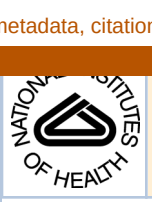

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Sexual behaviour and less frequent bathing are associated with higher human papillomavirus incidence in a cohort study of uncircumcised Kenyan men

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Abstract

Objectives—Data on the acquisition of human papillomavirus (HPV) infection in men are limited, especially from developing regions including Africa. The objective of this study was to characterise and determine the risk factors of HPV acquisition among a cohort of uncircumcised men participating in a randomised controlled trial (RCT) of male circumcision in Kisumu, Kenya.

Methods—Penile exfoliated cell specimens were collected at baseline, 6- and 12-month follow-up visits from the glans/coronal sulcus and shaft of men enrolled in the control arm of the RCT between 2002 and 2005. All participants were HIV seronegative, aged 17–24 years at baseline and remained uncircumcised over follow-up. Specimens were tested with GP5+/6+ PCR to detect 44 HPV types. Parametric frailty models were used to assess risk factors of HPV incidence.

Results—The median age of 966 participants was 20 years. The median follow-up time was 12.1 months. The incidence rate (IR) of any HPV infection was 49.3/1000 person-months with HPV16

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Contributors DMB drafted the manuscript and conducted statistical analyses. PJFS and CJLM contributed to the design and implementation of the HPV methods, including HPV testing. MGH gave his expertise in the analysis design and interpretation of the data. MB conducted HPV testing. RCB and SM contributed to the study conception and design of the RCT and HPV ancillary study and contributed to the interpretation of the data. KA and WA supervised the RCT and collected data on site in Kenya. JSS contributed to the HPV study conception, implementation and interpretation of the data. All authors reviewed the manuscript. All authors, external and internal, had full access to all of the data in the study, and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Competing interests PJFS is an occasional advisory board member to Gen-Probe, Roche and GSK, and has limited stock of Self-Screen, a spin-off company of VU University Medical Center (no payments made); CJLM is an occasional advisory member to QIAGEN, Roche, GSK, Merck and Gen-probe, a consultant to QIAGEN (finished 12/31/10), and has a small amount of shares of Self-Screen BV (no payments made). JSS has reviewed research grants or served as a consultant for GSK, Merck, Hologic, Genprobe and QIAGEN. For the remaining authors, no competing interests were declared.

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having the highest IR (10.9/1000 person-months). The strongest risk factors for overall HPV incidence were bathing less frequently than daily (adjusted HR=2.6; 95% CI 1.0 to 6.5) and having ≥2 female sexual partners in the past year (adjusted HR=1.6; 95% CI 1.2 to 2.1).

Conclusions—HPV IRs were notably high in this cohort of high-risk, uncircumcised men from Kisumu, Kenya, with the number of sexual partners and bathing frequency being the strongest risk factors.

INTRODUCTION

Carcinogenic human papillomavirus (HPV) infections are necessary for the development of invasive cervical cancer and are considered aetiological agents of other non-cervical cancers among both men and women.[1–4] While several previous studies have described HPV infections among women, data on the acquisition of HPV infection among men are relatively limited.[5]

Few prospective studies have been published on HPV incidence among men from North America, South America, Europe and Africa.[6–14] Incidence rates (IRs) of penile HPV infections for the first incident HPV type detected have ranged from 17.9 to 38.4/1000 person-months.[6–8, 14] Determining risk factors for HPV incidence among men could identify interventions to help prevent future HPV acquisition in men and transmission to women. A higher number of recent and lifetime sexual partners and history of smoking have been found to increase the rate for HPV acquisition among men in prior studies.[7, 14, 15] Data are especially needed on the rate and risk factors of HPV acquisition among men in less developed geographical regions, including sub-Saharan Africa, where the incidence of invasive cervical cancer among women is among the highest worldwide.[16, 17]

Randomised controlled trials (RCTs) of male circumcision have shown that circumcision reduces HPV acquisition among men.[10, 18] Given that some men may remain uncircumcised due to lack of access to services, religion or other reasons, we sought to characterise the type-specific incidence of HPV infection over a 12-month period among 966 uncircumcised men participating in the control arm of an RCT of male circumcision in Kisumu, Kenya. We also aimed to determine risk factors for HPV acquisition using parametric frailty models allowing for the analysis of clustered survival data.

