis and draft versions of the manuscript.

Conflicts of Interest
We declare that we have no conflicts of interest.

advanced stage of HIV disease (WHO stage 4) (RR 0.33, 95% CI 0.15–0.69) was associated with lower incidence.

Conclusions—The period prior to the initiation of ART is a critical period where increased attention should be focused on the detection and treatment of STIs. A successful effort to treat STIs in this period will likely reduce further HIV transmission and fits within a test-and-treat approach.

Keywords

Antiretroviral therapy; STI; health care; prevention of sexual transmission; Africa

INTRODUCTION

Sexually transmitted infections (STI) have long been known to enhance the probability of HIV transmission. While antiretroviral therapy (ART) clearly reduces HIV RNA replication, local genital tract inflammation, particularly inflammation caused by STIs, increases both HIV shedding and sexual infectiousness [1]. Furthermore, there is evidence that HIV immunosuppression increases susceptibility to other STIs [2,3]. As a result, HIV-STI co-infections significantly diminish the preventive effects of ART [4]. Genital ulcers, for example, increase male-to-female HIV transmission between 10 and 50-fold [5]. Each incident STI spikes viral shedding in the genital tract, recreating magnitudes of infectiousness that are otherwise only seen in acute infection [6].

There is limited data on the prevalence or incidence of STIs among adults living with HIV/AIDS. A systematic review found only 2 African studies of STIs among people already infected with HIV and one of them was among pregnant women [7,8,9]. Thus the majority of studies examining STI co-infections among people already infected with HIV were in Western Europe and North America, where prevalence, incidence and risk factors for STIs may differ in important ways from that of sub-Saharan Africa. Nevertheless, the review found that the overall mean point prevalence of confirmed STIs was approximately16% among people living with HIV/AIDS; the most common STIs were syphilis, gonorrhoea, chlamydia and trichamoniasis. STI prevalence was greatest at the time of HIV diagnosis, and the prevalence of STIs among people receiving ART (16.2%, SD 23.7) was not appreciably different compared to HIV-infected persons not yet on ART (16.5% SD 13.3; p=0.09). A more recent meta-analysis of 55 studies on the effect of ART on sexual risk behaviors and STIs found that sexual risk taking was lower among those receiving ART compared with those not on ART (OR=0.7; 95% CI=0.62–0.81) and that incidence of STIs was also lower among those on ART (OR=0.38; 95%CI=0.33–1.01) [10].

Establishing the burden of STIs among people already infected with HIV is important both at the individual and population-levels. For HIV-positive individuals, co-infection with syphilis can reduce CD4+ counts and increase plasma HIV RNA (viral load) [11] while co-infection with genital ulcer disease (particularly HSV-2) also increases plasma and genital tract viral load [12]. Furthermore, STIs increase sexual infectiousness and serve as a definitive marker of unprotected sexual transmission risk behaviors [13].

It has now been firmly established that ART for the treatment of HIV/AIDS has the potential to reduce HIV infectiousness and prevent HIV transmission [14–17]. The clinical studies that examined the role of ART in HIV transmission were carefully conducted trials in which participants were regularly screened and treated for other STIs. Because STIs in these studies were controlled, their impact on further HIV transmission was minimized. However, outside of clinical research, the majority of people infected with HIV do not receive comprehensive routine STI screening, suggesting that the reality of using HIV treatment as prevention may not reach its potential. Furthermore, mathematical models that have examined the population-level impact of expanding ART access as a prevention strategy largely ignore the role of other STIs. Failing to include population or individual-level estimates of the prevalence and incidence of STIs likely inflates the expected impact of ART as prevention [17–18].

In the current study, we examined, among a cohort of HIV-infected adults, the incidence of seeking treatment for STIs at all clinics in the City of Cape Town, South Africa. We collected data on STI treatment sought by the same people both prior to and since initiating ART, allowing us to compare the incidence of seeking treatment for STIs in the period prior to ART initiation versus the period while on ART.

METHODS AND MATERIALS

Study design and participants

We used data from the Patient Record and Health Management Information System (PREHMIS), an electronic medical records system maintained by the City of Cape Town's Department of Health (hereafter City Health) that captures all visits to all 78 City of Cape Town medical clinics to measure the incidence rate of treatment-seeking for sexually transmitted infections in the period prior to initiation of ART and the period while on ART among adults currently receiving ART at one Cape Town clinic. Patients were selected if they were 14 years or older at the time of enrolment at the HIV clinic, had confirmed HIV-positive status at entry and started ART during follow-up.

