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Circumcision and Human Papillomavirus Infection in Men: A Site-Specific Comparison

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Abstract

Background—Lack of circumcision has been identified as a risk factor for male genital human papillomavirus (HPV) infection, although this association has not been consistently supported.

Methods—Specimens for HPV testing were collected from a cohort of 379 (primarily heterosexual) adult males. HPV prevalence in the glans penis and coronal sulcus, penile shaft, scrotum, semen, and urine was compared by circumcision status.

Results—Overall, HPV DNA prevalence ranged from 6% in semen to 52% in the penile shaft. The prevalence of any HPV infection in the glans/corona was significantly higher in uncircumcised men (46%) than in circumcised men (29%) (odds ratio [OR], 1.96 [95% confidence interval {CI}, 1.02-3.75], adjusted for demographic characteristics and sexual history). Uncircumcised men also had an increased risk of oncogenic HPV infection (adjusted OR, 2.51 [95% CI, 1.11-5.69]) and infection with multiple HPV types (adjusted OR, 3.56 [95% CI, 1.50-8.50]). Among uncircumcised men, HPV prevalence in the foreskin (44%) was comparable to that in the glans/corona, and type-specific positivity was observed between the 2 sites ($\kappa = 0.52$).

Conclusions—Uncircumcised men have an increased risk of HPV infection, including with oncogenic HPV, specifically localized to the glans/corona, possibly because of its proximity to the foreskin, which may be particularly vulnerable to infection.

Human papillomavirus (HPV) infection is the principal cause of cervical cancer [1] and is an etiologic agent of other malignancies [2-6]. The natural history of human papillomavirus (HPV) infection is well-characterized in women, and most female infections are acquired through sexual contact with men [7]. HPV infection is also common in men and is usually asymptomatic, although prevalence estimates vary widely, from 1% to 73% [8-19].

There is evidence that HPV infection and genital warts occur more frequently in uncircumcised men than in circumcised men [14-16,18-21] and that uncircumcised men have an increased risk of penile cancer [22-25]. An observed elevated risk of cervical cancer among partners of uncircumcised men [18] suggests that lack of circumcision may also enhance the transmission of HPV to female partners.

Nevertheless, a relationship between circumcision and HPV has not been supported by all studies [10,19,23,26,27]. Inconsistencies across studies may be due to differences in sites

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sampled, sampling methods, outcome measures (i.e., HPV DNA vs. clinical lesions), HPV DNA testing methods, and populations studied.

In examining the association between HPV infection and circumcision status, it is critical to include site-by-site comparisons of genital sites, which permit distinction between the external genitals and the urethra and between individual penis subsites. The present study examined the prevalence of HPV by circumcision status in multiple, specific, external genital sites and in semen and urine in a cohort of multiethnic and predominantly heterosexual adult men.

SUBJECTS, MATERIALS, AND METHODS

Study design and recruitment

The study was approved by the Committee on Human Studies of the University of Hawaii. Written, informed consent was obtained from all study subjects. Study participants were primarily recruited from a university population in Hawaii. The study was promoted through campus flyers, newspaper advertisements, and invitations sent to the E-mail addresses of enrolled male undergraduate and graduate students. Eligible men were ≥18 years old, English speaking, and had no history of blood-clotting disorders. Between July 2004 and December 2006, 379 adult males were recruited and followed at 2-month intervals. Study visits were conducted at the University Health Services of the University of Hawaii. The present report focuses on the baseline HPV status of cohort members.

Specimen collection

Trained clinicians collected exfoliated cell samples for HPV DNA detection. Separate specimens were collected from the glans penis and corona sulcus (hereafter referred to as “glans/corona”), penile shaft, scrotum, and inner foreskin (among uncircumcised men) by means of a method described elsewhere in which textured paper and a salinemoistened swab are used [9,10]. Visible warts and lesions were avoided in sampling the genitals. Disposable gloves worn by clinicians were changed between sampling of each site to minimize the risk of contamination between sites. First-catch urine (30 mL), in which the measurement of HPV was considered to be a proxy for urethral infection, was self-collected at the clinic. Semen specimens were self-collected at home via masturbation with latex gloves within 24 h of each visit.

