Published in final edited form as:

J Infect Dis. 2009 January 1; 199(1): 7–13. doi:10.1086/595567.

Associations between Male Anogenital Human Papillomavirus Infection and Circumcision by Anatomic Site Sampled and Lifetime Number of Female Sex Partners

Carrie M. Nielson[1], **Melody K. Schiaffino**[2], **Eileen F. Dunne**[3], **Jason L. Salemi**[2], and **Anna R. Giuliano**[2]

[1]Oregon Health and Science University, Portland [2]H. Lee Moffitt Cancer Center and Research Institute, Tampa, Florida [3]Division of STD Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

Background—Male circumcision may lower men's risk of human papillomavirus (HPV) infection and reduce transmission to sex partners. Reported associations between circumcision and HPV infection in men have been inconsistent.

Methods—Four hundred sixty-three men in 2 US cities were tested at 6 anogenital sites and in semen for 37 types of HPV. Men were eligible if they reported sex with a woman within the past year, no history of genital warts or penile or anal cancer, and no current diagnosis of a sexually transmitted infection. Participants completed a self-administered questionnaire. Circumcision status was assessed by the study clinician. Logistic regression was used to examine associations between circumcision and HPV detection at each site and in semen, with adjustment for potential confounders.

Results—Seventy-four men (16.0%) were uncircumcised. Adjusted odds ratios (AORs) for any HPV genotype and circumcision were 0.53 (95% confidence interval [CI], 0.28–0.99) for any anatomic site/specimen, 0.17 (95% CI, 0.05–0.56) for the urethra, 0.44 (95% CI, 0.23–0.82) for the glans/corona, and 0.53 (95% CI, 0.28–0.99) for the penile shaft. AORs were <1.0 but not statistically significant for the scrotum, semen, anal canal, and perianal area.

Conclusions—Circumcision may be protective against HPV infection of the urethra, glans/corona, and penile shaft.

Human papillomavirus (HPV) is the cause of cervical cancer and is associated with penile cancer, other anogenital cancers, and precursor lesions in both men and women. The risk of

Reprints or correspondence: Dr. Anna Giuliano, Risk Assessment, Detection, and Intervention Program, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Dr., MRC-CANCONT, Tampa, FL 33612-9416 (anna.giuliano@moffitt.org).

Potential conflicts of interest: A.R.G. is on the speakers' bureau of Merck and has served as a consultant for Merck's male human papillomavirus vaccine program. All other authors report no potential conflicts.

Presented in part: 24th International Papillomavirus Conference and Clinical Workshop, Beijing, 3–9 November 2007 (abstract PS8 – 44).

cervical cancer has been associated with characteristics of women's male sex partners, including circumcision and sexual behavior factors [1–3]. Indeed, even before the identification of HPV, the observation that Jewish women had a low incidence of cervical cancer led to the hypothesis that male circumcision reduces the risk of cervical cancer in female partners [4]. Circumcision of male partners has now been associated with cervical cancer risk as well as with HPV infection in men [1, 5–13]. Evidence also suggests that circumcision may reduce the risk of penile cancer by preventing phimosis, a significant risk factor for this HPV-related cancer [14, 15].

Although several studies have examined the association between circumcision and HPV infection in men, results are inconsistent. The use of different sampling methods, anatomic sites for sampling, study populations at varying risk for HPV infection, and methods for assessing circumcision status (self-reported vs. clinician) make it difficult to compare these studies [16, 17]. Two studies have provided insight into the differences in either associations across risk strata or anatomic site of sampling. First, Castellsague et al. [16] demonstrated a stronger association between circumcision and female partners' cervical cancer risk among men in a higher-risk stratum (defined by lifetime number of sex partners and age at first intercourse) than among those in lower-risk strata. Second, a recent evaluation of HPV infection and circumcision status at external genital sites and in semen and urine provided evidence of differences in associations across sample types [18]. The aims of the present analyses were to examine the associations between HPV infection and circumcision at the glans penis/coronal sulcus, penile shaft, and scrotum in addition to the urethra, semen, perianal area, and anal canal and to explore differences in these associations by risk strata, as defined by the lifetime number of female sex partners.

