



Published in final edited form as:

Sex Transm Dis. 2025 November 01; 52(11): 699–705. doi:10.1097/OLQ.0000000000002207.

Association between high-risk HPV prevalence and circumcision status among sexually experienced adult males, 2013–2016, United States

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Abstract

Background: Randomized control trials in sub-Saharan countries found male circumcision may prevent high-risk human papillomavirus (HR-HPV) acquisition. Using 2013–2016 National Health and Nutrition Examination Survey data, we explored the association between circumcision and HR-HPV among sexually experienced 18–59-year-old males.

Methods: Self-collected penile specimens were tested for HPV DNA. We estimated weighted HR-HPV prevalence (positivity to ≥ 1 HR type: HPV16/18/31/33/35/39/45/51/52/56/58/59/66/68) by circumcision status. The association between circumcision and HR-HPV was assessed using multivariable logistic regression models. Effect modification by circumcision on the association between number of lifetime sex partners and HR-HPV was explored.

Results: Overall, 77.7% of males reported being circumcised, with large variation by race/ethnicity and country of birth. HR-HPV prevalence was significantly higher among circumcised (25.7%) than uncircumcised (20.4%) males; this was attenuated after adjustment for lifetime and new past-year sex partners (adjusted prevalence ratio: 1.10, 95%CI: 0.92–1.32). There was evidence circumcision modified the association between lifetime partners and HR-HPV, but HR-HPV prevalence increased with increasing number of partners in circumcised and uncircumcised males.

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RL, JG, and LM designed the study. TQ and EU were responsible for overseeing specimen testing and laboratory processes. RL and SB performed data analysis and drafted the initial manuscript. All authors contributed to interpretation of the data, development of the final manuscript, and offered scientific expertise.

Conflicts of interest: The authors declare no potential conflicts of interest.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conclusions: Our observed lack of statistical association between circumcision and HR-HPV may differ from randomized trial results due to the differences between circumcised and uncircumcised males or differences in anatomic site sampled or timing of circumcision.

Summary

Among adult males in the United States in 2013–2016, circumcised and uncircumcised males had similar high-risk human papillomavirus prevalence after adjusting for sexual behavior.

Keywords

Human papillomavirus; prevalence; male circumcision; National Health and Nutrition Examination Survey

Introduction

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States.(1) Most infections will become undetectable within 1–2 years;(2) however, persistent infection may lead to HPV-attributable disease, including anogenital warts and penile, anal, and oropharyngeal cancers in males.(3, 4) In 2013–2016, approximately 23% of males in the United States had at least one high-risk, or oncogenic, penile HPV type.(1)

In the United States, HPV vaccination is routinely recommended for all adolescents at age 11–12 years with catch-up through age 26 years. Since the end of 2016, only a 9-valent vaccine has been available in the United States; this vaccine protects against the two non-high-risk types that cause nearly all cases of anogenital warts and seven high-risk types that cause most HPV-attributable cancers.(5)

In addition to vaccination, the role of male circumcision (hereafter referred to as circumcision) as an HPV prevention tool has been explored.(6–8) Circumcision is a recognized prevention strategy for other viral sexually transmitted infections, including human immunodeficiency virus (HIV) and herpes simplex II.(9) Clinical trials initially designed to determine the efficacy of circumcision against incident HIV infection have evaluated efficacy against HPV acquisition as a secondary objective.(6–8) These trials, conducted in Africa among adult men, showed rates of incident high-risk HPV (HR-HPV) infection were 30–40% lower among males who received adult male circumcision than those who remained uncircumcised. Observational studies exploring the association between circumcision and prevalent HPV infection have included persons likely circumcised at a variety of ages (e.g., infancy, adulthood) and have been less consistent.(10–12) To further explore this association in the United States, we assessed HR-HPV penile prevalence by circumcision status and evaluated circumcision as an effect modifier on the association between sexual activity and HR-HPV among sexually experienced males aged 18–59 years from a nationally representative sample.