METHODS

Study population and enrolment

Uncircumcised men were screened between February 2002 and September 2005 in Kisumu, Kenya, to participate in an RCT of male circumcision.[19] The primary aim of the RCT was to determine the efficacy of male circumcision in reducing HIV incidence. In brief, inclusion criteria included being uncircumcised, aged 18–24 years, HIV seronegative and sexually active. Participants were recruited from sexually transmitted infection clinics, workplaces and community organisations. The study protocol was approved by the Institutional Review Boards of the Universities of Illinois at Chicago, Manitoba, Nairobi and North Carolina; RTI International; and the VU University Medical Center.

Questionnaire and specimen collection

After undergoing informed consent, participants were administered a standardised questionnaire on sociodemographic characteristics, hygiene practices, including how often they normally bathe (once/week, twice/week, every 2 days, every day), and sexual behaviour by a trained male interviewer. Penile exfoliated cells were collected for HPV DNA detection at baseline, 6- and 12-month study visits. At each visit, specimens were

taken separately from two anatomical sites: (i) shaft and external foreskin tissue (shaft specimen) and (ii) glans, coronal sulcus and inner foreskin tissue (glans specimen) using prewetted Type 3 Dacron swabs (Roche Diagnositics, Basel, Switzerland).[20]

Penile cell samples were placed into two individual 15 ml conical centrifuge tubes containing 2 ml 0.01 mol/l Tris-HCl, 7.4 pH, buffer and processed on the day of collection at the clinical laboratory of the Universities of Nairobi, Illinois and Manitoba by centrifugation at high speed (maximum, 3000 g) for 10 min. Excess Tris-HCl buffer was discarded using a Pasteur pipette, and the remaining cell pellet was resuspended in Tris-HCl buffer, and vortexed. Diluted cell pellets were frozen at −75°C. All samples were sent using a dry shipper to the Department of Pathology, VU University Medical Center, Amsterdam, The Netherlands, for HPV DNA testing.

HPV DNA and sexually transmitted infection testing

DNA was isolated from penile exfoliated cell samples using NucleoSpin 96 Tissue kit (Macherey-Nagel, Germany) and a Microlab Star robotic system (Hamilton, Germany), according to manufacturers' instructions. Presence of human DNA was evaluated by β-globin-specific PCR followed by agarose gel electrophoresis. HPV positivity was assessed by GP5+/6+ PCR followed by hybridisation of PCR products using an enzyme immunoassay readout with two HPV oligoprobe cocktail probes that, together, detect 44 HPV types. Subsequent genotyping was performed by reverse line blot (RLB) hybridisation of PCR products, as described previously.[21, 22] HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68 were considered high-risk types. Low-risk types included all other HPV types. HPV types detected by enzyme immunoassay, but not by RLB genotyping, were designated as HPV-X, indicating a type, subtype or variant not detectable with probes used for RLB hybridisation.

At the baseline visit, urine samples were tested for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections by PCR-based methods (Roche Diagnostics, Basel, Switzerland). Serum specimens were tested for herpes simplex virus type 2 (HSV-2) antibody (Kalon Biological, Aldershot, UK).

Statistical methods

Inclusion criteria required men to be enrolled in the control arm of the RCT, have HPV DNA results available from the baseline and 6-month visits, and remain uncircumcised until the 6-month visit. Of 1393 uncircumcised men enrolled in the control arm, 1140 had an HPV test result at baseline, of which 972 also had an HPV result from the 6-month visit. Of these, 966 men remained uncircumcised until the 6-month visit and were included in analyses. HPV prevalence at baseline and IRs for HPV detected over the 12-month follow-up period were estimated for individual HPV types and for specific HPV type groupings (eg, any HPV, high-risk HPV). An incident, or acquired, infection was defined as detection of a type-specific HPV infection during follow-up that was not present at baseline.