To obtain the study sample, we abstracted data from the paper records of the 1,465 patients currently on ART at one Cape Town clinic. Patients had been enrolled into care in 2009, 2010 and 2011. From these clinic records, we obtained data on dates of birth, enrolment to and discontinuation from the HIV care and treatment program, and death or loss-to-follow-up. Next, City Health extracted available clinical data on the selected patients from PREHMIS. Each time a patient visits a City clinic, a series of barcodes are scanned to indicate a diagnosis and the services that were delivered on that visit. The data were stripped of all identifying information before being shared with the study team. Because some people may seek STI services from clinics other than where they receive their HIV treatment, data from any one clinic would be incomplete. However, the City's centralized medical record system overcomes this problem because it captures all visits to all City clinics, identifying each patient with a unique number that is bar-coded and is consistent across clinics. This enables us to quantify all STI diagnoses associated with members of the study sample including those diagnoses made in other clinics in the City of Cape Town.

City Health follows the WHO guidelines for treating STI syndromically [19] and therefore does not confirm STI diagnoses with laboratory testing; furthermore, PREHMIS codes do not distinguish between different syndromes, instead grouping all STI symptoms into one broad category. As a result, we are unable to report or measure the prevalence of any specific STI, syndrome or reproductive tract infection.

Measures

Outcome variable—We assessed the incidence of seeking care for a STI among HIV-positive patients on ART and compared the incidence in the period prior to ART to the incidence once on ART. We included all new diagnoses of STI from participants' clinical histories recorded at each clinic visit and contained in PREHMIS.

Covariates—Data on participants' gender and age at enrolment to the ART clinic as well as CD4+ cell count, WHO stage of HIV disease and tuberculosis (TB) diagnosis at the start of ART were collected. WHO stage was determined using standard clinical criteria and TB diagnosis was made through combined radiological, clinical and bacteriological examination for acid-fast bacilli.

Statistical analysis

The goal of the analysis was to compare the incidence density of treatment seeking for STIs among HIV infected individuals in the periods before and during ART. We used a mixed effects Poisson model to assess the relative rates of occurrence of treatment seeking for an STI among HIV infected individuals in the periods prior to initiation of ART and while on ART. This modeling framework was chosen because the outcome was a count variable, to account for correlation due to clustering of incident STI treatment seeking on individuals, and to quantify random variation among participants with regard to incidence STI treatment seeking. We categorized age into 3 groups of <25, 25–34 and ≥ 35 years old and dichotomized CD4+ cell count into <200 cells per milliliter and ≥ 200 cells per milliliter. For the analysis, we combined participants in WHO stages 1 and 2 into one group to augment sample size and thus improve precision. Analysis was performed in Revolution R Enterprise version 6.2. A two-sided *P*-value of 0.05 was considered statistically significant.

Sensitivity analysis—We examined whether modeling age and CD4+ cell count as continuous variables would materially alter the findings. We also checked whether the association between seeking treatment for incident STI and treatment period differed by gender, age and CD4+ cell count. Additionally, we performed a sub-analysis that excluded infections reported on the day of study entry to assess the possibility of bias associated with visits for prevalent rather than incident infection. Finally, we analysed a subgroup of participants who contributed similar pre- and on-ART person time (each with less than a 1 year difference in amount of pre- and on-ART follow-up) to enhance comparability and check the potential impact of differential distribution of individual follow-up time.

RESULTS

We collected data on 1,465 participants for a total follow-up time of 4,214 person-years, distributed nearly equally between the pre-ART and the on-treatment periods [Table 1]. Women made up 65% of the sample and contributed 70% of the person-time of follow-up. The mean age at entry was 32.9 (SD = 8.5); men were on average 5 years older than women (36.2 years versus 31.1 years).

We observed a total of 232 events of individuals reporting to City of Cape Town health clinics for the treatment of STIs. Of those, 203 (87.5%) were observed in the period prior to ART initiation with the remaining 12.5% occurring during ART treatment; 67% (155/232) of those events were among women. Among men, 85.7% of incident STI treatment events were in the period prior to ART initiation while among women 88.4% of the events occurred during the pre-ART period.