METHODS

The design and methods of the HPV Detection in Men study have been described elsewhere in detail [19]. Briefly, a cross-sectional study of HPV infection in 463 men in 2 US cities (Tucson, Arizona, and Tampa, Florida) was completed during 2002–2005. Men were eligible if they (1) were 18–40 years old, (2) had had sexual intercourse with a woman within the past year, (3) acknowledged no previous diagnosis of genital warts or penile or anal cancer, (4) had no current penile discharge or pain during urination, and (5) had no current diagnosis of a sexually transmitted disease, such as chlamydia or gonorrhea.

All participants gave informed consent, and the University of Arizona Human Subjects Protection Program, the Centers for Disease Control and Prevention Institutional Review Board, the US Department of Defense, and the University of South Florida Institutional Review Board approved all procedures.

Men collected a semen sample by masturbation 12–36 h before the clinical visit. They were instructed to abstain from having sex with a partner or washing the genitals during the 24 h before the study visit. The study clinician examined each participant's genital, abdominal, and anal areas for lesions or warts. If present, lesions or warts were sampled by rubbing with a saline-wetted Dacron swab. The clinician also recorded whether the participant was circumcised. The clinician used a calcium alginate or Dacron urethral swab to sample the

first 2 cm of the urethral epithelium. The clinician sampled the other anogenital sites by rubbing them with separate saline-wetted Dacron swabs, sampling the entire surface of the (1) glans penis/coronal sulcus, (2) penile shaft (including the prepuce, if present), (3) scrotum, and (4) perianal area. The anal canal was sampled with another saline-wetted Dacron swab. The urethral sample was optional, and the urethral and semen samples were eliminated in the third year of the study. Men completed a self-administered questionnaire that asked about whether they were circumcised, their history of sexually transmitted infections, and their current and past sexual behaviors.

HPV DNA detection and genotyping

HPV was detected in swabbed cellular material and semen by polymerase chain reaction (PCR) amplification of a fragment of the L1 gene, using the PGMY 09/11 L1 consensus primer system [20]. HPV genotyping was conducted using the reverse line blot method on all samples, regardless of the HPV PCR result [20]. This detection method uses the HPV L1 consensus PCR products labeled with biotin to detect 37 HPV types.

Definition of HPV outcomes

The oncogenic HPV types associated with cervical dysplasia and cancer include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66 [21]. The nononcogenic types detected with the Roche line blot method are 6, 11, 26, 40, 42, 53–55, 61, 62, 64, 67–73, 81–84, IS39, and CP6108. An HPV-positive result was defined as the detection of any of these 37 HPV genotypes. A negative result was defined as the absence of any HPV DNA in a sample positive for human β-globin. Samples in which β-globin or any of the 37 detectable HPV genotypes was not detected were deemed inadequate for evaluation and treated as missing. Men who tested positive for any of the 37 HPV types were considered positive for “any HPV.” Of these men, those who had a positive result for any oncogenic HPV type *or* for both oncogenic and nononcogenic types were considered positive for “oncogenic HPV,” whereas men positive for *only* a nononcogenic HPV type were considered positive for “nononcogenic HPV.”

Statistical analysis

The frequencies and means of the responses to the questionnaire items and the results from the clinical examination were compared between circumcised and uncircumcised men. A t test was used to compare continuous measures, and a χ^2 test was used for categorical variables.

Logistic and log-binomial regression were used to model the associations between circumcision and the detection of oncogenic, nononcogenic, and any HPV infection. Odds ratios (ORs) were calculated to facilitate comparison with findings published elsewhere. Because HPV infection is a common outcome, prevalence ratios were also calculated using log-binomial regression [22]. For each outcome, we generated separate models for (1) HPV infection at any site and (2) HPV infection at each site independently of infection at other sites. Associations between circumcision and the detection of multiple HPV types were also evaluated for any site, glans/corona, shaft, and scrotum. These were the sites with enough multiple-type infections to allow for the calculation of ORs. We considered potential

confounders, including current smoking status and smoking history, lifetime number of female sex partners, different female partners in the past 3 months, frequency of sexual intercourse in the past 3 months and the past 1 month, frequency of condom use with vaginal sex in the past 3 months, history of various sexually transmitted disease diagnoses, and detection of genital warts during the clinical sampling visit.

