Published in final edited form as:
Sex Transm Infect. 2013 March ; 89(2): 122–127. doi:10.1136/sextrans-2012-050524.

High-risk human papillomavirus prevalence is associated with HIV infection among heterosexual men in Rakai, Uganda

Aaron AR Tobian[1,2], **Mary K Grabowski**[2], **Godfrey Kigozi**[3], **Patti E Gravitt**[2,4], **Kevin P Eaton**[5], **David Serwadda**[3,6], **Fred Nalugoda**[3], **Maria J Wawer**[2,3], **Thomas C Quinn**[5,7], and **Ronald H Gray**[2,3]

[1]Department of Pathology, School of Medicine, Johns Hopkins University, Baltimore, Maryland, USA [2]Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA [3]Rakai Health Sciences Program, Entebbe, Uganda [4]Perdana University Graduate School of Medicine, Serdang, Malaysia [5]Department of Medicine, School of Medicine, Johns Hopkins University, Baltimore, Maryland, USA [6]School of Public Health, Makerere University, Kampala, Uganda [7]Division of Intramural Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA

Abstract

Objectives—Human papillomavirus (HPV) infection causes genital warts, penile cancer and cervical cancer. Africa has one of the highest rates of penile and cervical cancers, but there are little data on high-risk human papillomavirus (HR-HPV) prevalence in heterosexual men. Knowledge of HR-HPV prevalence, risk factors and genotype distribution among heterosexual men is important to establish risk-reduction prevention strategies.

Methods—1578 uncircumcised men aged 15–49 years who enrolled in male circumcision trials in Rakai, Uganda, were evaluated for HR-HPV from swabs of the coronal sulcus/glans using Roche HPV Linear Array. Adjusted prevalence risk ratios (adjPRRs) were estimated using modified Poisson multivariable regression.

Results—HPV prevalence (either high risk or low risk) was 90.7% (382/421) among HIV-positive men and 60.9% (596/978) among HIV-negative men (PRR 1.49, 95% CI 1.40 to 1.58). HIV-positive men had a significantly higher risk of infection with three or more HR-HPV genotypes (PRR = 5.76, 95% CI 4.27 to 7.79). Among HIV-positive men, high-risk sexual behaviours were not associated with increased HR-HPV prevalence. Among HIV-negative men, HR-HPV prevalence was associated with self-reported genital warts (adjPRR 1.57, 95% CI 1.07 to 2.31). Among all men (both HIV negative and HIV positive), HR-HPV prevalence was associated with more than 10 lifetime sexual partners (adjPRR 1.30, 95% CI 1.01 to 1.66), consistent condom use (adjPRR 1.31, 95% CI 1.08 to 1.60) and HIV infection (adjPRR 1.80, 95% CI 1.60 to 2.02).

Correspondence to, Dr Aaron Tobian, Department of Pathology, Johns Hopkins University, Carnegie 667, 600 N. Wolfe Street, Baltimore, MD 21287, USA; atobian1@jhmi.edu.

Contributors All authors contributed to the study design, data collection, data analysis, writing and reviewing the paper.

Competing interests None.

Ethics approval The trials were approved by the HIV Subcommittee of the Ugandan National Council for Research and Technology (Kampala, Uganda), and by three institutional review boards: the Science and Ethics Committee of the Uganda Virus Research Institute (Entebbe, Uganda), the Johns Hopkins University Bloomberg School of Public Health IRB (Baltimore, Maryland, USA) and the Western Institutional Review Board (Olympia, Washington, USA).

Provenance and peer review Not commissioned; externally peer reviewed.

HR-HPV prevalence was lower among men who reported no sexual partners during the past year (adjPRR 0.47, 95% CI 0.23 to 0.94).

Conclusion—The burden of HR-HPV infection is high among heterosexual men in sub-Saharan Africa and most pronounced among the HIV-infected individuals.

INTRODUCTION

Human papillomavirus (HPV) infection is one of the most common sexually transmitted infections, and persistent infection leads to genital warts, penile and anal cancers in men, as well as cervical cancer in women.[12] Cervical cancer is the leading cause of female cancer mortality in Eastern Africa,[2] and women co-infected with HIV have substantially higher numbers of HR-HPV genotypes and more rapid progression to neoplasia.[3] Among women in heterosexual relationships, male HPV prevalence is a key component of HPV transmission.[1]

An HPV vaccine has been shown to reduce HPV in heterosexual men, although vaccine efficacy is lower among previously exposed men.[4] Knowledge of high-risk human papillomavirus (HR-HPV) prevalence, risk factors and genotype distribution among heterosexual men are important to establish prevention strategies and vaccine programmes. It is also important to know genotype distribution to assess the frequency of non-vaccine HR-HPV genotypes.