The time at risk of acquiring an incident HPV infection at either anatomical site was estimated assuming the incident infection was acquired at the midpoint between the last HPV-negative result and first HPV-positive result. Participants were censored at their last visit prior to circumcision if they were circumcised before their 12-month visit or at their last study visit if they remained HPV-negative. IR estimates for each HPV type or type grouping were estimated only among participants who were negative for the given individual type or grouping at baseline. Men with multiple HPV types were considered to have a high-risk HPV infection if ≥1 high-risk types were detected and a low-risk infection if only low-risk types were detected. Acquisition of multiple high-risk HPV types at the

same visit was considered a single acquisition event. Men with untyped HPV infections were excluded from high-risk and low-risk categorisations unless a high-risk type was concurrently detected. IR analyses were repeated for any, high-risk and low-risk HPV for the glans and shaft specimens separately. Confidence intervals (CIs) for IRs were estimated by modelling the number of incident HPV infections as a Poisson variable.[6, 23] Hazard ratios (HRs) comparing IRs for high-risk versus low-risk HPV infections and for glans versus shaft infections were estimated using the Wei–Lin–Weissfeld method to adjust for correlated data within subjects.[24]

HRs and corresponding 95% CIs for potential risk factors of HPV incidence, among men who were HPV negative at baseline, were estimated via age-adjusted parametric frailty models assuming a Weibull distribution and allowing one man to contribute >1 incident infection to analyses.[25] HPV infections were right censored if they were not detected during follow-up. All other HPV infections were interval censored with the upper limit of the interval corresponding to the visit the infection was first detected and the lower limit corresponding to the last visit where the infection was absent. Multivariate parametric frailty models were used to estimate adjusted HRs and 95% CIs. The full multivariate model included age (≤19, 20–21, ≥22 years), condom use in the last 6 months and education, believed a priori to be variables of interest, and variables with significant marginal associations for HPV incidence (employment status, bathing frequency and number of sexual partners in the past 12 months (≤1, ≥2 partners)). The final multivariate model included age and variables remaining significant in the multivariate model after a backwards elimination process. Statistical significance was determined by likelihood ratio tests. Age-adjusted and final multivariate models were then estimated using high-risk HPV incidence as the outcome.

β-Globin positivity in the glans and shaft specimens was 57.7% and 36.0% at baseline, 57.9% and 35.8% at the 6-month visit, and 68.3% and 46.3% at the 12-month visit, respectively. Results did not differ substantially when analyses were restricted to β-globin-positive samples; thus, reported analyses used HPV DNA data from all penile exfoliated cell specimens unless otherwise stated.

RESULTS

The median age of the 966 participating men at enrolment was 20 years (range 17–24) (table 1). Most men did not live with their sexual partner at baseline (94.6%) and had at least a secondary education (63.6%). No participant reported having a male sexual partner. Approximately a quarter (25.8%) of men reported never using a condom in the past 6 months. The prevalence of HSV-2 seropositivity was 26.5%, with *Chlamydia trachomatis* (4.0%) and *Neisseria gonorrhoeae* (1.6%) laboratory-diagnosed infections being less common.

Overall baseline prevalence of HPV infection was 50.1%, with multiple HPV infections found among 29.0% of participants (table 2). High-risk and low-risk HPV infections were detected in 37.5% and 10.6% of participants, respectively, at baseline. The four most common HPV types were HPV16 (9.9%), 56 (6.3%), 67 (5.8%) and 52 (5.4%) within single or multiple infections. All other known HPV types detected had a prevalence of <5%.

The median time of study follow-up was 12.1 months (inter-quartile range (IQR) 0.5), including 65 (7%) of men who had two visits and 901 (93%) with three visits. The median time between study visits was 6.1 months (IQR 0.4) from baseline to the 6-month visit, and 6.0 months (IQR 0.2) from the 6- to 12-month visits.

IR analysis

The IR of any HPV infection was 49.3/1000 person-months for the first HPV type detected at either the glans or shaft (table 2). Incident infections of multiple HPV types were common with an incidence of 24.3/1000 person-months. The IR of high-risk HPV was higher than low-risk HPV (HR=1.6; 95% CI 1.3 to 2.0). The individual types with the highest IRs in either single or multiple infections were HPV16 (10.9/1000 person-months), HPV35 (6.0/1000 person-months), HPV JC9710 (6.0/1000 person-months) and HPV56 (5.5/1000 person-months). All other HPV types had IRs ≤5.0/1000 person-months.