Materials and Methods

Data source and analytic sample

The National Health and Nutrition Examination Survey (NHANES) is a continuous cross-sectional survey administered by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC). Data are released in 2-year nationally representative cycles; detailed methodology is described in the NHANES website. (13) Relevant to the present analysis, demographic information is collected during an in-home interview. Self-collected penile swabs and self-reported sexual behavior information (including circumcision status) are collected during an examination at a mobile examination center. Participants were instructed through written and pictorial instructions to swab the entire surface of the penis including the top, bottom, and both sides from the base of the shaft to tip of the penis, and if uncircumcised, under the foreskin (after pulling back the foreskin). Informed consent was obtained from each adult participant. Data collection was approved by the NCHS Ethics Review Board.

The analysis was restricted to sexually experienced males aged 18–59 years; sexually experienced was defined as ever having had anal, oral, or vaginal sex. Participants with missing or inadequate penile specimens, missing circumcision status, or missing number of lifetime sex partners were excluded, resulting in a final sample of 2867 males. Circumcision status was self-reported; participants were presented medical illustrations of a circumcised penis and an uncircumcised penis and were asked to select the picture illustrating the appearance of their penis.(14) Data from the 2013–2014 and 2015–2016 cycles were combined to achieve more stable estimates. Detailed response rates and inclusion criteria are described in Figure 1.(13)

Demographic and sexual behavior information

Age was categorized as 18–29, 30–39, 40–49, and 50–59 years. Self-reported race/ethnicity was categorized as non-Hispanic White, non-Hispanic Black, Mexican American, Other Hispanic, non-Hispanic Asian, and other non-Hispanic race/ethnicity. Country of birth was dichotomized as born in the United States (50 US states or Washington, D.C) or Other. Poverty income ratio (PIR) was based on self-reported income and year-specific federal poverty guidelines that account for household size and geographic location; we classified PIR <1 as below poverty.(13) Insurance status was categorized as having private insurance, any other insurance, or no insurance. Number of lifetime sex partners, including same-sex and opposite-sex partners, was categorized as 1–2, 3–5, 6–9, 10–15, and ≥16 partners. New sex partner in the past year was categorized as yes or no. While self-reported HPV vaccination status is available in NHANES and was considered for inclusion in the study, this was ultimately not included because a majority of participants were never age-eligible to receive vaccine and coverage was low in this period.(15)

Laboratory methods

Self-collected penile swab specimens were shipped to CDC for HPV detection and typed with the Research Use Only Linear Array HPV Genotyping Test (Roche Diagnostics, Indianapolis, IN), which uses L1 consensus PCR followed by type-specific hybridization for

qualitative detection of 37 HPV types (6/11/16/18/26/31/33/35/39/40/42/45/51/52[XR]/53/54/55/56/58/59/61/62/64/66/67/68/69/70/71/72/73/81/82/83/84/89/IS39) and β -globin. Of note, these types reflect the types listed in the Linear Array product manual. There have been some changes to the classification of these types since the product was released. IS39 is now classified as a subtype of HPV82, meaning Linear Array detects 36 individual types rather than 37; HPV64 is now classified as a subtype of HPV34; and HPV 55 is now classified as a subtype of HPV 44. Samples negative for both HPV and β -globin were considered inadequate and excluded from analysis. Samples positive for HPV and negative for β -globin or negative for HPV and positive for β -globin were considered adequate. Detailed laboratory procedures are available on the NHANES website.⁽¹³⁾ Samples positive for at least one HR-HPV type (HPV16/18/31/33/35/39/45/51/52/56/58/59/66/68) were defined as positive for HR-HPV. Sensitivity analyses were conducted using additional outcomes, positivity to HPV 16 or 18 (HPV 16/18) and positivity to at least one non-HR-HPV type (HPV6/11/26/39/40/42/53/54/55/61/62/64/67/69/70/71/72/73/81/82/83/84/89/IS39).