The prevalence of male HR-HPV infection has been well documented in Europe, the USA and Latin America.[56] However, limited data are available for HPV prevalence among heterosexual men in Africa, and these studies have primarily been limited to either high-risk men attending STD clinics or HIV-negative populations.[5–9] The risk factors for HPV prevalence among HIV-positive heterosexual men and genotype distribution among the general population of heterosexual men in Africa is unknown. Here, we report the population-based risk factors and genotype distribution of prevalent HPV among HIV-positive and HIV-negative heterosexual men in sub-Saharan Africa.

MATERIALS AND METHODS

Clinical samples

Uncircumcised men aged 15–49 years were enrolled into two trials of male circumcision for HIV and STI prevention in Rakai District, Uganda. The design and results of the study have been reported previously.[1011] In brief, eligible persons were informed of study procedures and risks, provided written informed consent prior to screening and an additional written consent for enrolment. HIV-positive men with CD4 counts <350 cells/mm^3 or WHO stage 4 disease were excluded from the trials. At enrolment, serologic testing for HIV, herpes simplex virus type 2 (HSV-2) and syphilis, physical examinations and interviews to ascertain socio-demographic characteristics and sexual risk behaviours were conducted. Samples were collected by trained staff and the sera were stored at −80°C. All subjects were provided free HIV counselling and testing, health education and condoms. All participants found to be HIV positive were referred to an HIV treatment programme funded by the Presidential Emergency Fund for AIDS Relief.

Of 6396 men enrolled in the trials, a total of 1578 men (24.7%) were evaluated for HR-HPV. Men were randomly selected from the trial population. However, married men were oversampled to permit study of HPV transmission to their female partners and HIV-positive men were oversampled to provide sufficient power to evaluate risk factors in this group. Of the 1578 men, 179 (11.3%) had penile swabs with no detectable cellular β globin and no

detectable HPV and were excluded from this analysis since the adequacy of the sample collection could not be ensured. Thus, there were 1399 men (978 HIV negative and 421 HIV positive) included in this study.

The trials were approved by the HIV Subcommittee of the Ugandan National Council for Research and Technology (Kampala, Uganda) and by three institutional review boards: the Science and Ethics Committee of the Uganda Virus Research Institute (Entebbe, Uganda), the Johns Hopkins University Bloomberg School of Public Health IRB (Baltimore, Maryland, USA) and the Western Institutional Review Board (Olympia, Washington, USA). The trials were overseen by independent Data Safety Monitoring Boards[1011] and were registered with Clinical.Trials.Gov numbers NCT00425984 and NCT00124878.

HPV, HSV-2, HIV and syphilis detection

Moistened Dacron swabs from the coronal sulcus and glans were stored in Digene specimen transport media at −80°C until assay. HPV genotyping was performed using the Roche HPV Linear Array (Roche Diagnostics, Indianapolis, Indiana, USA), which detects 37 genotypes.[12] HPV genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68 were considered the primary HR-HPV genotypes.

HSV-2 infection was determined by HSV-2 ELISA (Kalon Biological Ltd, Guilford, UK) using an index value of 1.5 as positive, as previously described.[111314] HIV status was determined using two separate ELISAs and confirmed by HIV-1 Western Blot, as previously described.[10] Active *Treponema pallidum* infection was determined by a positive rapid plasma reagin followed by a positive *T pallidum* particle agglutination assay.[11]

Statistical analysis

Exploratory analyses assessed socio-demographic characteristics and behaviours at enrolment associated with prevalent HR-HPV. Since timing of HR-HPV infection was unknown and could have preceded enrolment by several years, we assessed both long-term and short-term risk behaviours. Prevalence risk ratios (PRRs) and 95% CIs of prevalent HR-HPV were estimated using modified Poisson regression with robust variance.[15] A non-parametric trend test developed by Cuzick, which is an extension of the Wilcoxon rank-sum test, was used to assess decreasing HR-HPV prevalence associated with increasing age. Risk factors with a p value <0.15 in univariate analysis were entered into a Poisson multivariable model to estimate adjusted prevalence risk ratios (PRRs). The multivariable model included all covariates listed in table presenting the multivariate results. A test for variance inflation factor was used to evaluate for multicollinearity and did not find any variables that were considered a linear combination of independent variables. A multivariable model of only HIV-positive men was not performed since only genital ulcer disease and age at sexual debut had a p value <0.15 in the univariate analysis. Analyses were performed using Stata software (V.11, StataCorp).