The incidence of any HPV infection was 44.4/1000 person-months in the glans compared with 21.6/1000 person-months in the shaft (HR=2.1; 95% CI 1.7 to 2.4) (table 3). IRs of high-risk and low-risk infections in the glans were 27.3 and 18.8/1000 person-months, respectively, with lower rates for high-risk and low-risk HPV infections in the shaft (13.1 and 7.8/1000 person-months, respectively). The incidence of multiple HPV type infections was higher in the glans versus shaft (HR=2.9; 95% CI 2.3 to 3.6). When restricting analyses to β-globin-positive samples, IRs for overall HPV in the glans and shaft (47.9 and 22.4/1000 person-months, respectively) were similar to the corresponding IRs observed among all samples.

Risk factors for HPV incidence

The strongest risk factors for incident HPV infections in age-adjusted models were bathing less frequently than daily (HR=3.0; 95% CI 1.2 to 7.9), having ≥2 female sexual partners in the year prior to enrolment (HR=1.6; 95% CI 1.2 to 2.2) and being employed (HR=1.4; 95% CI 1.1 to 1.9) (table 4). Other potential risk factors assessed, including HSV-2 seropositivity, living with one's partner and condom use in the last 6 months, were not significantly associated with HPV IRs. In the final model, having ≥2 sexual partners in the past year (HR=1.6; 95% CI 1.2 to 2.1) remained associated with HPV incidence, after controlling for age, employment status and bathing frequency. Less frequent bathing (HR=2.6; 95% CI 1.02 to 6.5) and employment status (HR=1.4; 95% CI 1.1 to 1.9) also remained significant in the final model. Results were similar when modelling incident high-risk HPV infections as the outcome in both age-adjusted and multivariate models, except that employment status was not significant in the final model (table 4).

When analyses were restricted to β-globin-positive samples, the associations between overall HPV incidence and bathing frequency (HR=4.7; 95% CI 1.6 to 14.2) and the number of partners in the last 12 months (HR=1.8; 95% CI 1.2 to 2.6) remained significant albeit less precise, after adjusting for age, bathing frequency and number of sexual partners. Employment status, however, was no longer significant in the age-adjusted model (HR=1.3; 95% CI 0.9 to 2.0). Bathing frequency and the number of sexual partners in the past 12 months remained strong risk factors when modelling incident high-risk HPV as the outcome among β-globin-positive samples (results not shown).

DISCUSSION

Incident HPV infections were common among Kenyan men, with an IR of almost 50/1000 person-months. The incidence of high-risk HPV infections in the glans was higher than the incidence of low-risk infections in the glans and of HPV infections in the shaft. The strongest risk factors for overall HPV incidence were having at least two sexual partners in the year prior to enrolling in the RCT and bathing less frequently than daily.

This is the largest follow-up study of HPV infection, to our knowledge, among uncircumcised men to date. It is also one of the first to determine risk factors for HPVacquisition among men from sub-Saharan Africa. A sensitive GP5+/6+ PCR assay was

used to detect a wide range of HPV types in a central laboratory, and separate HPV laboratory testing for glans and shaft specimens allowed for stratified analyses by anatomical site. Novel parametric frailty models were used to assess several potential risk factors for HPV acquisition, which allow for the analysis of clustered survival data using arbitrary censoring.[25]

The IR of 49.3/1000 person-months found in our study is higher than previously reported IR estimates among men, ranging from 17.9/1000 person-months among military men from Mexico to 38.4/1000 person-months among men from Brazil, Mexico and the USA.[6–8, 14] The higher IR in our study could be due in part to the longer duration of 1 year between visits in the study from Mexico,[8] which may have underestimated the true IR, and the lower percentage of uncircumcised men in the international and US studies.[6, 7, 14] Our IR estimate for high-risk HPV infection in the glans (27.3/1000 person-months, equivalent to 32.8/100 person-years) was slightly higher than the corresponding IR in the glans among HIV-negative, married men participating in the control arm of an RCT of male circumcision in Uganda (IR=29.4/100 person-years).[10] The slightly higher IR found in our Kenyan study could be due to differences in age and marital status as the Uganda study had a higher median age and only included married participants.