Interview

A structured survey was administered by a trained interviewer at each study visit. At enrollment, a comprehensive survey queried social and demographic information and medical, sexual, and reproductive histories.

HPV DNA testing and genotyping

DNA was extracted from specimens by use of commercial reagents (Qiagen). The polymerase chain reaction used PGMY09/PGMY11 primers to amplify a 450-bp region of the L1 HPV genome [28].

HPV-positive specimens were subsequently genotyped using a reverse line blot detection method [29] for 37 different HPV types, including oncogenic/probable oncogenic types (HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51-53, 56, 58, 59, 66, 68, 73, 82, and IS39), nononcogenic types (HPV types 6, 11, 40, 42, 54, 61, 70, 72, 81, and CP6108), and types with undetermined risk status (HPV types 55, 62, 64, 67, 69, 71, 83, and 84) [30,31]. HPV-positive specimens that were subsequently found to be negative in the genotyping assay were considered to be unclassified HPV-positive specimens. The HPV testing and genotyping procedure has been detailed elsewhere [9].

All specimens were also tested using GH20 and PC04 primers to amplify a 268-bp region of the human β-globin gene as an internal control for sample sufficiency. Specimens testing negative for β-globin were considered to be insufficient and were excluded from analyses.

Statistical analysis

All analyses were conducted using SAS (version 8; SAS Institute). Because there is a strong interaction between HIV and HPV infections [32], the 28 men with a positive self-reported HIV history were excluded in all analyses of HPV, which focused on healthy males.

Characteristics of circumcised and uncircumcised men were compared using the χ^2 statistic of association for categorical variables and the 2-sample *t* test for continuous variables.

The association of possible risk factors with HPV status was evaluated using unconditional logistic regression. Univariate and multivariate analyses were used to calculate crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs).

The association between HPV status and circumcision status was compared by anatomic site. For each site, HPV-negative circumcised men were the reference category. Variables identified as possible confounders for the association between HPV infection and circumcision status were included as covariates in the multivariate logistic regression models.

The multivariate model included the following covariates: age (continuous), birthplace (United States/non-United States), race/ethnicity (white/nonwhite), years of education (continuous), age at initial sexual intercourse (continuous), lifetime number of female sex partners (continuous), history of sex with men (yes/no), condom use (ever/never), and history of genital warts (yes/no).

Anatomic sites were evaluated individually and as groups (external penis, external genitals, and any site). The external penis included the glans/corona and shaft. The external genitals included the glans/corona, shaft, and scrotum. Any site included the glans/corona, shaft, scrotum, urine, and semen.

For evaluation of associations, HPV types were grouped as follows: (1) any HPV, (2) oncogenic (including probable oncogenic), (3) nononcogenic/undetermined risk status/unclassified types, and (4) multiple HPV types (positivity for>1 HPV type). Estimation of risk associated with oncogenic types included specimens positive for other types. Likewise, risk estimation for nononcogenic/undetermined risk status/unclassified types included specimens concurrently positive for oncogenic types.

Concordance in type-specific HPV detection between different anatomic sites of the same individual was evaluated using the κ statistic. κ values >0.40 were considered to be indicative of agreement beyond that expected by chance [33].

RESULTS

The present analysis included 379 men enrolled in the cohort. The mean age of participants was 29 years. The majority of men were white, single (never married), and had at least some post-secondary education. Seventy-seven percent of men were heterosexual. Fifty-three percent reported a total of 6 or more female sex partners during their lifetimes. A history of soliciting female commercial sex workers was reported by 13% of men. HIV infection was reported by 7% of men. HIV-positive individuals were excluded from all analyses of HPV status, resulting in 351 men for subsequent analyses.

In univariate analysis, cigarette smoking, history of sex with men, lifetime number of female sex partners, history of genital warts, and circumcision status were associated with HPV status at 1 or more anatomic sites. Age, race/ethnicity, birthplace, education level, marital status, age at initial sexual intercourse with a female, and condom use were not associated with HPV status.