RESULTS

The prevalence of any HPV (high risk or low risk) was 90.7% (382/421) among HIV-positive men and 60.9% (596/978) among HIV-negative men (PRR = 1.49, 95% CI 1.40 to 1.58) (table 1). The prevalence for the two low-risk HPV genotypes that cause genital warts was higher in the HIV-infected than HIV-uninfected men (table 1).

The prevalence of HR-HPV was 74.1% (312/421) among HIV-positive men and 38.6% (378/978) among HIV-negative men (PRR = 1.92, 95% CI 1.74 to 2.11). Among HIV-negative men, HR-HPV 16 (7.8%) and HR-HPV 51 (7.0%) were the two most common genotypes detected. Among HIV-positive men, HR-HPV 58 (20.7%) and HR-HPV 16

(20.0%) were the two most common genotypes detected. Genotype-specific prevalence was significantly higher in HIV-infected than HIV-negative men for all HR-HPV genotypes tested, and HIV-positive men had significantly higher risk of multiple (three or more) HR-HPV infections (PRR = 5.76, 95% CI 4.27 to 7.79).

Among the youngest men in this study (15–19 years old) that included both HIV-positive and HIV-negative men, HPV prevalence for genotype 6 was 2.1% (2/96), genotype 11 was 5.2% (5/96), genotype 16 was 7.3% (7/96) and genotype 18 was 6.2% (6/96).

The univariate associations of HR-HPV prevalence stratified by enrolment HIV status are shown in table 2. Among HIV-negative men, prevalence of any HR-HPV genotype was 29.4% among men aged 15–19 years old and increased to 47.7% among men aged 20–24 years. Among men aged 20 years and older, HR-HPV prevalence continually decreased with increasing age after 25 years (p = 0.001). HR-HPV prevalence was higher among men with non-marital relationships, men with increased number of sexual partners over their lifetime, men who reported condom use and men who reported genital warts (PRR = 1.86, 95% CI 1.16 to 2.99). HR-HPV prevalence was lower among men who reported no female sexual partners during the past year.

Among HIV-positive men in the univariate analysis, associations between risk factors and HR-HPV prevalence showed similar trends to the HIV-negative men. However, except for genital ulcer disease (PRR = 1.16, 95% CI 1.04 to 1.29), there were no statistically significant associations.

Among all HIV-negative and HIV-positive men, HR-HPV prevalence was associated with both HIV-positive serostatus (PRR = 1.92, 95% CI 1.74 to 2.11, table 1) and HSV-2-positive serostatus (PRR = 1.37, 95% CI 1.21 to 1.54, table 2).

The adjPRRs estimated using multivariate Poisson regression are shown in table 3. Among HIV-negative men, HR-HPV prevalence was associated with self-reported genital warts (adjPRR 1.57, 95% CI 1.07 to 2.31), multiple sexual partners during the past year (adjPRR 2.83, 95% CI 1.00 to 8.04) and consistent condom use (adjPRR 1.45, 95% CI 1.09 to 1.93). There was no statistically significant association between HR-HPV prevalence and age, education, non-marital relationships, age at sexual debut, lifetime number of sexual partners and alcohol use with sexual intercourse. Among all men in the study (both HIV negative and HIV positive), HR-HPV prevalence was associated with HIV infection (adjPRR 1.80, 95% CI 1.60 to 2.02), more than 10 lifetime sexual partners (adjPRR 1.30, 95% CI 1.01 to 1.66) and consistent condom use (adjPRR 1.31, 95% CI 1.08 to 1.60). HR-HPV prevalence was lower among men who reported no sexual partners during the past year (adjPRR 0.47, 95% CI 0.23 to 0.94). Genital warts and age at sexual debut were of borderline statistical significance, and there was no association between HR-HPV prevalence and HSV-2 serostatus, age, education, non-marital relationships, drinking alcohol, alcohol consumption with sexual intercourse, genital ulcer disease, urethral discharge and dysuria.