To facilitate comparisons with studies that combined sampling sites or specimens, we conducted additional analyses, combining results from (1) semen and the urethra and (2) the glans, shaft, and scrotum. Separate models were used to evaluate the association between circumcision and each of these outcomes. Men were included in these combined-site analyses if they had no missing results for any of the sites in the combination, and men who had an HPV-positive result at any of the sites were considered to have positive results at the combined site.

To explore whether sexual history moderated the associations between circumcision and HPV infection status, we examined the associations stratified by lifetime number of female sex partners and tested the interaction between stratum and circumcision status. The median life time number of female sex partners ($n = 9$) was used to define the strata. ORs, prevalence ratios, and 95% confidence intervals (CIs) were calculated. Statistical analyses were performed with SAS software (version 9.1.3; SAS Institute).

RESULTS

Overall and site-specific prevalences of any and unclassified HPV types in this study have been reported elsewhere [19]. Overall, 47.5% of men had any of the 37 HPV genotypes detected in at least 1 of the samples collected. Site-specific prevalence ranged from 4.7% in semen to 40.8% at the penile shaft.

Demographics, sexual history, and behavioral characteristics by circumcision status are presented in table 1. Seventy-four men (16.0%) were uncircumcised. Uncircumcised men were slightly younger, less likely to be white, and more likely to be Hispanic. With regard to HPV-related risk factors, circumcised men were more likely to smoke ≥10 cigarettes per day (13.1% vs. 1.4%; $P < .01$), to have had at least 1 female sex partner in the past 3 months ($P = .02$), and to have had a partner with an abnormal Pap smear result ($P = .02$). We observed a marginally significant difference in the use of condoms at least half the time (44.3% vs. 55.9% in circumcised vs. uncircumcised men; $P = .09$).

The associations between circumcision and any, oncogenic, and nononcogenic HPV detection by site or semen sample are presented in table 2. All multivariate models were adjusted for the date of laboratory analysis, smoking ≥10 cigarettes per day, lifetime number of female sex partners, and use of condoms during vaginal sex in the past 3 months. Therefore, multivariate models excluded men who reported no sex in the past 3 months. For the glans penis/coronal sulcus, urethra, semen, and perianal area, the odds of HPV detection observed among circumcised men were lower with the crude ORs, and the adjusted ORs (AORs) showed a stronger association. For other sites, the crude ORs were near 1.00 but were lower after adjustment. Circumcision was strongly associated with reduced odds of

detecting any HPV (AOR, 0.44 [95% CI, 0.23–0.82]) or oncogenic HPV (AOR, 0.47 [95% CI, 0.22–0.99]) at the glans penis/coronal sulcus. The reduction in the odds of nononcogenic HPV detection was not statistically significant. At the urethra, a significant association was observed for any HPV (AOR, 0.17 [95% CI, 0.05–0.56]) and nononcogenic HPV (AOR, 0.04 [95% CI, 0.01–0.23]) but not for oncogenic HPV (table 2).

The strength of the association between circumcision and HPV detection appeared to decrease somewhat as distance from the urethra/prepuce increased, with a marginally significant reduction in any HPV (AOR, 0.53 [95% CI, 0.28–0.99]) and oncogenic HPV (AOR, 0.50 [95% CI, 0.25–1.00]; $P = .05$) detected at the shaft. We found no association between circumcision and HPV detection at the scrotum. Significant associations between circumcision and HPV infection were observed when the urethra and semen samples were combined for any HPV (AOR, 0.29 [95% CI, 0.11–0.81]) and nononcogenic HPV (AOR, 0.09 [95% CI, 0.02–0.39]), but the reduction in odds with this combination of samples was not significant for oncogenic HPV (AOR, 0.96 [95% CI, 0.20–4.64]). When glans, shaft, and scrotum results were combined, AORs were between 0.56 and 0.91 for the 3 HPV outcomes; however, none of these was significant (table 2). The odds of HPV detection were usually lower at the perianal area and anal canal among circumcised men, but AORs were not significant.