In multivariate analysis (adjusting for age, birthplace, race/ethnicity, education level, lifetime number of female sex partners, history of sex with men, age at initial sex, condom use, history of genital warts, cigarette smoking, and circumcision status), only sex with men, lifetime number of female sex partners, and circumcision status were associated with HPV status. History of sex with men was inversely associated with HPV infection of the shaft (adjusted OR, 0.44 [95% CI, 0.21-0.94]). Lifetime number of female sex partners was positively associated with HPV infection of the shaft and scrotum (adjusted ORs of 6.93 [95% CI, 2.34-20.48] [$P_{trend} < .0001$] and 3.54 [95% CI, 1.14-10.96] [$P_{trend} = .003$], respectively, for >15 partners relative to <2 partners).

Circumcision status was based on clinical examination; 79% of men were circumcised. Four men who reported being circumcised were observed to have a foreskin on examination and were classified as uncircumcised. Visible genital warts were observed in 4% of study participants.

Compared with circumcised men, uncircumcised men had an older age distribution ($P = .01$), were more likely to be of Asian or other racial/ethnic background ($P = .003$), were more likely to be born outside of the United States ($P < .001$), had a broader distribution by education level ($P = .003$), and were less likely to have a history of genital warts ($P = .007$) (table 1). There were no differences between circumcised and uncircumcised men with respect to sexual history, condom use, cigarette smoking history, and history of sexually transmitted infections other than genital warts.

Overall, 90% (2001/2226) of specimens were sufficient on the basis of β-globin detection. There was no difference in specimen sufficiency by circumcision status for any anatomic site (data not shown).

The overall HPV prevalence was highest in the penile shaft (52%) followed by the scrotum (40%), glans/corona (32%), urine (10%), and semen (6%) (table 2). Among uncircumcised men, HPV prevalence in the foreskin (44%) was comparable to that in the glans/corona (46%).

In comparisons by circumcision status, uncircumcised men had a higher prevalence of any HPV infection of the glans/corona (46% vs. 29%; adjusted OR, 1.96 [95% CI, 1.02-3.75]). Uncircumcised men also had an increased risk of oncogenic infection (31% vs. 16%; adjusted OR, 2.51 [95% CI, 1.11-5.69]) and infection with multiple HPV types in the glans/corona (31% vs. 12%; adjusted OR, 3.56 [95% CI, 1.50-8.50]).

The highest prevalence of HPV was observed in the penile shaft for both groups. HPV prevalence for circumcised men (50%) was lower than for uncircumcised men (60%), although differences between the 2 groups were not statistically significant. No association with circumcision status was observed for sites other than the glans/corona.

Overall, 33 different HPV genotypes were detected across all sites (data not shown). The indeterminate risk type HPV-84 was the most common type found overall and in the shaft (14%), foreskin (14%), scrotum (10%), and urine (7%).

In the glans/corona, the distribution of oncogenic HPV types varied by circumcision status (table 3). HPV-84 was the most common HPV type detected in the glans/corona of both

uncircumcised and circumcised men. The most common oncogenic HPV types detected in the glans/corona were HPV-16 and HPV-39 among circumcised men and HPV-66 followed by HPV-52, -53, and -73 among uncircumcised men. The most common nononcogenic type detected in the glans/corona in both circumcised and uncircumcised men was CP6108.

Correlation in type-specific HPV detection was evaluated between paired anatomic sites from the same individuals. Among uncircumcised men, type-specific agreement was observed between the foreskin and the glans/corona ($\kappa = 0.52$ [95% CI, 0.30-0.74]) and the foreskin and the shaft ($\kappa = 0.43$ [95% CI, 0.22-0.65]). Among circumcised men, type-specific agreement in HPV infection was observed between the shaft and scrotum ($\kappa = 0.56$ [95% CI, 0.45-0.67]), but this association was not among uncircumcised men ($\kappa = 0.39$ [95% CI, 0.19-0.59]).

DISCUSSION

We have demonstrated that HPV infection of the exterior genitals is common in adult males and that its prevalence varies by circumcision status. Specifically, uncircumcised men had an increased risk of HPV infection of the glans/corona. Lack of circumcision was associated with an increased risk of any HPV infection, oncogenic HPV infection, and infection with multiple HPV types in the glans/corona.

