Incidence and predictors of sexually transmitted infections among adult HIV-positive patients receiving antiretroviral therapy at Themba Lethu HIV clinic in Johannesburg, South Africa

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Background. Sexually transmitted infections (STIs) among people living with HIV/AIDS can facilitate the spread of HIV.
Objectives. To estimate STI incidence and identify predictors of STI acquisition among HIV-positive patients during their first 24 months of antiretroviral therapy (ART) in Johannesburg, South Africa.
Methods. We conducted a cohort study using prospectively collected routine data on patients who initiated ART between January 2004 and January 2015 at the Themba Lethu HIV clinic in Johannesburg. Kaplan-Meier analysis was used to estimate STI incidence rates (based on evidence of laboratory diagnosis and STI syndromic treatment prescription records). STI predictors were identified using Cox regression analysis.
Results. Among 26 762 adult patients on ART, there were 1 906 (7.1%) cases of STI (incidence 4.8/100 person-years; 95% confidence interval (CI) 4.7 - 5.1). Non-pregnant women were 60% more likely than men to be diagnosed with an STI (adjusted hazard ratio (aHR) 1.6; 95% CI 1.4 - 1.8). The risk of STI decreased with increasing baseline CD4 count (aHR 0.8, 0.5 and 0.4 for CD4 counts 101 - 200, 201 - 350 and >350 cells/μL, respectively, compared with CD4 count <100 cells/μL). Patients with advanced baseline World Health Organization (WHO) clinical stages had a higher risk (aHR 1.6 for WHO stage 4; 95% CI 1.3 - 1.9) compared with those with WHO stage 1. However, there was a 20% increase in the risk of STI among obese patients compared with underweight patients (aHR 1.3; 95% CI 1.0 - 1.7). Over 80% of obese patients diagnosed with an STI had a CD4 count <200 cells/μL.
Conclusions. STIs are common in HIV-infected patients who are receiving ART. While both ART and the syndromic management of STIs are high-impact interventions for controlling the spread of HIV, closer monitoring of STI occurrences is warranted, particularly among immunologically vulnerable patients.

Sexually transmitted infections (STIs) constitute important public health concerns in developing countries, where they account for 17% of illness-related economic losses.[1] In South Africa (SA), a Spectrum model estimation exercise in 2017 reported *Chlamydia trachomatis* (CT) prevalence at 14.7% for men and 6.0% for women, *Neisseria gonorrhoeae* (NG) prevalence at 6.6% for men and 3.5% for women, and active syphilis prevalence at 0.5% for men and 0.97% for women.[2] The 2015 SA antenatal care (ANC) survey reported syphilis prevalence of 2.0% among pregnant women attending public sector facilities, similar to levels observed in 2007 - 2008.[3] In a 2013 study among adults in Johannesburg, 20.4% of all participants self-reported an STI episode (19.9% among HIV-infected participants).[4]

Untreated STIs can lead to long-term sequelae of infection. In adults, such manifestations occur in the reproductive system (genital ulceration, infertility, pelvic inflammatory disease),

neurological system or cardiovascular system, and in infants, blindness or severe neurological disability is common.[5-7] The prevention and early treatment of STIs are particularly crucial for SA because of the country's high HIV burden. SA was estimated to have 7.9 million individuals living with HIV in 2017.[8] Considering the high probability of HIV transmission when either sexual partner has an STI,[9,10] a high STI incidence among individuals living with HIV has considerable implications for containing the spread of HIV in general.