The AOR for multiple-type HPV infection was similar to those for any type and for oncogenic HPV when any site was considered (AOR, 0.54 [95% CI, 0.30 – 0.98]). Likewise, the associations with multiple-type infections were similar to those for infection with oncogenic, nononcogenic, and any HPV at the glans penis/coronal sulcus (AOR, 0.46 [95% CI, 0.22– 0.94]) and scrotum (AOR, 0.77 [95% CI, 0.27–2.16]). At the shaft, the AOR for multiple-type infection was 0.88 (95% CI, 0.43–1.80).

When adjusted prevalence ratios (APRs) were examined, a similar pattern of associations was observed. However, as expected, prevalence ratios were closer to 1.00 than were ORs. The APR for circumcision and detection of any HPV at any site was 0.77 (95% CI, 0.53–1.12; $P = .17$). Associations were stronger and significant at the glans penis/coronal sulcus (APR, 0.62 [95% CI, 0.39–0.97]) and the urethra (APR, 0.25 [95% CI, 0.09–0.67]). APRs for the remaining single sites were between 0.51 (for semen) and 0.82 (for anal canal) and were not statistically significant. The APR for the combination of urethra and semen was 0.37 (95% CI, 0.16–0.89), and that for the glans/ shaft/scrotum was 0.84 (95% CI, 0.57–1.25).

The associations between circumcision and any HPV detection were similar between the 2 strata of lifetime number of female sex partners (≥9 vs. <9; data not shown). A test of interaction by stratum did not show significant interaction ($P = .8$). We observed similar reductions in the odds of HPV detection across strata for any site and for each of the external genital sites and the urethra. For example, for men with ≥9 partners, the AOR was 0.56 (95% CI, 0.22–1.40), compared with an AOR of 0.52 (95% CI, 0.23–1.20) for men with <9 partners. However, the only associations that were significant were for men with ≥9 partners for samples taken from the glans penis/coronal sulcus (AOR, 0.43 [95% CI, 0.19–0.99]),

urethra (AOR, 0.23 [95% CI, 0.06–0.85]), and the combination of urethra and semen (AOR, 0.22 [95% CI, 0.06–0.80]).

DISCUSSION

This is the first study to report the associations between HPV infection and circumcision at multiple, individually sampled, internal and external anogenital sites and semen. In this study of asymptomatic men in the United States, the odds of HPV detection at the urethra, the combined urethra and semen, the shaft, and the glans penis/coronal sulcus were lower among circumcised men than among uncircumcised men. The association was not significant for results from the scrotum or anal sites alone or combined with other external genital sites. This reduction in the odds of HPV detection among circumcised men persisted across strata of men reporting a lifetime number of female sex partners above or below the median for this study.

Most published studies (7 of 10) have shown that circumcised men have lower odds of HPV infection than uncircumcised men [1, 5–12, 18]. AORs in these studies ranged from 0.76 (95% CI, 0.58–1.01) among male partners of women with cervical cancer [5] to 0.20 (95% CI, 0.06–0.6) among men attending a sexually transmitted disease clinic in Denmark [10] and 0.20 (95% CI, 0.1–0.4) among men attending vasectomy clinics in Mexico [11]. Comparison of published results has been problematic, because most studies sampled only a single site or a pooled combination of a few sites for the detection of HPV. Studies sampling the urethra were some of the first to report a protective effect among circumcised men and their risk of HPV infection and lesions [5, 6]. Aynaud et al. [5] reported an inverse association between circumcision and HPV infection at the urethra (OR, 0.76 [95% CI, 0.58–1.01]), and a subsequent case-control study by Castellsague et al. [1] showed an even stronger association with sampling of the urethra and glans penis/coronal sulcus (OR, 0.37 [95% CI, 0.16–0.85]). Our results are similar to those reported in other studies that sampled the urethra [1, 5]. Furthermore, the associations we report for other sites sampled, including the glans penis/coronal sulcus, shaft, and scrotum, aid in comparing results with those of other studies. Two studies also demonstrated reduced odds of HPV detection at external penile sites when the urethra was not sampled [7, 10].