Our results are consistent with the results of other studies reporting an inverse association of circumcision and genital HPV infection [14-16,18,20]. Ours is the first such study to include separate evaluation of penis subsites as well as the scrotum, semen, and urine.

In the present study, the foreskin of uncircumcised men was retracted when sampling the glans/corona and the inner foreskin. The mechanism by which circumcision may protect against HPV infection is unclear. The glans/corona of an uncircumcised man is normally covered by the unretracted foreskin. During sexual intercourse, the foreskin becomes retracted, exposing both the glans/corona and inner foreskin. The inner foreskin is comprised of variably keratinized squamous mucosal epithelia [34]. It has been suggested that retraction of the foreskin during intercourse exposes the inner mucosal surface to HPV and that access to basal cells is further facilitated through tears and abrasions, which can occur during intercourse [18,35]. If this hypothesis is correct, removal of the foreskin may reduce the surface area exposed to HPV from an infected partner and decrease trauma to the mucosal surface [18].

The increased risk of multiple HPV infection among uncircumcised men may simply reflect an enhanced vulnerability of the foreskin to multiple episodes of infection by different HPV types over time.

The comparable prevalence of HPV in the glans/corona and foreskin of uncircumcised men and the type-specific concordance between these sites may be evidence of autoinoculation, whereby HPV is acquired in inner foreskin on retraction and subsequently transmitted to the glans/corona on contact. Alternatively, it may also reflect multifocal infections acquired contemporaneously at the 2 proximate sites from the same infected partner.

The role played by circumcision has been examined in the etiology of other sexually transmitted infections. Circumcision has been demonstrated to reduce the risk of HIV infection [36,37]. This protection may be afforded through removal of the foreskin, a rich source of cells targeted by HIV, notably $CD4^+$ T cells and Langerhans cells [35,38]. There also is evidence that circumcision may protect against such sexually transmitted infections [39] as gonorrhea [26], syphilis [26,35], and chancroid [35] but not others, such as herpes simplex virus type 2 infection [35,40].

We observed that urethral HPV was not correlated with typespecific detection at any site and that its prevalence was much lower than that at the external penis. This distinguishes HPV infection from other sexually transmitted infections for which the urethra is the primary site of infection, such as chlamydia and gonorrhea [41].

In the present study, uncircumcised men were less likely than circumcised men to report a history of genital warts. This is consistent with the fact that genital warts are caused by nononcogenic types [42], and we did not observe an increased risk of nononcogenic HPV infection for uncircumcised men at any site, including the glans/corona. Our findings are in accordance with some studies in finding an increased prevalence of genital warts among circumcised men [23,26]. One study observed an increased risk of genital warts in the external penis but not in the urethra of uncircumcised men [21].

In addition to the overall increased risk of HPV infection, we demonstrated that the glans/corona of uncircumcised men was at increased risk of infection with oncogenic types. Baldwin et al. [20] also reported an association between circumcision status and oncogenic infection. Interestingly, we observed some differences in the distribution of oncogenic HPV types in the glans/corona by circumcision status. For example, the most common oncogenic type was HPV-16 in circumcised men and HPV-66 in uncircumcised men.

It is not clear why the glans/corona of uncircumcised men would be particularly vulnerable to oncogenic genotypes. However, the observation is notable given that the glans is the most common subsite of penile carcinomas [43] and given the evidence that uncircumcised men are at greater risk for penile cancers [22-25]. Relative to cervical cancers, cancers of the penis are rare in the United States and other developed countries, accounting for <1% of malignancies among men [44]. The estimated proportion of penile cancers associated with HPV varies from 29% to 82%, based on recent studies of archival tissue [22,23,45-47]. There is geographic variation in penile cancer, with the highest incidences occurring in countries in Southeast Asia, Latin America, and eastern and southern Africa and in India [44]. One of the lowest incidences of penile cancer is observed in Israel, which has one of the highest rates of circumcision [44]. It is also possible that circumcision status reflects cultural factors (including sexual experiences) that influence HPV infection. Uncircumcised men in our population were more likely to be foreign born. In our diverse student population, this included both Asian-born and European-born males.