Several studies in developing countries have shown that treating STIs among HIV-infected patients significantly reduces the risk of transmission by reducing levels of HIV in genital secretions.[2,9] In 1995, SA adopted the syndromic approach to STI management, which entails the rapid treatment of STI cases identified by symptom screening rather than specific aetiology.[11] Slight increases in STI prevalence were observed between 1990 and 2005 for NG

(52.5% to 54.4% among women and 30.7% to 31.7% among men), while decreases were noted for trichomoniasis (30.9% to 24.2% among women and 5.9% to 4.0% among men), CT (11.5% to 10.1% among women and 8.7% to 7.1% among men) and syphilis (7.7% to 1.9% among women and 7.4% to 2.2% among men). Genital herpes simplex virus (HSV-2) prevalence appears to have increased slightly over time (52.5% to 54.4% among women and 30.7% to 31.7% among men).[2,9] There is some evidence to suggest that genital ulcers are more likely to occur among HSV-2-infected individuals who are HIV-immunocompromised, and as the HIV epidemic matures, the contribution of HSV-2 to HIV transmission also increases.[12] However, the proportion of new HIV infections in adults that were attributable to curable STIs also declined, from 39% in 1990 to 14% in 2010.[2,9]

Despite its widespread benefits, syndromic STI management limits opportunities for diagnosis of asymptomatic infections and has been associated with poor reporting of STI cases.[11,13] Many of the modelled STI prevalence estimates in SA rely heavily on data from ANC surveys, research studies and clinical trials. There is limited information on STI incidence rates across both HIV-infected and uninfected populations, and even fewer data for HIV-infected individuals who are receiving antiretroviral therapy (ART).[2,14]

Objectives
To estimate the incidence of STIs among HIV-positive adults receiving care at the Themba Lethu HIV clinic in Johannesburg, SA.

Methods
Study population
We conducted a cohort study using prospectively collected data on adult HIV-positive (age ≥18 years) patients accessing standard first-line ART[15] at the Themba Lethu HIV clinic in Johannesburg from January 2004 to January 2015. At the time of data collection, clinical data at Themba Lethu were routinely captured and stored in an electronic patient management system (TherapyEdge-HIV; Devex, USA). SA follows the syndromic approach for managing STIs, where patients are given a combination regimen based on the outcomes of a symptom screen during a medical visit. An STI symptom screen is recommended for all Themba Lethu ART patients every 3 months. Study participants were followed up via medical record review over 24 months after ART initiation to identify incident STIs. Incident STIs were determined from laboratory data, clinical notes and treatment prescription records, as defined in Table 1.[16] As such, patients prescribed regimens consisting of recommended drugs for syndromic STI management on the clinic visits were also identified as incident STI cases in consultation with a prescribing clinician at the HIV clinic.

Demographic variables collected at the time of ART initiation (baseline) include age, gender, highest level of education (categorised as no education, primary school and secondary school), history of smoking (yes/no), history of alcohol use (yes/no) and employment status (employed/unemployed). Baseline clinical data include CD4 count, World Health Organization (WHO) clinical stage and body mass index (BMI). The primary outcome variable was the occurrence of an incident STI over 24 months after first-line ART initiation. Person-time accrued from the date of ART initiation to the first occurrence of an STI or the last time seen at the clinic (for patients who were lost to follow-up or transferred out, or died), or to the end of the observation period (24 months). Data were fully anonymised before statistical analysis. The study was approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (ref. no. M170564).

Statistical analysis
Continuous variables were described using medians and interquartile ranges (IQRs). Categorical variables were described using percentages. Kaplan-Meier analyses were conducted to determine STI incidence rates. Predictors of incident STIs among treated HIV-positive patients were modelled using Cox proportional hazards modelling. As our goal was to identify predictors and not assess causation, variables with a p-value <0.1 in crude analyses were included in a multivariate model. Schoenfeld residuals were used to test the assumption of proportional hazards. Variables were excluded from the model when the inclusion of the interaction term did not resolve the proportional hazards assumption violation, in which case the model was stratified.

Results
Cohort description and baseline characteristics
Table 2 shows the distribution of baseline demographic and clinical characteristics of the 26 762 eligible patients. The overall median (IQR) age of the participants was 36.7 (31.0 - 43.4) years. Overall, 61.4% of participants were female. Female subjects were more likely than males to be ≤30 years old at ART initiation (29.2% v. 15.0%). Overall, 49.0% of the study participants were unemployed and 79.1% had a secondary-school level of education at ART initiation. Furthermore, a higher proportion of males than females reported a baseline history of alcohol consumption (24.8% v. 5.4%) or a history of smoking (18.6% v. 5.7%).