The recent study by Hernandez et al. [18], which examined HPV detection in men at various sites is, to our knowledge, the only comparable assessment of the role played by circumcision in HPV detection. We observed similar AORs for the association between circumcision and any HPV detection at the coronal sulcus/glans penis. Our additional sampling of the urethra and semen allowed us to detect a strong association with circumcision at the urethra alone and when urethra and semen sample results were combined. Although our AORs are similar to those previously published, our more conservative APRs, though closer to the null, remained significant for the glans penis/coronal sulcus and urethra. These prevalence ratios may provide a better estimate of the protective effect of circumcision on the incidence of HPV infection. In light of the results of the present study and of the published literature, it appears that circumcision is inversely associated with HPV detection at the urethra and coronal sulcus/glans penis and is marginally associated with lower odds of HPV detection at the penile shaft.

Circumcision may provide protection among men with higher-risk behavior. Our analyses demonstrate significant reductions in the odds of HPV detection at the glans penis/coronal sulcus and urethra among men at highest risk of exposure to HPV infection. Although these AORs were not significantly different across exposure strata, there may be reason to suspect that men at the highest risk of HPV exposure might benefit more than those at lower risk. Castellsague et al. [1] noted a stronger association between men's circumcision status and cervical cancer in female partners among high-risk men (AOR, 0.18 [95% CI, 0.04–0.89]) than among intermediate-risk men (AOR, 0.50 [95% CI, 0.27–0.94]) or low-risk men (AOR, 1.61 [95% CI, 0.86–3.02]), when risk was defined by lifetime number of sex partners and age at first intercourse. Such a difference in effect by risk stratum has also been hypothesized for effect of circumcision in preventing HIV infection [23]. Further studies will be required to elucidate the interplay among circumcision and other risk factors for HPV infection in men. In the present study, associations became apparent or were stronger when men who had not had sex in the past 3 months were excluded and after adjustment for smoking, lifetime number of female sex partners, and condom use in the past 3 months.

The limitations of this study include the low proportion (16.0%) of uncircumcised men, which reflects the common practice of circumcising male newborns in the United States This trend may vary across subpopulations of men in the United States The prevalence of circumcision in the United States varies by race and ethnicity and by birth cohort; 88% of non-Hispanic white men and 42% of Mexican American men aged 14–59 years were circumcised. Those born in the 1980s were significantly less likely to be circumcised than those born in the 1970s [24]. Larger studies may be able to detect additional site-specific associations between HPV infection and circumcision or to evaluate additional cofactors, such as country of origin and birth cohort. Continued research is needed regarding circumcision and HPV detection, infection, and persistence, in addition to the cost-effectiveness of circumcision for preventing HPV disease. The duration of HPV infection may be key to transmission and carcinogenesis; therefore, the association between circumcision and HPV detection in men should be addressed in longitudinal studies. Studies currently under way to evaluate the efficacy of circumcision on the prevention of HPV infection may provide additional insights.

Acknowledgments

Financial support: This project was supported under a cooperative agreement from the Centers for Disease Control and Prevention through the Association of American Medical Colleges (grant U36/CCU319276; AAMC ID no. MM-0579-03/ 03). C.M.N. was supported by the National Cancer Institute (grant R25 CA078447).