Previous studies have observed an increased risk of cervical cancer in partners of uncircumcised men [18]. This is consistent with our results of an increased prevalence of oncogenic HPV types in uncircumcised men. Although it has not been demonstrated that women are more likely to acquire HPV from sex with uncircumcised men than with circumcised men, it is intuitive that a higher HPV prevalence in men could lead to an increased risk of transmission to female partners. Whether HPV is more efficiently transmitted to females due to the presence of a foreskin is unknown.

There are factors that could influence the association between circumcision and HPV that were not considered. We could not determine whether the association between HPV and circumcision varies by the age at which the procedure is done, because this information was not collected, although the majority of circumcisions in the United States are performed on neonates [40]. We also did not collect information on and could not determine the influence of the degree of foreskin removal, which can vary in circumcised men [34,48].

Other etiologic factors that may influence the etiology of penile carcinomas include history of cigarette smoking, poor hygiene, and phimosis [4,22-25,49]. Two studies found that the increased risk of invasive penile cancer among uncircumcised men may be mediated by phimosis (the inability to completely retract the foreskin over the glans), which can result in

inflammation and predispose to carcinogenesis [22,23]. We did not collect information on phimosis or genital hygiene and were unable to investigate these potential confounders.

The present analysis provides a baseline evaluation of HPV infection in a university-based, primarily heterosexual, multiethnic population of men. The prevalence of circumcision in our population (79%) was identical to recent national estimates for the United States [40]. The HPV prevalence and type distribution in our study population is comparable to that recently reported in another US population for which similar sites were sampled and the same testing and genotyping methods were used [50]. In addition, the prevalence of urethral infection in this mainland US cohort was identical to the prevalence of HPV in urine in our cohort, which affirms its suitability as a proxy measure for urethral infections. To what extent our results can be generalized to other populations of sexually active US men in other respects is not clear.

This cross-sectional analysis did not allow for an evaluation of causality of circumcision with respect to HPV infection; however, as more results become available, the effect of circumcision on the acquisition, clearance, and persistence of infection will be studied prospectively in this male cohort. Understanding the natural history of HPV in men and women is important for the long-term control of this common infection. The increased risk of HPV infection among uncircumcised men observed in the present study has important implications regarding HPVassociated malignancies in men and their female partners. The promotion of circumcision as a means of controlling HPV and other sexually transmitted infections is controversial. Our study adds to a growing body of knowledge that will be important to future public health strategies, including possible prophylactic vaccination of males and other primary prevention measures.

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Table 1

Characteristics of the male cohort, by circumcision status

Characteristic	Circumcised (*n* = 299)	Uncircumcised (*n* = 80)	*P*[a]
Age, mean (SD), years	28.8 (11.9)	29.5 (12.3)	.66
Race/ethnicity[b]			.003
White	175 (59)	46 (58)	
Asian	25 (8)	10 (13)	
Pacific Islander	38 (13)	1 (1)	
Other (single race)	15 (5)	11 (14)	
Mixed race/ethnicity	45 (15)	12 (15)	
Birthplace			<.001
United States	266 (89)	41 (51)	
Other than United States	33 (11)	39 (49)	
Education[b]			.003
No college	7 (2)	8 (10)	
Some college	207 (70)	44 (55)	
College degree	51 (17)	13 (16)	
Graduate/professional degree	33 (11)	15 (19)	
Cigarette smoking[b]			.50
Never	202 (68)	51 (64)	
Ever	96 (32)	29 (36)	
Sexual history[c]			.91
Sex with women only	228 (77)	61 (76)	
Sex with women and men	53 (18)	14 (18)	
Sex with men only	9 (3)	2 (3)	
No sex	7 (2)	3 (4)	
Condom use[d]			.88
Within past 4 months	145 (51)	37 (49)	
>4 months ago	121 (43)	35 (46)	
Never	16 (6)	4 (5)	
Self-reported history of genital warts	39 (13)	2 (2)	.007

NOTE. Data are no. (%) of subjects, unless otherwise specified. Total percentages may be slightly greater or less than 100% because of rounding.