Overall, 6.7% of the study sample had a history of tuberculosis at the time of ART initiation.

STIs in HIV-positive adults on ART
A total of 1 906 (7.1%) STI cases were identified. Of these, 708 were identified using clinical notes with prescribed medicines, and the remaining 1 198 were determined using the prescription information. Table 3 shows the proportions of STIs using the clinical notes with prescribed medication and prescription information (syndromic management). Of the 708 patients, 16.3% had anogenital warts, 13.7% had HSV-2 and only 2% had chancroid. The regimen-based STI cases were mostly prescribed metronidazole + ciprofloxacin (32.8%), metronidazole + ciprofloxacin + doxycycline (27.5%) or metronidazole + doxycycline (19.3%) (Table 4).

The incidence of STIs was 4.9/100 person-years (py) (95% confidence interval (CI) 4.7 - 5.1). Among patients who had an incident STI on ART, 126 (6.6%) had two or more episodes during the period of observation. Only 213 (11.2%) of STI cases had HIV viral load data up to 6 months before or after the STI episode, and 74.2% of these were virally suppressed. The median (IQR) time to the first STI episode was 3.1 (0.7 - 9.9) months from the time of ART initiation.

Table 5 presents predictors of incident STIs among HIV-positive patients on ART. Women who were not pregnant at ART initiation were 60% more likely than men to have an incident STI (adjusted hazard ratio (aHR) 1.6; 95% CI 1.4 - 1.8) (Fig. 1). The risk of STI decreased with increasing age (aHR 0.6 for patients aged 41 - 50 years compared with ≤30 years; 95% CI 0.5 - 0.7). Patients with a low baseline CD4 count (<100 cells/µL) were at increased risk of incident STIs, with the risk decreasing with increasing baseline CD4 count (aHR 0.8, 0.5 and 0.4 for CD4 counts 101 - 200, 201 - 350 and >350 cells/µL, respectively, compared with CD4 count <100 cells/µL).

Table 1. Summary of the syndromic management of STIs in South Africa

	Additional indications	Metronidazole	Ceftriaxone/ciprofloxacin	Azithromycin/doxycycline	Clotrimazole/fluconazole	Benzathine penicillin	Acyclovir
Dosage		Oral, 2 g stat/400 mg 12-hourly for 7 days	IM, 250 mg stat	Oral, 1 g stat	Vaginal pessary 500 mg stat/cream 12-hourly for 7 days	IM, 2.4 MU stat/doxycycline (oral, 100 mg 12-hourly for 14 days) if allergic to penicillin	Oral, 400 mg 8-hourly for 7 days
LAP	Lower abdominal tenderness and UTI and no indication for gynaecological/surgical assessment, if allergic to penicillin then omit ceftriaxone and increase azithromycin dose to 2 g	✓	✓	✓			
VDS	No LAP, if allergic to penicillin then omit ceftriaxone and increase azithromycin dose to 2 g	✓	✓ patient <35 years old	✓ patient <35 years old	✓		
MUS	If allergic to penicillin then omit ceftriaxone and increase azithromycin dose to 2 g	✓ if partner has VDS	✓	✓			
SSW	No indication for surgical assessment		✓	✓			
GUS	Sex within the last 3 months			✓ if no improvement		✓	✓
Syphilis						✓	
BAL					✓	✓	✓
Treatment of more than one STI syndrome							
MUS + SSW	Treat according to SSW flowchart	✓ if partner has VDS	✓	✓			
MUS + BAL	Treat according to MUS flowchart	✓ if partner has VDS	✓	✓	✓		
MUS + GUS			✓	✓			✓
VDS + LAP	Treat according to LAP flowchart and treat for candidiasis, if required	✓	✓	✓			
VDS + GUS	Treat for candidiasis, if required	✓	✓	✓			✓
LAP + GUS		✓	✓				✓
SSW + GUS			✓				✓

STI = sexually transmitted infection; stat = immediately as a single dose; IM = intramuscular; MU = million units; LAP = lower abdominal pain; UTI = urinary tract infection; VDS = vaginal discharge syndrome; MUS = male urethritis syndrome; SSW = scrotal swelling; GUS = genital ulcer syndrome; BAL = balanitis/balanoposthitis.