References

1. Castellsague X, Bosch FX, Munoz N, et al. Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners. N Engl J Med. 2002; 346:1105–12. [PubMed: 11948269]
2. Agarwal SS, Sehgal A, Sardana S, Kumar A, Luthra UK. Role of male behavior in cervical carcinogenesis among women with one lifetime sexual partner. Cancer. 1993; 72:1666–9. [PubMed: 8348498]
3. Zunzunegui MV, King MC, Coria CF, Charlet J. Male influences on cervical cancer risk. Am J Epidemiol. 1986; 123:302–7. [PubMed: 3753819]

4. Kessler II. Venereal factors in human cervical cancer: evidence from marital clusters. Cancer. 1977; 39:1912–9. [PubMed: 192439]
5. Aynaud O, Ionesco M, Barrasso R. Penile intraepithelial neoplasia: specific clinical features correlate with histologic and virologic findings. Cancer. 1994; 74:1762–7. [PubMed: 8082079]
6. Aynaud O, Piron D, Bijaoui G, Casanova JM. Developmental factors of urethral human papillomavirus lesions: correlation with circumcision. BJU Int. 1999; 84:57–60. [PubMed: 10444125]
7. Baldwin SB, Wallace DR, Papenfuss MR, Abrahamsen M, Vaught LC, Giuliano AR. Condom use and other factors affecting penile human papillomavirus detection in men attending a sexually transmitted disease clinic. Sex Transm Dis. 2004; 31:601–7. [PubMed: 15388997]
8. Lajous M, Mueller N, Cruz-Valdez A, et al. Determinants of prevalence, acquisition, and persistence of human papillomavirus in healthy Mexican military men. Cancer Epidemiol Biomarkers Prev. 2005; 14:1710–6. [PubMed: 16030106]
9. Shin HR, Franceschi S, Vaccarella S, et al. Prevalence and determinants of genital infection with papillomavirus, in female and male university students in Busan, South Korea. J Infect Dis. 2004; 190:468–76. [PubMed: 15243918]
10. Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJ, van den Brule AJ. Risk factors for genital HPV DNA in men resemble those found in women: a study of male attendees at a Danish STD clinic. Sex Transm Infect. 2002; 78:215– 8. [PubMed: 12238658]
11. Vaccarella S, Lazcano-Ponce E, Castro-Garduno JA, et al. Prevalence and determinants of human papillomavirus infection in men attending vasectomy clinics in Mexico. Int J Cancer. 2006; 119:1934–9. [PubMed: 16708372]
12. Weaver BA, Feng Q, Holmes KK, et al. Evaluation of genital sites and sampling techniques for detection of human papillomavirus DNA in men. J Infect Dis. 2004; 189:677–85. [PubMed: 14767822]
13. Castellsague X, Bosch FX, Munoz N. The male role in cervical cancer. Salud Publica Mex. 2003; 45(Suppl 3):S345–53. [PubMed: 14746027]
14. Tsen HF, Morgenstern H, Mack T, Peters RK. Risk factors for penile cancer: results of a population-based case-control study in Los Angeles County (United States). Cancer Causes Control. 2001; 12:267–77. [PubMed: 11405332]
15. Daling JR, Madeleine MM, Johnson LG, et al. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. Int J Cancer. 2005; 116:606–16. [PubMed: 15825185]
16. Castellsague X, Albero G, Cleries R, Bosch FX. HPV and circumcision: a biased, inaccurate and misleading meta-analysis. J Infect. 2007; 55:91–3. author reply 93–6. [PubMed: 17433445]
17. Van Howe RS. Human papillomavirus and circumcision: a meta-analysis. J Infect. 2007; 54:490–6. [PubMed: 16997378]
18. Hernandez BY, Wilkens LR, Zhu X, et al. Circumcision and human papillomavirus infection in men: a site-specific comparison. J Infect Dis. 2008; 197:787–94. [PubMed: 18284369]
19. Nielson CM, Flores R, Harris RB, et al. Human papillomavirus prevalence and type distribution in male anogenital sites and semen. Cancer Epidemiol Biomarkers Prev. 2007; 16:1107–14. [PubMed: 17548671]
20. Gravitt PE, Peyton CL, Alessi TQ, et al. Improved amplification of genital human papillomaviruses. J Clin Microbiol. 2000; 38:357–61. [PubMed: 10618116]
21. Cogliano V, Baan R, Straif K, et al. Carcinogenicity of human papillomaviruses. Lancet Oncology. 2005; 6:204. [PubMed: 15830458]
22. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol. 2005; 162:199–200. [PubMed: 15987728]
23. Wawer MJ, Reynolds SJ, Serwadda D, Kigozi G, Kiwanuka N, Gray RH. Might male circumcision be more protective against HIV in the highly exposed? An immunological hypothesis. AIDS. 2005; 19:2181–2. [PubMed: 16284475]
24. Xu F, Markowitz LE, Sternberg MR, Aral SO. Prevalence of circumcision and herpes simplex virus type 2 infection in men in the United States: the National Health and Nutrition Examination Survey (NHANES), 1999–2004. Sex Transm Dis. 2007; 34:479–84. [PubMed: 17413536]