Table 2 presents incidence rates and incidence rate ratios for STI treatment seeking in the periods prior to and during ART treatment. Individuals were approximately 6.9 times more likely to seek care for an STI in the period prior to ART initiation compared to the period on treatment. While the crude incidence rates were higher in men than women (6.1 versus 5.2 per 100 person-years), the ratio of infections occurring in the 2 time periods was roughly the same, with men being 7.6 times more likely to seek treatment for an STI prior to initiation of ART and women being 6.8 times more likely to seek treatment prior to initiation of ART, compared to the period once on ART.

Table 3 presents multivariable analysis of factors associated with seeking care for STIs. Individuals had on average a seven-fold higher rate of seeking treatment for STIs in the period prior to initiating ART compared to the period when they were on ART when controlling for gender, age at study entry, CD4+ cell count, WHO stage of disease and the presence of TB at ART start; all while allowing for random variation with regard to STI treatment seeking at the level of each individual.

In addition, males had approximately 70% higher rate of STI treatment seeking compared to females; rates of STI treatment seeking decreased with increasing age; and those with a higher CD4+ cell count had a higher rate, albeit statistically non-significant. Incidence rates for those with a WHO stage 3 of disease and below at ART start were statistically similar, but those with stage 4 disease at ART start had much lower rates; while those with TB at ART start also had lower, but non-statistically significant rates.

Among the 1,465 participants, 1,292 (88.2%) did not seek care for an STI during the follow-up period. Among the rest, 131 had 1 STI episode, 32 had 2 episodes, 6 people had 3 episodes and 4 people had 4 or more episodes.

Among the 131 participants with a single STI infection during follow-up, 37 (28%) of the infections were reported at the entry visit. Among the 101 infections in the 42 participants who had more than 1 infection during follow up, 17 (16%) occurred on the first visit date/ entry. The majority of infections among both groups therefore did not occur at intake but rather during the follow-up period.

To further assess the possibility of bias, we performed a sensitivity analysis that excluded infections recorded at the day of a participant's entry to the study. The results were similar to those of the main analysis (Table 1 in Web Appendix). We also checked whether participants may have been spending a short amount of time in the pre-ART phase and then initiating ART. The distribution of times between a clinic visit for an STI and ART initiation indicated that only 6.9% and 28.1% of visits occurred within 1 and 6 months before ART initiation, respectively. The median time between pre-ART clinic visits and ART initiation was 485 days (Figure 1 in Web Appendix). Finally, we conducted an additional analysis using a subgroup of participants that contributed similar amounts of pre- and on-ART person time (a difference of less than 1 year between an individual's pre- and on-ART person time), and obtained estimates similar to the main findings (Table 2 in Web Appendix).

The full model allowing for heterogeneity in patient-specific rates of treatment seeking for incident STI (random intercepts on patients) as well as heterogeneity in incidence rates per patient per treatment period (random coefficients on treatment period) did not provide a better statistical fit when compared to the parsimonious model that only accounted for patient-specific variation regardless of treatment group ($P = 0.175$). This suggests that the large decrease in incidence rates that we observed during the on-ART period occurred systematically across participants. Interactions between treatment period and CD4+ cell count, age and gender were not statistically significant (*P*-values from likelihood ratio tests 0.466, 0.092 and 0.889, respectively), indicating that the rates of treatment seeking for incident STIs did not vary differentially by treatment period according to gender, age at enrolment to the clinic, and CD4+ cell count ART start. In addition, sensitivity testing showed that modelling age and CD4+ cell count as linear continuous variables did not materially alter the findings.

DISCUSSION

To our knowledge, this study is the first to systematically examine treatment for STIs among those already infected with HIV in the periods prior to and since ART initiation. We found that, controlling for other potential confounders, those on ART were approximately 7 times more likely to seek treatment for an STI in the period prior to ART initiation compared to the period once on ART. Furthermore, the timing of infections indicate that only about a quarter of them occurred at the time of HIV diagnosis, while the majority occurred thereafter, indicating the strong possibility that these were incident infections that were not present at the time of enrolment into the system.

We found that men were significantly more likely to have STI clinic visits than women. One possible explanation for this gender difference may be that women are more likely to receive care in community or Provincial clinics that were not captured in our data. The difference is more likely due to high rates of asymptomatic STIs among women [20] resulting in a higher prevalence of clinic visits among men. We also found that younger patients were more likely to have STI, a finding that is consistent with the broader pattern of STI outside of people living with HIV [21]. These associations between demographic characteristics and STI visits may help inform targeted prevention for HIV positive patients receiving clinical care.