Table 2. Demographic characteristics of patients on ART in a public hospital in Johannesburg, South Africa, by sex and pregnancy status at ART start (among females)

	Female, pregnant at ART start (*N*=280), *n* (%)	Female, not pregnant at ART start (*N*=16 150), *n* (%)	Male (*N*=10 332), *n* (%)	Total (*N*=26 762), *n* (%)
Age (years) at ART start				
≤30	148 (52.9)	4 649 (28.8)	1 550 (15.0)	6 347 (23.7)
31 - 40	130 (46.4)	6 652 (29.3)	4 844 (46.9)	11 629 (43.4)
41 - 50	1 (0.4)	3 489 (39.4)	2 790 (27.0)	6 280 (23.5)
≥51	1 (0.4)	4 409 (27.1)	1 148 (11.1)	2 509 (9.4)
Employment status at ART start				
No	154 (55.6)	4 374 (43.4)	4 393 (43.2)	12 779 (49.0)
Yes	123 (44.4)	5 693 (56.6)	5 766 (56.8)	13 325 (51.0)
Education level at ART start				
No education	8 (3.5)	720 (5.5)	514 (6.1)	1 242 (5.7)
Primary education	21 (9.3)	1 866 (14.2)	1 406 (16.8)	3 293 (15.2)
Secondary education	197 (87.2)	10 537 (80.3)	6 448 (77.1)	17 182 (79.1)
CD4 (cells/µL) at ART start				
0 - 100	70 (29.9)	5 858 (44.1)	4 571 (52.5)	10 499 (47.2)
101 - 200	95 (40.6)	4 284 (32.2)	2 518 (28.9)	6 897 (31.0)
201 - 350	56 (23.1)	2 437 (18.3)	1 319 (15.1)	3 810 (17.1)
>350	15 (6.4)	715 (5.4)	302 (3.5)	1 032 (4.6)
BMI (kg/m²) at ART start				
<18.5	15 (6.7)	1 898 (15.1)	1 937 (24.1)	3 850 (18.7)
18.5 - 24.9	113 (50.4)	6 245 (50.8)	5 075 (63.1)	11 433 (55.6)
25 - 29.9	66 (29.5)	2 652 (21.6)	844 (10.4)	3 562 (17.3)
≥30	30 (13.4)	1 506 (12.2)	183 (2.3)	1 719 (8.4)
WHO stage at ART start				
1	218 (77.9)	10 921 (67.6)	6 362 (61.6)	17 501 (65.4)
2	2 (0.7)	201 (1.2)	98 (0.9)	301 (1.1)
3	49 (17.5)	4 049 (25.1)	3 042 (29.3)	7 140 (26.7)
4	11 (3.9)	979 (6.1)	830 (8.0)	1 820 (6.8)
History of alcohol consumption at ART start				
No	212 (92.6)	12 513 (92.5)	6 409 (75.2)	18 869 (85.8)
Yes	9 (3.9)	993 (7.5)	2 113 (24.8)	3 117 (14.2)
History of smoking at ART start				
No	215 (96.8)	12 147 (90.0)	6 332 (72.9)	18 691 (83.4)
Yes	9 (3.9)	737 (5.5)	2 058 (18.6)	2 359 (10.5)
STI in the first 24 months of ART				
No	265 (94.6)	14 786 (91.6)	9 805 (94.9)	24 856 (92.9)
One or more episodes	15 (5.4)	1 364 (8.4)	527 (5.1)	1 906 (7.1)
History of TB at ART start				
Yes	23 (8.2)	959 (5.9)	803 (7.8)	1 785 (6.7)
No	257 (91.8)	15 191 (94.1)	9 529 (92.2)	24 977 (93.3)

ART = antiretroviral therapy; BMI = body mass index; WHO = World Health Organization; STI = sexually transmitted infection; TB = tuberculosis.