Table 1

Characteristics of participants in the HPV Detection in Men study, by circumcision status (n = 463).

Characteristic	Participants, no. (%)		*P*
	Circumcised (n = 389)	Uncircumcised (n = 74)	
Age			.06
18–19 years (n = 50)	42 (10.8)	8 (10.8)	
20–24 years (n = 181)	142 (36.5)	39 (52.7)	
25–29 years (n = 90)	76 (19.5)	14 (18.9)	
30–34 years (n = 63)	57 (14.7)	6 (8.1)	
35–40 years (n = 79)	72 (18.5)	7 (9.5)	
Race			<.001
White (n = 324)	297 (76.4)	27 (36.5)	
Black (n = 9)	5 (1.3)	4 (5.4)	
Asian/Pacific Islander (n = 19)	7 (1.8)	12 (16.2)	
American Indian/Alaska Native (n = 33)	25 (6.4)	8 (10.8)	
Other/unknown (n = 78)	55 (14.1)	23 (31.1)	
Ethnicity			<.001
Non-Hispanic (n = 384)	337 (86.6)	47 (63.5)	
Hispanic (n = 79)	52 (13.4)	27 (36.5)	
No. of cigarettes currently smoked per day			<.01
0–9 (n = 404)	331 (86.9)	73 (98.7)	
≥10 (n = 51)	50 (13.1)	1 (1.4)	
Lifetime no. of female sex partners			.82
1–5 (n = 158)	130 (34.9)	28 (40.6)	
6–10 (n = 92)	79 (21.2)	13 (18.8)	
11–20 (n = 105)	89 (23.9)	16 (23.2)	
≥21 (n = 87)	75 (20.1)	12 (17.4)	
No. of female sex partners in the past 3 months			.02
0 (n = 61)	46 (11.9)	15 (20.3)	
1 (n = 274)	240 (62.2)	34 (45.9)	
≥2 (n = 125)	100 (25.9)	25 (33.8)	
Condom use with vaginal sex in the past 3 months			.09
Less than half the time (n = 221)	194 (55.9)	27 (44.3)	
At least half the time (n = 187)	153 (44.1)	34 (55.7)	
Genital wart(s) found during clinic visit			.06
No (n = 445)	371 (95.4)	74 (100)	
Yes (n = 18)	18 (4.6)	0 (0)	
Ever had a sex partner with an abnormal Pap smear result			.02
No (n = 153)	122 (31.4)	31 (41.9)	
Yes (n = 107)	99 (25.5)	8 (10.8)	

Characteristic	Participants, no. (%)		*P*
	Circumcised (*n* = 389)	Uncircumcised (*n* = 74)	
Don't know (*n* = 203)	168 (43.2)	35 (47.3)	

NOTE. Not all categories total 463 because of missing responses. HPV, human papillomavirus.

Table 2

Associations between circumcision and any, oncogenic, or nononcogenic human papillomavirus (HPV) detection in the HPV Detection in Men study, by genital anatomic site(s) or semen.