The high rates of STIs in the period prior to ART initiation raises several important issues. First, additional attention should be devoted to the screening and treatment of STIs during earlier periods of care prior to initiating ART. The failure to detect and treat STIs increases the likelihood of further HIV and STI transmission to uninfected partners [22]. The high rates of STIs in the period prior to ART initiation may undermine the projected efficacy of universal treatment as a prevention strategy, primarily because of the increased infectiousness of people with HIV/STI co-infections. The significant impact of early ART on HIV transmission in HPTN 052 occurred in the context of routine STI screening, diagnostic testing, and treatment [14]. HIV treatment as prevention in this and similar settings will be further bolstered if it includes aggressive STI testing and treatment as the standard of care.

This study has several limitations. Because of the structure of the available data, we were not able to verify STI diagnoses with appropriate laboratory analysis and were forced to group all STIs into one broad category. In addition, since we did not interview individuals in the study, we do not have any behavioural data; thus we cannot say whether the different rates of STIs we observed in the two periods were a result of changes in sexual risk behaviors, of ART itself, or of a combination of the two.

It is also likely that the rates of STI treatment seeking that we observed underestimate the true rate of STIs in this population. This is likely the case because 1) many STIs are asymptomatic and people who are asymptomatic are unlikely to seek treatment; 2) people who sought care from private treatment providers, clinics managed by the Provincial Department of Health or clinics outside of Cape Town would not be counted in our analysis since PREHMIS includes only City of Cape Town clinics; and 3) we included only people in clinical care who were on ART. Those who never initiated ART are not in our sample, and are likely to have had a higher burden of STIs compared to those who successfully initiated treatment. Furthermore, the use of ID numbers to link patients to the electronic database may have resulted in some undercounting of cases. For these reasons we believe that our estimate of the burden of disease in this population is indeed a conservative one.

The high rates of STIs that we observed among people already infected with HIV during the period prior to ART initiation represents an important opportunity for prevention and suggests a more comprehensive approach to HIV transmission is needed beyond ART. Systematically including STI detection and treatment in the standard of care for people living with HIV will likely result in both a reduction in further transmission and increased viral suppression once people are on ART. Sustained risk reduction counselling that includes STI diagnosis and treatment, assistance with partner notification, HIV status disclosure decision-making, and condom use is essential at all stages of HIV infection, perhaps most urgently prior to initiating ART.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We would also like to thank Carolyn Crisp for analysis of a similar, smaller dataset.

This work was funded in part by NIH grants to ML (Grant numbers 1R01MH083539, 1R24HD077976) and SK (Grant number R01HD074560).