HPV16, the most prevalent HPV type in this population (9.9%), also had the highest incidence (10.9/1000 person-months). A high incidence of HPV16 has been similarly reported in other studies among both men[6, 7, 9, 14] and women.[26] The high rate of acquisition of HPV16 has a clear implication for increasing cancer risk among men and their sexual partners, as HPV16 is the most common HPV type found in penile cancer among men;[2] cervical, vulvar and vaginal cancers among women;[1, 27] and in anal and oropharyngeal cancers in both sexes.[3, 4]

Penile HPV IRs in our study were higher in the glans specimen, including the inner foreskin, compared with the shaft (HR=2.1; 95% CI 1.7 to 2.4). Our results are in contrast to the findings of a US study of 240 men.[7] In this highly circumcised US population, the cumulative probability of incident HPV infection did not differ by anatomical site (44.3% in glans vs 45.4% in shaft). Among uncircumcised men, there may be a larger disparity in HPV acquisition by penile site, potentially attributable to keratinisation of the glans epithelium and removal of the inner foreskin after circumcision.

Our findings indicate that less frequent bathing was a strong risk factor for HPV incidence. These findings are similar to those in a previous report among this population that found less frequent bathing to be the strongest risk factor for cross-sectional HPV point-prevalence.[20] To our knowledge, no other studies of penile HPV acquisition among men have investigated overall bathing frequency as a potential risk factor. Three studies of penile HPV infection reported no association with the time since last bath or shower[7] nor with genital washing after intercourse.[8, 28] Similarly, we did not find an association between the number of hours until bathing after sex and HPV acquisition. Little is known about the effect of improved penile hygiene on HPV infection. While bathing more frequently may not completely prevent HPV infection in men, our findings provide evidence that more frequent bathing is associated with a decreased risk of HPV acquisition. To assess whether more frequent bathing reduces incident HPV infections, RCTs should be conducted to examine the effect of male bathing on incident HPV infections. Our results indicated that men who reported a higher number of recent sexual partners also had higher HPV IRs, as was found in previous studies of HPV incidence in men.[7, 9] We also found a slightly elevated risk of overall HPV incidence among men who were employed, but this association was not associated with high-risk HPV incidence.

The 6-month interval between each visit was a limitation of this study as participants in our study could have acquired a new HPV infection and cleared it before their subsequent follow-up visit, potentially underestimating HPV incidence in our study. β-Globin positivity was also relatively low in our study; however, it has been previously indicated that β-globin-PCR-negative samples may contain detectable HPV as HPV copies may often exceed those of the β-globin gene.[20] When restricting our analyses to β-globin-positive samples, IRs for overall HPV in the glans and shaft (47.9 and 22.4/1000 person-months, respectively) were similar to the IRs observed in the glans and shaft among all samples (44.4 and 21.6/1000 person-months, respectively). Bathing frequency and number of recent sexual partners also remained strong risk factors of HPV incidence among β-globin-positive samples.

The generalisability of our findings may be somewhat limited, given that participants were a select population of primarily unmarried, uncircumcised men with at least a secondary education who met eligibility criteria for an RCT that entailed circumcision. Uncircumcised men may be more likely to acquire HPV infections than circumcised men[10, 18] and risk factors, such as less frequent bathing, may be modified by circumcision status; thus, caution should be taken when comparing our findings with those of circumcised populations.

In conclusion, we found a high incidence of high-risk HPV in the glans among uncircumcised men. Male circumcision has been found to be an effective intervention for decreasing high-risk HPV acquisition among men.[10, 18] For men who remain uncircumcised, reducing the number of recent sexual partners and improving penile hygiene could potentially reduce HPV acquisition.

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Key messages

- Data on human papillomavirus (HPV) acquisition are needed among men from developing regions including Africa.
- HPV incidence rates were notably high among high-risk uncircumcised men from Kisumu, Kenya.
- Reducing the number of sexual partners and improving penile hygiene could potentially reduce HPV acquisition among uncircumcised men.