Table 3. Proportions of sexually transmitted infections in ART patients in a public hospital in Johannesburg, South Africa

Sexually transmitted infection	*n* (%)
Chancroid	2 (0.1)
Chlamydia	10 (0.5)
Syphilis	15 (0.8)
Gonococcal infection	11 (0.6)
Herpex simplex	261 (13.7)
Trichomoniasis	18 (0.9)
Anogenital warts	310 (16.3)
Unspecified sexually transmitted	81 (4.2)
Syndromic management	1 198 (67.1)

ART = antiretroviral therapy.

Similarly, the risk of STI diagnosis was higher among patients who were in WHO stages 3 (aHR 1.1; 95% CI 1.0 - 1.3) or 4 (aHR 1.6; 95% CI 1.3 - 1.9) at ART start compared with those in WHO stage 1. In contrast, there was a 20% increase in the risk of STI diagnosis among obese patients compared with those who were underweight at ART initiation (aHR 1.3; 95% CI 1.0 - 1.7). However, >80% of obese patients who experienced an incident STI had a CD4 count <200 cells/µL.

Discussion
We sought to determine the incidence of STIs among HIV-positive adult patients in their first 24 months of HIV treatment in Johannesburg. Overall, 7% of our sample had at least one STI episode in the first 2 years on ART, at an incidence rate of 4.8/100 py. This

Table 4. Drug regimen used to identify incident sexually transmitted infections including vaginal discharge syndrome, male urethritis syndrome and lower abdominal pain

Drug regimen	Female (*N*=911), *n* (%)	Male (*N*=287), *n* (%)	Total (*N*=1 198), *n* (%)
Metronidazole + ciprofloxacin	239 (26.2)	154 (53.7)	393 (32.8)
Metronidazole + ciprofloxacin + doxycycline	277 (30.4)	52 (18.1)	329 (27.5)
Metronidazole + doxycycline	208 (22.5)	23 (8.0)	231 (19.3)
Metronidazole + clotrimazole	53 (5.8)	0	53 (4.4)
Doxycycline + ciprofloxacin	21 (2.3)	27 (9.4)	48 (4.0)
Metronidazole + doxycycline + acyclovir	38 (4.2)	6 (2.1)	44 (3.7)
Fluconazole + acyclovir	28 (3.1)	12 (4.2)	40 (3.3)
Metronidazole + doxycycline + amoxicillin	24 (2.6)	5 (1.7)	29 (2.4)
Other	23 (2.5)	8 (2.8)	31 (2.6)
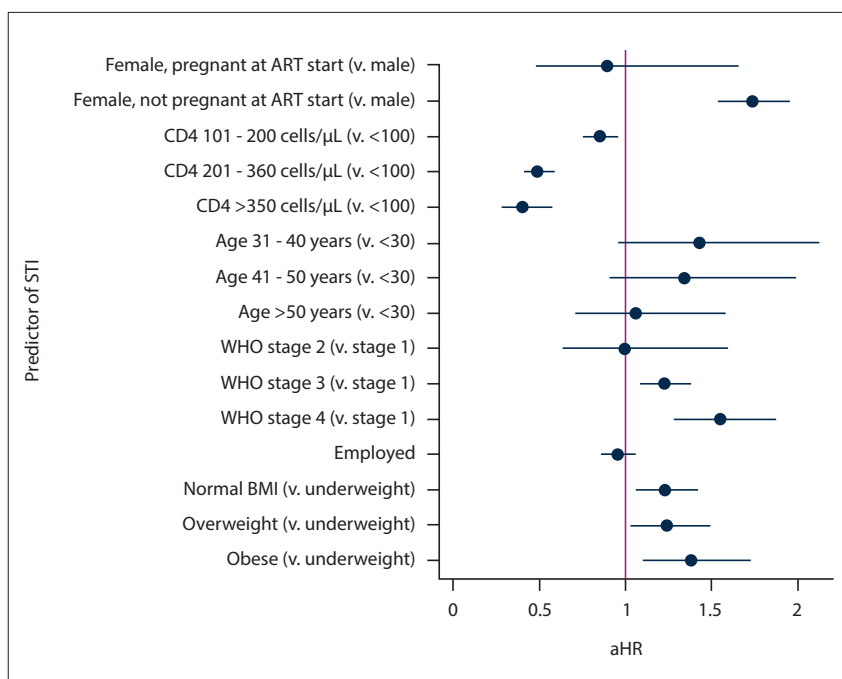
Fig. 1. Adjusted baseline predictors of incident STI among HIV-positive patients receiving ART at the Themba Lethu HIV clinic in Johannesburg, South Africa. (STI = sexually transmitted infection; ART = antiretroviral therapy; WHO = World Health Organization; BMI = body mass index; aHR = adjusted hazard ratio.)