Site, genotype	HPV positive, no. (%)		OR	AOR[a] (95% CI)
	Circumcised	Uncircumcised		
Any site				
Any type (*n* = 463)	199 (51.2)	38 (51.4)	0.99	0.53 (0.28–0.99)
Oncogenic (*n* = 463)	112 (28.8)	23 (31.1)	0.90	0.56 (0.30–1.06)
Nononcogenic (*n* = 463)	87 (22.4)	15 (20.3)	1.13	0.84 (0.43–1.67)
Glans penis/coronal sulcus				
Any type (*n* = 444)	111 (29.8)	25 (35.2)	0.79	0.44 (0.23–0.82)
Oncogenic (*n* = 444)	52 (13.9)	13 (18.3)	0.72	0.47 (0.22–0.99)
Nononcogenic (*n* = 444)	59 (15.8)	12 (16.9)	0.92	0.62 (0.29–1.29)
Shaft				
Any type (*n* = 449)	152 (40.2)	29 (40.9)	0.97	0.53 (0.28–0.99)
Oncogenic (*n* = 449)	80 (21.2)	18 (25.4)	0.79	0.50 (0.25–1.00[b])
Nononcogenic (*n* = 449)	72 (19.1)	11 (15.5)	1.28	0.85 (0.40–1.80)
Scrotum				
Any type (*n* = 441)	96 (25.9)	17 (24.3)	1.09	0.73 (0.37–1.44)
Oncogenic (*n* = 441)	48 (12.9)	9 (12.9)	1.01	0.68 (0.29–1.62)
Nononcogenic (*n* = 441)	48 (12.9)	8 (11.4)	1.15	0.86 (0.36–2.06)
Urethra				
Any type (*n* = 278)	18 (7.8)	7 (14.9)	0.48	0.17 (0.05–0.56)
Oncogenic (*n* = 278)	9 (3.9)	1 (2.1)	1.86	1.24 (0.14–10.80)
Nononcogenic (*n* = 278)	9 (3.9)	6 (12.8)	0.28	0.04 (0.01–0.23)
Semen				
Any type (*n* = 343)	12 (4.2)	4 (7.1)	0.57	0.48 (0.12–1.96)
Oncogenic (*n* = 343)	9 (3.1)	2 (3.6)	0.87	0.52 (0.10–2.78)
Nononcogenic (*n* = 343)	3 (1.1)	2 (3.6)	0.29	0.41 (0.03–5.07)
Anal canal				
Any type (*n* = 386)	33 (10.3)	6 (9.1)	1.15	0.80 (0.28–2.30)
Oncogenic (*n* = 386)	14 (4.4)	3 (4.6)	0.96	0.48 (0.09–2.57)
Nononcogenic (*n* = 386)	19 (5.9)	3 (4.6)	1.33	1.07 (0.29–3.95)
Perianal area				
Any type (*n* = 436)	35 (9.5)	10 (14.5)	0.62	0.46 (0.20–1.04)
Oncogenic (*n* = 436)	14 (3.8)	4 (5.8)	0.64	0.31 (0.51–1.11)
Nononcogenic (*n* = 436)	21 (5.7)	6 (8.7)	0.64	0.58 (0.21–1.60)
Urethra/semen				
Any type (*n* = 268)	26 (11.7)	9 (19.6)	0.55	0.29 (0.11–0.81)

Site, genotype	HPV positive, no. (%)		OR	AOR[a] (95% CI)
	Circumcised	Uncircumcised		
Oncogenic (n = 268)	14 (6.3)	2 (4.4)	1.48	0.96 (0.20–4.64)
Nononcogenic (n = 268)	12 (5.4)	7 (15.2)	0.32	0.09 (0.02–0.39)
Glans/shaft/scrotum				
Any type (n = 421)	171 (48.3)	30 (44.8)	1.15	0.68 (0.36–1.27)
Oncogenic (n = 421)	92 (26.0)	19 (28.4)	0.89	0.56 (0.29–1.11)
Nononcogenic (n = 421)	104 (29.4)	16 (23.9)	1.33	0.91 (0.47–1.78)

NOTE. AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.

[a] Adjusted for date of analysis, smoking status, lifetime no. of female sex partners, and condom use in the past 3 months.

[b] $.05 < P < .10$.