Table 1

Baseline characteristics of 966 uncircumcised men enrolled in the control arm of a male circumcision trial between 2002 and 2005 in Kisumu, Kenya

Variable	n (%)*
Age (years)†	20 (17–24)‡
Number of female partners in last 12 months	2 (0–28)‡
Lifetime number of female sexual partners	4 (1–86)‡
Living with female sexual partner	
No	910 (94.6)
Yes	52 (5.4)
Education	
Primary or none	352 (36.4)
Secondary or tertiary	614 (63.6)
Employment status	
Unemployed	623 (64.5)
Employed	343 (35.5)
Condom use in last 6 months	
Never	219 (25.8)
≤50%	333 (39.2)
>50%	298 (35.1)
Herpes simplex virus type 2 seropositive	
No	678 (73.5)
Yes	244 (26.5)
Presence of *Chlamydia trachomatis*	
No	915 (96.0)
Yes	38 (4.0)
Presence of *Neisseria gonorrhoeae*	
No	938 (98.4)
Yes	15 (1.6)
Bathing frequency	
Less than daily	20 (2.1)
Daily	937 (97.9)

*Percentages do not include missing values for living with partner status (n=4), condom use (n=116), HSV-2 seropositivity (n=44), presence of *Chlamydia trachomatis* (n=13), presence of *Neisseria gonorrhoeae* (n=13) and bathing frequency (n=9).

†The study inclusion criteria required participants be aged 18–24 years; there was one protocol violation resulting in one 17-year-old included in this study.

‡Median (range); n=10 missing number of female partners in last 12 months; n=74 missing lifetime number of female sexual partners.

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Table 2

Prevalence and incidence of HPV Infection among 966 uncircumcised men in Kisumu, Kenya

HPV type	Baseline HPV prevalence (%)	Incident HPV infections (n)	Subjects at risk (n)	Person-months	IR*	95% CI
Any HPV	50.1	218	482	4419.7	49.3	43.0 to 56.3
Multiple	29.0	176	686	7216.3	24.3	20.9 to 28.3
High-risk HPV†	37.5	179	581	5758.7	31.1	26.7 to 36.0
16	9.9	107	870	9848.8	10.9	8.9 to 13
18	3.6	40	931	11 016.0	3.6	2.6 to 4.9
31	3.7	35	930	11 059.7	3.2	2.2 to 4.4
33	1.4	21	952	11 375.1	1.8	1.1 to 2.8
35	3.2	66	935	10 929.7	6.0	4.7 to 7.7
39	2.3	28	944	11 264.7	2.5	1.7 to 3.6
45	4.6	29	922	10 965.1	2.6	1.8 to 3.8
51	4.2	39	925	10 935.8	3.6	2.5 to 4.9
52	5.4	33	914	10 831.2	3.0	2.1 to 4.3
56	6.3	58	905	10 575.2	5.5	4.2 to 7.1
58	3.9	43	928	10 950.7	3.9	2.8 to 5.3
59	4.2	27	925	11 043.7	2.4	1.6 to 3.6
66	4.6	51	922	10 816.9	4.7	3.5 to 6.2
68	1.3	9	953	11 465.2	0.8	0.4 to 1.5
Low-risk HPV†	10.6	173	822	8733.3	19.8	17.0 to 23.0
6	3.4	49	933	10 990.5	4.5	3.3 to 5.9
11	2.1	28	946	11 265.4	2.5	1.7 to 3.6
26	1.2	17	954	11 430.0	1.5	0.9 to 2.4
30	1.4	15	952	11 439.4	1.3	0.7 to 2.2
32	1.3	19	953	11 392.9	1.7	1.0 to 2.6
34	0.1	0	965	11 669.7	0.0	0.0 to 0.3
40	3.5	38	932	11 057.3	3.4	2.4 to 4.7
42	4.9	54	919	10 778.4	5.0	3.8 to 6.5
43	3.7	43	930	10 964.5	3.9	2.8 to 5.3
44	0.0	1	966	11 671.5	0.1	0.0 to 0.5