In a sensitivity analysis, men (both HIV positive and HIV negative) with (n = 1399) and without (n = 179) detectable cellular DNA (either β globin or viral) were evaluated. HR-HPV prevalence was 70.6% (312/443) among HIV-positive men and 33.3% (378/1135) among HIV-negative men. Identical to the primary analysis that only included men with detectable cellular DNA, HR-HPV prevalence was significantly higher among men with HIV infection, more than 10 lifetime sexual partners, consistent condom use and genital warts. HR-HPV prevalence was lower among men who reported no sexual partners during the past year.

DISCUSSION

Data are limited on HR-HPV prevalence among heterosexual men in sub-Saharan Africa, even though the rates of penile (2.7/100 000 persons) and cervical cancers (52.4/100 000) are highest in this region.[216] The prevalence of HR-HPV was 74.1% among HIV-positive men and 38.7% among HIV-negative men. It is difficult to compare risks across studies. However, the prevalence of HR-HPV among heterosexual men in this study appears to be higher than most previously published risks in Europe, North America, Latin America and Asia.[56] HR-HPV prevalence was significantly higher among HIV-positive compared with HIV-negative men. HR-HPV prevalence was not associated with high-risk sexual behaviours among HIV-positive men (table 2). The overall high HR-HPV prevalence among HIV-positive men (>74%) likely obscured any further association between HR-HPV prevalence and high-risk sexual behaviours. Among all HIV-negative and HIV-positive men, HR-HPV prevalence was associated with HIV infection, condom use and increased number of sexual partners both over a lifetime and within the past year.

HR-HPV prevalence increased until 20–24 years in univariate models and then HR-HPV prevalence significantly decreased with age. However, age was not statistically significant in the adjusted model, which suggests that age effects were likely due to age-specific sexual behaviours. Even at the youngest age group of 15–19 years, HR-HPV prevalence was 29.4% among HIV-negative men. Since the HPV vaccination is not as effective against previously exposed individuals, it is important to initiate immunisation prior to sexual debut in this population.

The role of condom use for HR-HPV prevention is debatable among heterosexual men. Some studies have shown condom use is associated with lower HPV infection,[17–19] whereas other studies have found condoms not to be protective.[1920] While this study is limited by its cross-sectional nature, we found that HR-HPV prevalence at the coronal sulcus was higher among men who reported condom use. The variation in the protective effect of condom use is likely due to the multifocal nature of HPV infection including areas such as the scrotum, perineum, anal canal and urethra, which are not protected by a condom. Thus, autoinoculation from these unprotected areas might explain the lack of condom efficacy.[21] Additionally, condom use is associated with higher numbers of sexual partners in this society, and thus, the effects on HR-HPV may be confounded by correlated sexual behaviours.

Both the number of sexual partners over the man’s lifetime and also the number of sexual partners within the past year were associated with HR-HPV prevalence. The reduction in HR-HPV prevalence among men who reported no sexual partners during the past year is likely due to the relatively rapid clearance of HR-HPV infections within 6–18 months[2223] such that prevalence reflects proximal rather than distant sexual exposures.

HIV-positive men had a significantly higher prevalence of HR-HPV. While HIV-positive men reported similar risk behaviours to the HIV-negative men during the previous year, the HIV-induced immune dysfunction likely increases HR-HPV prevalence due to more persistent infections among HIV-positive men compared with HIV-negative men.[2425] It is likely that the high prevalence of HPV infection and the increased number of genotypes among HIV-positive men obscured associations between HR-HPV infection and high-risk sexual behaviours.

This study has limitations. While the study population was composed of men who were randomly selected from a rural population-based male circumcision trial, married men and HIV-positive men were oversampled. In addition, the HPV detection assay in this study utilised a β-globin-positive control to ensure adequate sample collection of cellular material,

and 11.3% were excluded because of the absence of detectable cellular or viral DNA. However, HR-HPV prevalence was not significantly elevated and the risk factors for HR-HPV were identical even when β-globin-negative men were included in a sensitivity analysis. The impact of male circumcision on HR-HPV prevalence was not assessed in this study since inclusion criteria for the trial required men to be uncircumcised. However, we and others have previously demonstrated that male circumcision reduces HR-HPV infection among HIV-negative men, female partners of HIV-negative men and HIV-positive men,[1125–29] and consequently also HPV-associated penile lesions.[30] The demographics and risk behaviours are self-reported and thus men may be affected by recall or social desirability bias. The findings are not applicable to all men with HIV since only men with CD4 cell counts ≥350 cells/ml and no evidence of AIDS-related illnesses were enrolled in the trials.