[a] χ^2 test of association.

[b] One subject declined to respond.

[c] Two subjects declined to respond.

[d] Most recent use with a female partner; excludes men who have sex with men exclusively and men who have no history of sex.

Table 2

Association between circumcision and human papillomavirus (HPV) prevalence, by anatomic site

Site[a]	Any HPV		Oncogenic HPV[b]		Nononcogenic/undetermined risk/unclassified HPV[c]		Multiple HPV	
	+	-	+	-	+	-	+	-
Penis foreskin	…	…	…	…	…	…	…	…
Circumcised	NA	NA	NA	NA	NA	NA	NA	NA
Uncircumcised	28 (44)	35 (56)	14 (29)	35 (71)	24 (41)	35 (59)	14 (29)	35 (71)
Adjusted OR (95% CI)[d]	NA	NA	NA	NA	NA	NA	NA	NA
Glans/corona	100 (32)	208 (74)	50 (19)	208 (81)	72 (26)	208 (74)	40 (16)	208 (84)
Circumcised	69 (29)	172 (71)	34 (16)	172 (84)	49 (22)	172 (78)	24 (12)	172 (88)
Uncircumcised	31 (46)	36 (54)	16 (31)	36 (69)	23 (39)	36 (61)	16 (31)	36 (69)
Adjusted OR (95% CI)[d]	1.97 (1.03-3.77)		2.51 (1.11-5.69)		1.92 (0.93-4.00)		3.58 (1.50-8.50)	
Penile shaft	175 (52)	159 (48)	84 (35)	159 (65)	143 (47)	159 (53)	71 (31)	159 (69)
Circumcised	133 (50)	131 (50)	67 (34)	131 (66)	107 (45)	131 (55)	55 (30)	131 (70)
Uncircumcised	42 (60)	28 (40)	17 (38)	28 (62)	26 (56)	28 (44)	16 (36)	28 (44)
Adjusted OR (95% CI)[d]	1.60 (0.82-2.37)		1.43 (0.66-3.09)		1.69 (0.86-3.34)		1.74 (0.78-3.89)	
Urine	20 (10)	180 (91)	3 (2)	180 (98)	18 (9)	180 (91)	2 (1)	180 (99)
Circumcised	13 (8)	143 (90)	2 (1)	143 (99)	11 (7)	143 (99)	0 (0)	143 (100)
Uncircumcised	7 (16)	37 (84)	1 (3)	37 (97)	7 (16)	37 (84)	2 (5)	37 (95)
Adjusted OR (95% CI)[d]	3.22 (0.86-12.13)		5.42 (0.13-225.81)		3.57 (0.91-14.00)		…	
Semen	12 (6)	185 (94)	3 (2)	185 (98)	11 (6)	185 (94)	2 (1)	185 (99)
Circumcised	10 (6)	143 (94)	3 (2)	143 (98)	9 (6)	143 (94)	2 (1)	143 (99)
Uncircumcised	2 (5)	42 (95)	0 (0)	42 (100)	2 (5)	42 (95)	0 (0)	42 (100)
Adjusted OR (95% CI)[d]	0.92 (0.14-5.97)		…		1.16 (0.17-7.76)		…	
Scrotum	123 (40)	187 (60)	47 (20)	187 (80)	94 (33)	187 (67)	33 (15)	187 (85)
Circumcised	97 (40)	148 (60)	37 (20)	148 (80)	73 (33)	148 (67)	24 (14)	148 (86)
Uncircumcised	26 (40)	39 (60)	10 (20)	39 (80)	21 (35)	39 (65)	9 (19)	39 (81)
Adjusted OR (95% CI)[d]	1.22 (0.04-2.32)		1.28 (0.54-3.03)		1.45 (0.70-3.01)		1.89 (0.75-4.77)	
External penis[e]	187 (59)	129 (41)	43 (25)	129 (75)	59 (31)	129 (69)	33 (20)	129 (80)
Circumcised	140 (57)	106 (43)	36 (25)	106 (75)	46 (30)	106 (70)	26 (20)	106 (80)
Uncircumcised	47 (67)	23 (33)	7 (23)	23 (77)	13 (36)	23 (64)	7 (23)	23 (77)
Adjusted OR (95% CI)[d]	1.72 (0.88-3.35)		1.22 (0.42-3.54)		1.65 (0.68-4.02)		1.94 (0.64-5.87)	
External genitals[f]	194 (65)	106 (35)	43 (29)	106 (71)	59 (36)	106 (64)	33 (24)	106 (76)
Circumcised	146 (63)	86 (37)	36 (30)	86 (70)	46 (35)	86 (65)	26 (23)	86 (77)
Uncircumcised	48 (71)	20 (29)	7 (26)	20 (74)	13 (39)	20 (61)	13 (26)	20 (74)
Adjusted OR (95% CI)[d]	1.69 (0.85-3.39)		1.16 (0.39-3.44)		1.57 (0.64-3.90)		1.85 (0.75-4.58)	
Any site[g]	201 (79)	53 (21)	66 (56)	53 (44)	86 (64)	53 (38)	35 (40)	53 (60)
Circumcised	153 (78)	43 (22)	52 (55)	43 (45)	66 (61)	43 (39)	28 (39)	43 (61)
Uncircumcised	48 (83)	10 (17)	14 (58)	10 (42)	20 (67)	10 (33)	7 (41)	10 (59)
Adjusted OR (95% CI)[d]	2.03 (0.78-5.28)		2.62 (0.78-8.80)		2.39 (0.80-7.14)		2.85 (0.70-11.69)	