HPV type	Baseline HPV prevalence (%)	Incident HPV infections (n)	Subjects at risk (n)	Person-months	IR*	95% CI
53	1.0	9	956	11 470.9	0.8	0.4 to 1.5
54	0.9	8	957	11 521.2	0.7	0.3 to 1.4
55	1.2	21	954	11 405.9	1.8	1.1 to 2.8
57	0.0	2	966	11 660.1	0.2	0.0 to 0.6
61	0.0	1	966	11 671.6	0.1	0.0 to 0.5
64	0.0	2	966	11 662.3	0.2	0.0 to 0.6
67	5.8	46	910	10 676.5	4.3	3.1 to 5.7
69	1.0	22	956	11 428.0	1.9	1.2 to 2.9
70	2.3	35	944	11 213.5	3.1	2.2 to 4.3
71	0.0	2	966	11 663.2	0.2	0.0 to 0.6
72	0.8	7	958	11 530.7	0.6	0.2 to 1.3
73	1.4	32	952	11 301.5	2.8	1.9 to 4.0
81	3.3	38	934	11 025.6	3.4	2.4 to 4.7
82	0.6	12	960	11 529.4	1.0	0.5 to 1.8
83	1.7	32	950	11 280.5	2.8	1.9 to 4.0
84	0.3	4	963	11 625.6	0.3	0.1 to 0.9
85	0.3	8	963	11 592.0	0.7	0.3 to 1.4
86	0.1	9	965	11 615.9	0.8	0.4 to 1.5
89	2.1	24	946	11 292.3	2.1	1.4 to 3.2
JC9710	4.6	65	922	10 769.8	6.0	4.7 to 7.7
X	5.4	47	914	10 820.2	4.3	3.2 to 5.8

Estimates of prevalence and IR were based on HPV detection at either anatomical site (glans or shaft).

*IR per 1000 person-months for the first type detected in the glans or shaft.

†Infections with multiple HPV types were considered high-risk if one or more high-risk HPV types were detected. All other multiple infections were considered low-risk types unless they included HPV-X.

HPV, human papillomavirus; IR, incidence rate.

Table 3

Incidence of HPV infection stratified by anatomical site among 966 uncircumcised men in Kisumu, Kenya

HPV type	Incident HPV infections in glans (n)	IR (95%CI)*	Incident HPV infections in shaft (n)	IR (95% CI)*	HR (95% CI)
Any HPV	215	44.4 (38.4 to 50.4)	184	21.6 (18.6 to 25.0)	2.1 (1.7 to 2.4)
High-risk HPV†	173	27.3 (23.4 to 31.7)	121	13.1 (10.9 to 15.6)	2.1 (1.7 to 2.6)
Low-risk HPV†	167	18.8 (16.0 to 21.9)	81	7.8 (6.2 to 9.7)	2.4 (1.9 to 3.1)
Multiple	164	21.6 (18.4 to 25.2)	79	7.5 (6.0 to 9.4)	2.9 (2.3 to 3.6)
HPV16	88	8.6 (6.9 to 10.6)	48	4.4 (3.2 to 5.8)	2.0 (1.4 to 2.7)
HPV18	35	3.1 (2.2 to 4.4)	17	1.5 (0.9 to 2.4)	2.1 (1.4 to 3.3)

*IR=incidence per 1000 person-months.

†Infections with multiple HPV types were considered high-risk if one or more high-risk HPV types were detected: HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68. All other multiple infections were considered low-risk if they did not include HPV-X.

HPV, human papillomavirus; IR, incidence rate.

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Table 4

Risk factors of incident HPV infection at the glans or shaft over 12 months among 482 men in Kisumu, Kenya, who were HPV-negative at the baseline visit