The burden of HR-HPV infection is high among heterosexual men in this rural sub-Saharan African population, even in men as young as 15–19 years. Novel prevention strategies, such as a polyvalent HPV vaccine, for both men and women are critical to reducing genital warts, penile cancer and cervical cancer in Africa.

Acknowledgments

We are most grateful to the study participants and the Rakai Community Advisory Board whose commitment and cooperation made this study possible.

Funding The trial was funded by the Bill and Melinda Gates Foundation (#22006.02) and the National Institutes of Health (#U1AI51171). The Fogarty International Center (#5D43TW001508 and #2D43TW000010-19-AITRP) contributed to training. National Institute of Allergy and Infectious Diseases (NIAID), NIH grants U01-AI-068613 and 3U01-AI075115-03S1 and the NIAID Intramural Program provided laboratory support. AART was supported by the NIH 1K23AI093152-01A1, Doris Duke Charitable Foundation Clinician Scientist Development Award (#22006.02) and the Johns Hopkins University Clinician Scientist Award.

Disclosures PG received research funding from Roche Molecular Diagnostics who manufacture the HPV genotyping test used in this study.

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Key messages

- This population-based study of HIV-negative and HIV-positive heterosexual men in rural sub-Saharan Africa demonstrates that the burden of both low-risk and high-risk human papillomavirus (HR-HPV) infection is high.
- HIV-negative men with a history of risky sexual behaviour are more likely to be infected with HR-HPV.
- HR-HPV prevalence is significantly higher among HIV-positive heterosexual men.
- HR-HPV prevalence is not associated with high-risk sexual behaviours among HIV-positive men. The overall high HR-HPV prevalence among HIV-positive men (>74%) likely obscures any further association between HR-PV prevalence and high-risk sexual behaviours.

Table 1

HPV genotype-specific prevalence stratified by HIV

	HIV negative		HIV positive		
	HPV positive		HPV positive		
	n = 978	%	n = 421	%	HIV positive/HIV negative PRR (95% CI)
Any HPV (LR and HR)	596	60.94	382	90.74	1.49 (1.40 to 1.58)
Any LR-HPV	449	45.91	348	82.66	1.80 (1.66 to 1.95)
Any HR-HPV	378	38.65	312	74.11	1.92 (1.74 to 2.11)
LR-HPV genotype					
6	51	5.21	72	17.1	3.28 (2.33 to 4.61)
11	65	6.65	79	18.76	2.82 (2.08 to 3.84)
HR-HPV genotype					
16	76	7.77	84	19.95	2.57 (1.92 to 3.42)
18	37	3.78	57	13.54	3.58 (2.40 to 5.33)
31	41	4.19	40	9.50	2.27 (1.49 to 3.45)
33	28	2.86	44	10.45	3.65 (2.30 to 5.78)
35	38	3.89	75	17.81	4.58 (3.15 to 6.66)
39	28	2.86	43	10.21	3.57 (2.48 to 5.66)
45	51	5.21	56	13.30	2.55 (1.78 to 3.66)
51	68	6.95	70	16.63	2.39 (1.75 to 3.27)
52	49	5.01	44	10.45	2.09 (1.41 to 3.08)
56	17	1.74	29	6.89	3.96 (2.20 to 7.13)
58	45	4.60	87	20.67	4.49 (3.19 to 6.32)
59	49	5.01	77	18.29	3.65 (2.60 to 5.13)
66	37	3.78	47	11.16	2.95 (1.95 to 4.47)
68	39	3.99	71	16.86	4.23 (2.91 to 6.14)
Number of concurrent HR-HPV genotypes					
0	600	61.35	109	25.89	0.42 (0.36 to 0.50)
1	244	24.95	114	27.08	1.09 (0.90 to 1.31)
2	82	8.38	69	16.39	1.95 (1.45 to 2.64)
3+	52	5.32	129	30.64	5.76 (4.27 to 7.79)

HPV, human papillomavirus; HR-HPV, high-risk human papillomavirus; LR-HPV, low-risk human papillomavirus; PRR, prevalence risk ratio.