NOTE. Data are no. (%), unless otherwise indicated. CI, confidence interval; glans/corona, glans penis and coronal sulcus; NA, not applicable.

[a] Excludes specimens negative for β-globin and specimens from HIV-positive individuals. For foreskin, *n* = 63; for glans/corona, *n* = 308; for shaft, *n* = 334; for urine, *n* = 200; for semen, *n* = 197; for scrotum, *n* = 310.

[b] Includes oncogenic/probable oncogenic types (HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51-53, 56, 58, 59, 66, 68, 73, 82, and IS39); includes specimens concurrently positive for other types (nononcogenic, undetermined risk, and unclassified).

[c] Includes nononcogenic types (HPV types 6, 11, 40, 42, 54, 61, 70, 72, 81, and CP6108) and types with undetermined risk status (HPV types 55, 62, 64, 67, 69, 71, 83, and 84); also includes specimens concurrently positive for oncogenic types.

[d] Reference categories for all odds ratios (ORs) are HPV-negative circumcised men; ORs are adjusted for age, birthplace, race/ethnicity, education level, lifetime no. of female sex partners, history of sex with men, age at initial sex, condom use, history of genital warts, and history of cigarette smoking.

[e] Glans/corona and/or shaft.

[f] Glans/corona, shaft, and/or scrotum.

[g] Glans/corona, shaft, scrotum, urine, and/or semen.

Table 3

Distribution of human papillomavirus (HPV) genotypes detected in the glans penis and coronal sulcus, by circumcision status

Genotype	% of total HPV genotypes detected[a]	
	Circumcised men	Uncircumcised men
Nononcogenic		
6	4	0
42	0	5
54	3	3
61	2	3
70	0	2
72	0	2
CP6108	7	8
Oncogenic		
16	8	3
18	4	3
33	0	3
35	1	3
39	8	0
45	1	2
51	6	2
52	5	5
53	3	5
56	2	0
58	0	2
59	4	2
66	0	7
67	1	3
68	4	2
73	2	5
82	0	2
IS39	0	2
Undetermined risk status		
55	2	0
62	2	2
84	16	10
Unclassified types	18	16

[a] A total of 107 and 61 genotypes were detected in circumcised and uncircumcised men, respectively. Multiple genotypes detected within a single specimen are counted separately. Excludes specimens negative for β-globin and specimens from HIV-positive individuals. Totals do not sum to 100 because of rounding.