	Overall HPV		High-risk HPV	
Baseline risk factor	Age-adjusted model Age-adjusted HR (95% CI)*	Final multivariate model Adjusted HR (95% CI) †	Age-adjusted model Age-adjusted HR (95% CI)*	Final multivariate model Adjusted HR (95% CI) ‡
Age (years)				
17–19	1.0 (0.7 to 1.4)	1.0 (0.7 to 1.5)	1.3 (0.9 to 2.0)	1.3 (0.9 to 2.0)
20–21	1.0 (0.7 to 1.4)	1.0 (0.7 to 1.4)	1.1 (0.8 to 1.7)	1.2 (0.8 to 1.8)
22+	1	1	1	1
Employment status				
Unemployed	1	1	1	1
Employed	1.4 (1.1 to 1.9)	1.4 (1.1 to 1.9)	1.4 (1.0 to 1.9)	1.3 (0.9 to 1.9)
Education				
Primary or none	1.8 (1.0 to 3.1)		1.6 (0.8 to 3.0)	
Secondary	1.4 (0.8 to 2.4)		1.1 (0.6 to 2.1)	
Tertiary	1		1	
Presence of *Chlamydia trachomatis*				
No	1		1	
Yes	1.9 (0.9 to 4.1)		1.8 (0.7 to 4.2)	
Herpes simplex virus type 2 seropositive				
No	1		1	
Yes	1.3 (1.0 to 1.8)		1.4 (0.9 to 2.0)	
Bathing frequency				
Less than daily	3.0 (1.2 to 7.9)	2.6 (1.0 to 6.5)	3.5 (1.2 to 10.1)	3.0 (1.1 to 8.4)
Daily	1	1	1	1
Use of condom last partner				
No	1		1	
Yes	0.8 (0.6 to 1.0)		0.8 (0.5 to 1.1)	
Condom use last 6 months				
Never	1		1	
≤half time	1.3 (0.9 to 1.8)		1.5 (1.0 to 2.2)	
>half time	0.9 (0.7 to 1.3)		1.1 (0.7 to 1.6)	
Lifetime # of female partners				
1	1		1	
2–5	0.9 (0.6 to 1.4)		0.9 (0.6 to 1.4)	
6+	1.4 (1.0 to 2.1)		1.3 (0.8 to 2.1)	
Partners in last 12 months				
0–1	1	1	1	1
2+	1.6 (1.2 to 2.2)	1.6 (1.2 to 2.1)	1.6 (1.1 to 2.3)	1.5 (1.1 to 2.2)
Living with female sexual partner				
No	1		1	

	Overall HPV		High-risk HPV	
Baseline risk factor	Age-adjusted model Age-adjusted HR (95% CI)*	Final multivariate model Adjusted HR (95% CI) †	Age-adjusted model Age-adjusted HR (95% CI)*	Final multivariate model Adjusted HR (95% CI) ‡
Yes	1.8 (1.0 to 3.3)		1.7 (0.8 to 3.5)	
Age at first intercourse				
≤14	1.3 (0.9 to 1.8)		1.3 (0.8 to 1.9)	
15–16	1.1 (0.8 to 1.5)		1.2 (0.8 to 1.8)	
17+	1		1	
Years of sexual activity				
≤2	1		1	
3–4	1.2 (0.8 to 1.8)		1.4 (0.9 to 2.3)	
5–6	1.1 (0.7 to 1.7)		1.3 (0.8 to 2.1)	
7+	1.4 (0.9 to 2.1)		1.5 (0.9 to 2.6)	
Paid money for sex in last 6 months				
No	1		1	
Yes	1.0 (0.6 to 1.7)		1.1 (0.7 to 1.9)	
Travel to Nairobi in last 6 months				
No	1		1	
Yes	0.9 (0.6 to 1.3)		1.0 (0.7 to 1.6)	
Ever tasted alcohol				
No	1		1	
Yes	1.0 (0.7 to 1.4)		1.1 (0.8 to 1.6)	
Hours until washing penis after sex				
≤1	1		1	
2–5	0.8 (0.6 to 1.2)		0.8 (0.5 to 1.2)	
6+	1.2 (0.9 to 1.7)		1.0 (0.7 to 1.5)	
Penile cuts or abrasions during sex				
Never	1		1	
Ever	1.1 (0.8 to 1.5)		1.2 (0.9 to 1.7)	
Presence of sexually transmitted disease previous 6 months or current (self-reported)				
No	1		1	
Yes	0.8 (0.4 to 1.3)		0.5 (0.2 to 1.1)	

*Adjusted for age (<20, 20–21, >21 years).

†Adjusted for age, employment status, bathing frequency and partners in last 12 months (0–1, >1 partners).

‡Adjusted for age, bathing frequency and partners in last 12 months.

HPV, human papillomavirus.