proportion is substantially lower than the 19.9% estimate from a survey among HIV-positive adults in the Diepsloot community of Johannesburg.[13] However, only 10.2% of the participants in Diepsloot were receiving ART at the time.

Women who were not pregnant at ART initiation had a higher STI incidence (5.7/100 py) than men, which is much lower than the estimated 20/100 py incidence estimates among HIV-negative female trial participants in SA.[17] Similar to previous studies, our results also indicate that younger women had a higher STI risk than men.[17] The higher risk among non-pregnant women may be associated with their higher healthcare-seeking tendencies compared with men.[18]

Predictors of STIs included a low CD4 count, advanced WHO stage and high BMI at ART initiation. While we did not report on health status indicators at the time of the STI episodes, our findings are consistent with other studies showing that immunocompromised individuals are generally more vulnerable to STIs.[7] Patients with weak immune systems (as indicated by a low CD4 count) but in apparent good health (high BMI) seem to be at high risk. However, there could also be a potential diagnostic bias in a population that is already in HIV care. Patients with more severe HIV disease may have high healthcare-seeking behaviour, thereby increasing the likelihood of STI diagnosis. Also, patients with a low CD4 count may be subject to more intensive

investigations, including laboratory tests for STIs and other pathogens.

Nevertheless, STIs in this population primarily indicate high-risk sexual activity. Viral load data were minimal among patients with STI episodes. However, the majority of those with viral load data were suppressed. While HIV treatment reduces infectiousness by controlling viral load, this is only the case among ART-adherent and virally suppressed patients. The risk for onward HIV transmission remains a reality among patients with transient viral suppression, particularly during an STI episode.[19,20] Patients should therefore be encouraged to use barrier methods and to seek healthcare as soon as STI symptoms manifest.

Study limitations
The data for this analysis were drawn from a single HIV clinic in Johannesburg that may not be representative of other settings in SA. Furthermore, the reliance on diagnosis notes and prescription data does not take into account asymptomatic patients who did not present for care and introduces the potential for care-seeking and diagnostic bias. Also, the sensitivity of this indirect prescription-based STI identification method must be assessed against direct sample testing to establish the margin of error to expect in monitoring efforts under the syndromic management policy in SA. Nevertheless, further research is needed to explore methods for improving data for STI monitoring among patients in HIV care in SA.

Conclusions
STIs are common in HIV-infected patients who are receiving ART. While both ART and the syndromic management of STIs are high-impact interventions for controlling the spread of HIV, closer monitoring of STI occurrences is warranted, particularly among immunologically vulnerable patients.

Table 5. Predictors of STIs among ART patients in a public hospital in Johannesburg, South Africa