Table 2

Prevalence of high-risk human papillomavirus stratified by HIV status

	HIV negative			HIV positive			All men		
	Infected men	%	Unadjusted PRR (95% CI)	Infected men	%	Unadjusted PRR (95% CI)	Infected men	%	Unadjusted PRR (95% CI)
All participants	378/978	38.65		312/421	74.11		690/1399	49.32	
Age (years)									
15–19	27/92	29.35	1.00 (referent)	3/4	75.00	1.00 (referent)	30/96	31.25	1.00 (referent)
20–24	104/218	47.71	1.63 (1.15 to 2.30)	32/37	86.49	1.15 (0.65 to 2.06)	136/255	53.33	1.71 (1.24 to 2.35)
25–29	120/272	44.12	1.50 (1.07 to 2.12)	64/90	71.11	0.95 (0.53 to 1.70)	184/362	50.83	1.63 (1.19 to 2.23)
30–34	69/195	35.38	1.21 (0.83 to 1.74)	82/115	71.30	0.95 (0.53 to 1.70)	151/310	48.71	1.56 (1.13 to 2.14)
35+	58/201	28.86	0.98 (0.67 to 1.44)	131/175	74.86	1.00 (0.56 to 1.77)	189/376	50.27	1.61 (1.18 to 2.20)
Education									
No education	29/77	37.66	1.00 (referent)	25/36	69.44	1.00 (referent)	54/113	47.79	1.00 (referent)
Primary	273/664	41.11	1.09 (0.81 to 1.48)	237/319	74.29	1.07 (0.85 to 1.34)	510/983	51.88	1.09 (0.89 to 1.33)
Secondary or higher	76/237	32.07	0.85 (0.60 to 1.20)	50/66	75.76	1.09 (0.84 to 1.41)	126/303	41.58	0.87 (0.69 to 1.10)
Occupation									
Non-wage	254/660	38.48	1.00 (referent)	204/278	73.38	1.00 (referent)	458/938	48.83	1.00 (referent)
Wage	124/318	38.99	1.01 (0.86 to 1.20)	108/143	75.52	1.03 (0.92 to 1.16)	232/461	50.33	1.03 (0.92 to 1.15)
Marital status									
Not married	73/175	41.71	1.00 (referent)	44/54	81.48	1.00 (referent)	117/229	51.09	1.00 (referent)
Married (monogamous)	272/713	38.15	0.91 (0.75 to 1.12)	232/323	71.83	0.88 (0.76 to 1.02)	504/1036	48.65	0.95 (0.83 to 1.10)
Married (polygamous)	33/90	36.67	0.88 (0.64 to 1.21)	36/44	81.82	1.00 (0.83 to 1.21)	69/134	51.49	1.01 (0.82 to 1.24)
Non-marital relationships									
No	269/766	35.12	1.00 (referent)	239/322	74.22	1.00 (referent)	508/1088	46.69	1.00 (referent)
Yes	109/212	51.42	1.46 (1.24 to 1.72)	73/99	73.74	0.99 (0.87 to 1.13)	182/311	58.52	1.25 (1.12 to 1.40)
Age at sexual debut (years)									
≤15	106/279	37.99	1.00 (referent)	80/104	76.92	1.00 (referent)	186/383	48.56	1.00 (referent)
16–19	215/519	41.43	1.09 (0.91 to 1.31)	183/260	70.38	0.92 (0.80 to 1.04)	398/779	51.09	1.05 (0.87 to 1.23)
≥20	51/141	36.17	0.95 (0.73 to 1.24)	48/56	85.71	1.11 (0.96 to 1.29)	99/197	50.25	1.03 (0.87 to 1.23)
Lifetime number of sexual partners									
0–2	54/191	28.27	1.00 (referent)	12/17	70.59	1.00 (referent)	66/208	31.73	1.00 (referent)