References

1. Anderson BL, Wang CC, Delong AK, et al. Genital tract leukocytes and shedding of genital HIV type 1 RNA. Clinical Infectious Diseases. 2008; 47(9):1216–21. [PubMed: 18808359]
2. Johnson LF, Lewis DA. The effect of genital tract infections on HIV-1 shedding in the genital tract: a systematic review and meta-analysis. Sexually Transmitted Diseases. 2008; 35(11):946–59. [PubMed: 18685546]
3. Mclelland RS, Lavreys L, Katingima C, Overbaugh J, Chohan V, Mandaliya K, Ndinya-Achola J, Baeten JM. Contribution of HIV-1 infection to acquisition of sexually transmitted disease: a 10-year prospective study. Journal of Infectious Diseases. 2005; 191(3):333–338. [PubMed: 15633091]
4. Msuya SE, Uriyo J, Hussain A, Mbizvo EM, Jeansson S, Sam NE, Stray-Pedersen B. Prevalence of sexually transmitted infections among pregnant women with known HIV status in northern Tanzania. Reproductive Health. 2009; 6(4):1–8. [PubMed: 19126239]
5. Baeten JM, Overbaugh J. Measuring the infectiousness of persons with HIV-1: opportunities for preventing sexual HIV-1 transmission. Current HIV Research. 2003; 1(1):69–86. [PubMed: 15043213]
6. Mayer KH, Venkatesh KK. Antiretroviral therapy as HIV prevention: status and prospects. American Journal of Public Health. 2010; 100(10):1867–76. [PubMed: 20724682]
7. Kalichman SC, Pellowski J, Turner C. Prevalence of sexually transmitted co-infections in people living with HIV/AIDS: systematic review with implications for using HIV treatments for prevention. Sexually Transmitted Infections. 2011; 87:183–190. [PubMed: 21330572]
8. Machekano RN, Bassett MT, Zhou PS, et al. Report of sexually transmitted diseases by HIV infected men during follow up: time to target the HIV infected? Sexually Transmitted Infections. 2000; 76:188–192. [PubMed: 10961196]
9. Aboud S, Msamanga G, Read JS, et al. Genital tract infections among HIV-infected pregnant women in Malawi, Tanzania and Zambia. International Journal of Sexually Transmitted Diseases and AIDS. 2008; 19:824–832.
10. Doyle, JS.; Degenhardt, L.; Pedrana, A., et al. Effects of HIV antiretroviral therapy on sexual and injecting risk-taking behaviour: a meta-analytical review. Poster presented at the 7th IAS Conference on HIV Pathogenesis, Treatment and Prevention; Kuala Lumpur, Malaysia. 30 June – 3July 2013; WEPDB0105
11. Buchacz K, Patel P, Taylor M, et al. Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis. AIDS. 2004; 18(15):2075–2079. [PubMed: 15577629]
12. Duffus WA, Mermin J, Bunnell R, et al. Chronic herpes simplex virus type-2 infection and HIV viral load. International Journal of STDs and AIDS. 2005; 16(11):733–735.
13. Cohen MS, Pilcher CD. Amplified HIV transmission and new approaches to HIV prevention. Journal of Infectious Diseases. 2005; 191:1391–1393. [PubMed: 15809893]
14. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. New England Journal of Medicine. 2011; 365(6):493–505. [PubMed: 21767103]
15. Vernazza PL, Troiani L, Flepp MJ, et al. Potent antiretroviral treatment of HIV infection results in suppression of seminal shedding of HIV. AIDS. 2000; 14(2):117–121. [PubMed: 10708281]
16. Donnell D, Baeten JM, Kiarie J, et al. Heterosexual HIV transmission after initiation of antiretroviral therapy: a prospective cohort study. Lancet. 2010; 375(9731):2092–2098. [PubMed: 20537376]

17. Granich RM, Gilks CF, Dye C, et al. Universal voluntary testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet. 2009; 373(9657):45–57.

18. Hontelez JAC, de Vlas SJ, Tanser F, et al. The impact of the new WHO antiretroviral treatment guidelines on HIV epidemic dynamics and cost in South Africa. PloS One. 2011; 6(7):e21919. [PubMed: 21799755]

19. Department of Health, South Africa. First line comprehensive management and control of sexually transmitted infection according to the Essential Drug List. Pretoria: National Department of Health; 2008. p. 1-18.

20. Lewis DA, Chirwa TF, Smimang VM, et al. Urethritis/cervicitis pathogen prevalence and associated risk factors among asymptomatic HIV-infected patients in South Africa. Sexually Transmitted Diseases. 2012; 39(7):531–536. [PubMed: 22706215]

21. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sexually Transmitted Infections. 1999; 75(1):3–17. [PubMed: 10448335]

22. Cohen M. Classical Sexually Transmitted Diseases Drive the Spread of HIV-1: Back to the future. Journal of Infectious Diseases, 2012. 2012; 206:1–2.

Key Messages

- Little is know about the rate of sexually transmitted infections among HIV-infected people in Africa, yet STIs likely exacerbate risk of further HIV transmission;
- HIV-infected people were 7 times more likely to seek treatment for sexually transmitted infections before ART initiation compared to the period on ART;
- Where HIV and STI prevalence is high, testing and treatment for other STIs may further bolster test-and-treat strategies for HIV prevention.

Table 1

Number of STI episodes and amount of person-time of follow-up among HIV patients in a clinic in Cape Town, South Africa.

Characteristic (N=1,465)	Overall	Pre-ART	On-ART
STI episodes/events	232	203	29
Gender			
Male (*n*=516)	77	66	11
Female (*n*=949)	155	137	18
Age at study entry (years)			
<25 (*n*=252)	66	57	9
25 – 34 (*n*=715)	131	115	16
≥35 (*n*=498)	35	31	4
Person time (years)	4214	2121	2093
Gender			
Male	1253	551	702
Female	2961	1569	1392
Age at study entry (years)			
<25	879	540	339
25 – 34	2129	1058	1071
≥35	1206	523	683

STI, Sexually Transmitted Infection; ART, Anti-retroviral Therapy

Table 2

Unadjusted STI incidence rates and incidence rate ratios comparing pre- and on-ART periods among HIV patients in South Africa.