Variable	STI, n (%)	Person-time (100 py)	Failure, n	Incidence rate per 100 py (95% CI)	cHR (95% CI)	aHR (95%CI)
Sex						
Male	527 (5.1)	143.75	517	3.6 (3.3 - 3.9)	1	1
Female, pregnant	15 (5.4)	4.23	15	3.5 (2.1 - 5.8)	0.9 (0.6 - 1.7)	0.8 (0.4 - 1.5)
Female, not pregnant	1 364 (8.4)	235.68	1 341	5.7 (5.4 - 6.0)	1.6 (1.4 - 1.8)	1.6 (1.4 - 1.8)
Age at ART start (years)						
≤30	562 (8.9)	88.47	550	6.2 (5.7 - 6.7)	1	1
31 - 40	895 (7.7)	168.38	880	5.2 (4.9 - 5.6)	0.8 (0.7 - 0.9)	0.8 (0.7 - 0.9)
41 - 50	356 (5.7)	91.42	352	3.9 (3.5 - 4.3)	0.6 (0.5 - 2.0)	0.6 (0.5 - 0.7)
≥51	93 (3.7)	35.39	91	2.5 (2.1 - 3.2)	0.4 (0.3 - 0.5)	0.4 (0.3 - 0.5)
CD4 count (cells/µL) at ART start						
0 - 100	927 (8.8)	136.94	909	6.6 (6.2 - 7.1)	1	1
101 - 200	542 (7.9)	103.09	531	5.1 (4.7 - 5.6)	0.8 (0.7 - 0.9)	0.8 (0.7 - 0.9)
201 - 350	180 (4.7)	61.00	177	2.9 (2.5 - 3.3)	0.5 (0.4 - 0.7)	0.5 (0.4 - 0.6)
>350	42 (4.1)	16.01	42	2.6 (1.9 - 3.5)	0.4 (0.3 - 0.6)	0.4 (0.3 - 0.6)
Baseline BMI						
Underweight	292 (7.6)	48.19	284	5.9 (5.2 - 6.6)	1	1
Normal	955 (8.4)	166.41	936	5.6 (5.3 - 6.0)	1.0 (0.9 - 1.1)	1.1 (1.0 - 1.3)
Overweight	296 (8.3)	55.12	293	5.3 (4.7 - 6.0)	0.9 (0.8 - 1.1)	1.2 (1.0 - 1.5)
Obese	151 (8.8)	27.29	150	5.5 (4.7 - 6.5)	1.0 (0.8 - 1.2)	1.3 (1.0 - 1.7)
WHO staging						
1	1 087 (6.2)	263.59	1 074	4.1 (3.8 - 4.3)	1	1
2	24 (7.9)	4.62	24	5.2 (3.5 - 7.7)	1.3 (0.9 - 1.9)	0.9 (0.5 - 1.5)
3	620 (8.7)	94.78	609	6.4 (5.9 - 6.9)	1.5 (1.4 - 1.7)	1.1 (1.0 - 1.3)
4	175 (9.6)	20.66	166	8.0 (6.8 - 9.3)	1.9 (1.6 - 2.2)	1.6 (1.3 - 1.9)
Employment at ART start						
No	965 (7.5)	174.11	951	5.4 (5.1 - 5.8)	1	1
Yes	911 (6.8)	201.27	894	4.4 (4.1 - 4.7)	0.8 (0.8 - 0.9)	0.9 (0.8 - 1.0)
Education at ART start						
No education	82 (6.6)	17.15	80	4.6 (3.7 - 5.8)	1	
Primary school	222 (6.7)	47.60	218	4.5 (4.0 - 5.2)	1.0 (0.8 - 1.3)	
Secondary school	1 155 (6.7)	259.24	1 137	4.3 (4.2 - 5.5)	1.0 (0.8 - 1.2)	
History of alcohol consumption at ART start						
No	1 404 (7.5)	274.81	1 384	5.1 (4.8 - 5.3)	1	
Yes	200 (6.4)	40.81	197	4.8 (4.2 - 5.6)	0.9 (0.8 - 1.1)	
History of smoking at ART start						
No	1 436 (7.5)	279.50	1 416	5.1 (4.8 - 5.4)	1	
Yes	169 (6.2)	36.62	166	4.5 (3.9 - 5.3)	0.9 (0.7 - 1.0)	

STI = sexually transmitted infection; ART = antiretroviral therapy; py = person-years; CI = confidence interval; cHR = crude hazard ratio; aHR = adjusted hazard ratio; BMI = body mass index; WHO = World Health Organization.

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