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	HIV negative			HIV positive			All men		
	Infected men	%	Unadjusted PRR (95% CI)	Infected men	%	Unadjusted PRR (95% CI)	Infected men	%	Unadjusted PRR (95% CI)
3–5	154/380	40.53	1.43 (1.11 to 1.85)	91/126	72.22	1.02 (0.74 to 1.42)	245/506	48.42	1.53 (1.23 to 1.90)
6–10	112/272	41.18	1.46 (1.12 to 1.90)	110/152	72.37	1.03 (0.74 to 1.42)	222/424	52.36	1.65 (1.33 to 2.05)
11+	58/135	42.96	1.52 (1.13 to 2.05)	99/126	78.57	1.11 (0.81 to 1.53)	157/261	60.15	1.90 (1.52 to 2.37)
Number of sexual partners during past year									
None	6/56	10.71	0.30 (0.14 to 0.64)	4/7	57.14	0.79 (0.41 to 1.51)	10/63	15.87	0.34 (0.19 to 0.61)
1	182/507	35.90	1.00 (referent)	143/198	72.22	1.00 (referent)	325/705	46.10	1.00 (referent)
2+	190/415	45.78	1.28 (1.09 to 1.49)	165/216	76.39	1.06 (0.94 to 1.19)	355/631	56.26	1.22 (1.09 to 1.35)
Condom use in the past year *									
None	186/533	34.90	1.00 (referent)	137/189	72.49	1.00 (referent)	323/722	44.74	1.00 (referent)
Consistent use	30/57	52.63	1.51 (1.15 to 1.98)	20/26	76.92	1.06 (0.84 to 1.33)	50/83	60.24	1.35 (1.11 to 1.63)
Inconsistent use	156/332	46.99	1.35 (1.14 to 1.58)	151/199	75.88	1.04 (0.93 to 1.18)	307/531	57.82	1.29 (1.16 to 1.44)
Drink alcohol									
No	119/331	35.95	1.00 (referent)	66/87	75.86	1.00 (referent)	185/418	44.26	1.00 (referent)
Yes	259/647	40.03	1.11 (0.94 to 1.32)	246/334	73.65	0.97 (0.85 to 1.11)	505/981	51.48	1.16 (1.02 to 1.32)
Alcohol use with sexual intercourse *									
No	162/421	38.48	1.00 (referent)	81/104	77.88	1.00 (referent)	243/525	46.29	1.00 (referent)
Yes	210/501	41.92	1.09 (0.93 to 1.28)	227/310	73.23	0.94 (0.83 to 1.06)	437/811	53.88	1.16 (1.04 to 1.30)
Genital wart (self-reported)									
No	373/971	38.41	1.00 (referent)	298/405	73.58	1.00 (referent)	671/1376	48.76	1.00 (referent)
Yes	5/7	71.43	1.86 (1.16 to 2.99)	14/16	87.50	1.19 (0.98 to 1.44)	19/23	82.61	1.69 (1.39 to 2.06)
Genital ulcer disease (self-reported)									
No	337/887	37.99	1.00 (referent)	208/294	70.75	1.00 (referent)	545/1181	46.15	1.00 (referent)
Yes	41/91	45.05	1.19 (0.93 to 1.51)	104/127	81.89	1.16 (1.04 to 1.29)	145/218	66.51	1.44 (1.29 to 1.61)
Urethral discharge (self-reported)									
No	352/921	38.22	1.00 (referent)	266/364	73.08	1.00 (referent)	618/1285	48.09	1.00 (referent)
Yes	26/57	45.61	1.19 (0.89 to 1.60)	46/57	80.70	1.10 (0.96 to 1.27)	72/114	63.16	1.31 (1.13 to 1.53)
Dysuria (self-reported)									
No	346/907	38.15	1.00 (referent)	264/355	74.37	1.00 (referent)	610/1262	48.34	1.00 (referent)
Yes	32/71	45.07	1.18 (0.90 to 1.55)	48/66	72.73	0.98 (0.83 to 1.15)	80/137	58.39	1.21 (1.04 to 1.41)

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	HIV negative			HIV positive			All men		
	Infected men	**%**	**Unadjusted PRR (95% CI)**	**Infected men**	**%**	**Unadjusted PRR (95% CI)**	**Infected men**	**%**	**Unadjusted PRR (95% CI)**
Enrolment syphilis status									
Negative	365/937	38.95	1.00 (referent)	280/378	74.07	1.00 (referent)	645/1315	49.05	1.00 (referent)
RPR and TPPA positive	13/41	31.71	0.81 (0.52 to 1.28)	32/43	74.42	1.00 (0.83 to 1.21)	45/84	53.57	1.09 (0.88 to 1.34)
HSV-2 status									
Persistent negative	186/507	36.69	1.00 (referent)	46/58	79.31	1.00 (referent)	232/565	41.06	1.00 (referent)
Enrolment indeterminate	46/116	39.66	1.08 (0.84 to 1.39)	39/54	72.22	0.91 (0.74 to 1.13)	85/170	50.00	1.22 (1.02 to 1.46)
Prevalent positive	146/355	41.13	1.12 (0.95 to 1.33)	227/309	73.46	0.93 (0.80 to 1.07)	373/664	56.17	1.37 (1.21 to 1.54)