Characteristic	Crude incidence rates (95% CL) per 100 person-years of observation			Incidence rate ratio (95% CL) (Pre/On-ART)
	Overall	Pre-ART	On-ART	
Overall	5.50 (5.43, 5.58)	9.57 (9.44, 9.70)	1.29 (1.24, 1.34)	6.91 (4.68, 10.19)
Gender				
Male	6.15 (6.00, 6.29)	11.97 (11.68, 12.27)	1.57 (1.48, 1.66)	7.63 (4.03, 14.45)
Female	5.23 (5.15, 5.32)	8.73 (8.58, 8.88)	1.29 (1.23, 1.36)	6.75 (4.13, 11.03)
Age at study entry (years)				
<25	7.51 (7.33, 7.69)	10.55 (10.28, 10.83)	2.66 (2.48, 2.84)	3.97 (1.97, 8.03)
25 – 34	6.15 (6.04, 6.26)	10.87 (10.67, 11.08)	1.49 (1.42, 1.57)	7.28 (4.32, 12.28)
≥35	2.90 (2.81, 3.00)	5.92 (5.72, 6.14)	0.59 (0.53, 0.65)	10.12 (3.57, 28.67)
CD4 count at ART start				
<200	4.51 (4.42, 4.59)	8.80 (8.62, 8.97)	1.30 (1.24, 1.36)	6.76 (4.18, 10.92)
≥200	7.26 (7.12, 7.40)	10.49 (10.28, 10.70)	1.62 (1.51, 1.73)	6.48 (3.28, 12.81)
WHO stage at ART start				
Stages 1 and 2	6.18 (6.10, 6.27)	10.55 (10.39, 10.71)	1.51 (1.45, 1.57)	6.98 (4.63, 10.50)
Stages 3 and 4	1.83 (1.73, 1.94)	3.19 (2.98, 3.41)	0.80 (0.71, 0.90)	3.98 (1.08, 14.71)
Pregnant at ART start[a]				
Yes	4.69 (4.48, 4.91)	8.60 (8.20, 9.03)	0.96 (0.84, 1.11)	8.92 (2.06, 38.62)
No	5.32 (5.23,5.41)	8.75 (8.59, 8.92)	1.35 (1.28, 1.42)	6.48 (3.84, 10.91)
TB at ART start				
Yes	3.29 (3.17, 3.40)	4.80 (4.60, 5.00)	1.86 (1.74, 1.98)	2.58 (1.19, 5.61)
No	6.14 (6.06, 6.23)	10.89 (10.72, 11.05)	1.24 (1.19, 1.30)	8.76 (5.52, 13.90)

CL, Confidence Limits; ART, Anti-retroviral Therapy;

[a]Only among women

Table 3

Adjusted rate ratios and 95% confidence limits of STI incidence among 1,465 HIV-infected participants in South Africa.

Characteristic	*n*	Rate ratio[a] (95% CL)	*P* value
ART			
On ART	1,465	1 (Ref)	
Before ART	1,465	7.01 (4.64, 10.59)	<0.001
Gender			
Female	949	1 (Ref)	
Male	516	1.73 (1.18, 2.55)	0.005
Age at study entry (years)			
≥35	498	1 (Ref)	
25 – 34	715	2.46 (1.52, 3.97)	<0.001
<25	252	2.67 (1.53, 4.65)	0.001
CD4 count at ART start			
<200	991	1 (Ref)	
≥200	474	1.28 (0.90, 1.82)	0.168
WHO stage at ART start			
Stages 1 and 2	401	1 (Ref)	
Stage 3	812	0.92 (0.63, 1.35)	0.681
Stage 4	252	0.33 (0.15, 0.69)	0.003
TB at ART start			
No	1,083	1 (Ref)	
Yes	382	0.76 (0.46, 1.26)	0.289

[a] Adjustment made for ART status, age, gender, and CD4+ cell count, WHO stage of disease, and therapy for TB at the start of ART.

STI, Sexually Transmitted Infections; CL, Confidence Limits; ART, Anti-retroviral Therapy; TB, Tuberculosis.