*Condom use and alcohol use with sexual intercourse were only evaluated in sexually active individuals.

HSV-2, herpes simplex virus type 2; PRR, prevalence risk ratio; RPR, rapid plasma reagin; TPPA, *Treponema pallidum* particle agglutination assay.

Table 3

Adjusted prevalence risk ratios (adjPRR) for human papillomavirus infection

	HIV-negative men adjPRR (95% CI)	All men adjPRR (95% CI)
HIV status		
Negative	–	1.00 (referent)
Positive	–	1.80 (1.60 to 2.02)
Herpes simplex virus type 2 status		
Persistent negative	–	1.00 (referent)
Enrolment indeterminate	–	1.03 (0.87 to 1.23)
Prevalent positive or seroconverter	–	1.05 (0.92 to 1.19)
Age (years)		
15–19	1.00 (referent)	1.00 (referent)
20–24	1.13 (0.79 to 1.60)	1.12 (0.81 to 1.55)
25–29	1.01 (0.70 to 1.45)	0.96 (0.69 to 1.33)
30–34	0.82 (0.56 to 1.22)	0.84 (0.60 to 1.18)
35+	0.66 (0.43 to 1.00)	0.80 (0.57 to 1.11)
Education		
No education	1.00 (referent)	1.00 (referent)
Primary	0.96 (0.71 to 1.31)	1.02 (0.84 to 1.23)
Secondary or higher	0.70 (0.49 to 0.99)	0.84 (0.67 to 1.06)
Non-marital relationships		
No	1.00 (referent)	1.00 (referent)
Yes	1.15 (0.95 to 1.40)	1.07 (0.95 to 1.21)
Age at sexual debut (years)		
≤15	1.00 (referent)	1.00 (referent)
16–19	1.14 (0.95 to 1.36)	1.04 (0.92 to 1.16)
≥20	1.18 (0.89 to 1.57)	1.18 (1.00 to 1.39)
Lifetime number of sexual partners		
0–2	1.00 (referent)	1.00 (referent)
3–5	1.21 (0.93 to 1.58)	1.20 (0.96 to 1.50)
6–10	1.27 (0.95 to 1.70)	1.22 (0.96 to 1.54)
11+	1.33 (0.95 to 1.87)	1.30 (1.01 to 1.66)
Number of sexual partners during past year		
None	0.37 (0.13 to 1.02)	0.47 (0.23 to 0.94)
1	1.00 (referent)	1.00 (referent)
2+	2.83 (1.00 to 8.04)	1.05 (0.93 to 1.18)
Condom use in the past year		
None	1.00 (referent)	1.00 (referent)
Consistent use	1.45 (1.09 to 1.93)	1.31 (1.08 to 1.60)
Inconsistent use	1.18 (0.97 to 1.43)	1.10 (0.98 to 1.24)
Drink alcohol		
No	–	1.00 (referent)

	HIV-negative men adjPRR (95% CI)	All men adjPRR (95% CI)
Yes	–	0.98 (0.84 to 1.14)
Alcohol use with sexual intercourse		
No	1.00 (referent)	1.00 (referent)
Yes	1.13 (0.96 to 1.33)	1.03 (0.90 to 1.18)
Genital wart (self-reported)		
No	1.00 (referent)	1.00 (referent)
Yes	1.57 (1.07 to 2.31)	1.21 (0.98 to 1.48)
Genital ulcer disease (self-reported)		
No	–	1.00 (referent)
Yes	–	1.09 (0.98 to 1.22)
Urethral discharge (self-reported)		
No	–	1.00 (referent)
Yes	–	1.01 (0.85 to 1.20)
Dysuria (self-reported)		
No	–	1.00 (referent)
Yes	–	0.97 (0.81 to 1.17)