Statistical analysis

Prevalences of circumcision and HR-HPV were estimated overall and by participant characteristics and sexual behaviors. Wald Chi-squared tests were used to test the association between each characteristic/behavior and both circumcision and HR-HPV positivity. HR-HPV prevalence was estimated by circumcision status for each category of each participant characteristic and is provided as supplemental information (Supplemental Table 1).

To assess the association between HR-HPV positivity and circumcision, HR-HPV prevalence among circumcised males was compared to that among uncircumcised males using prevalence ratios (PR) estimated using predicted marginal prevalence estimates from multivariable logistic regression models. To understand the effect of adjusting for each characteristic/behavior on the association between circumcision status and HR-HPV positivity, PRs were estimated adjusting for each characteristic individually. Additionally, a directed acyclic graph (DAG) was used to identify potential confounders and minimal sufficient sets for adjustment (Supplemental Figure 1A, Supplemental Table 2). Minimal sufficient sets for adjustment were defined as a set of variables that, when adjusted for, closed all open backdoor pathways in the DAG using the fewest variables possible; confounding (i.e., open backdoor) pathways include at least one variable that is a common cause for both the exposure and outcome (i.e., confounder).⁽¹⁶⁾ Missingness for each variable was considered when selecting minimal sufficient sets; for example, in pathways that included poverty status and insurance status, insurance status was included in the set due to lower levels of missingness. Number of lifetime sex partners was included in all minimal sufficient sets due to the strength of the relationship between number of lifetime partners and HR-HPV status. Two minimal sufficient sets were identified for adjustment: number of lifetime partners and new partner in the past year (set 1) and number of lifetime partners, age group, race/ethnicity, insurance status, and country of birth (set 2). These analyses were repeated for HPV16/18 and non-HR-HPV prevalence.

Because HPV is sexually transmitted and is highly related to number of lifetime partners, we also sought to determine if circumcision may be an effect modifier of the association between number of lifetime partners and HR-HPV positivity. A second DAG was created modeling circumcision as an effect modifier (Supplemental Figure 1B). Because an interaction term between lifetime partners and circumcision status was found to be statistically significant (*Wald F test* $P = 0.023$), HR-HPV prevalence was estimated by circumcision status and number of lifetime sex partners; prevalence in each group was compared to prevalence among uncircumcised males with 1–2 lifetime partners using prevalence ratios from a multivariable logistic regression model.⁽¹⁷⁾ As a sensitivity analysis, the effect modification analysis was repeated restricted to persons born in the United States as a proxy for controlling for age at circumcision, which was unavailable in NHANES; in the United States, circumcision is typically performed during infancy, whereas adult circumcision was the focus of clinical trials assessing circumcision as an HPV prevention strategy. Adjusted prevalence ratios (aPRs) were estimated adjusting for the minimal sufficient set based on Supplemental Figure 1B: age group, race/ethnicity, country of birth, insurance, and new partner in the past year.

Data management was performed in SAS 9.4 (SAS Institute, Cary, NC), and analysis was performed using SAS-callable SUDAAN 11.0 (RTI International, Research Triangle Park, NC). As recommended by NCHS, complex survey analytic methods were used to account for survey design, and all analyses were weighted using the mobile examination center weights provided by NHANES to account for non-response and sampling methods.⁽¹³⁾ Statistical significance was defined as $P < 0.05$ for Chi-Squared tests and 95% confidence intervals that did not include 1 for PRs.

Results

The overall prevalence of circumcision in 2013–2016 was 77.7% among US adult males. (Table 1) Prevalence of circumcision differed significantly by age group, race/ethnicity, country of birth, poverty status, insurance status, and number of lifetime partners (all $P \leq 0.01$); the largest absolute differences were seen by race/ethnicity (non-Hispanic White, 90.6%; other non-Hispanic race/ethnicity, 81.6%; non-Hispanic Black, 75.2%; Other Hispanic, 47.7%; non-Hispanic Asian, 44.1%; Mexican American, 37.3%) and country of birth (United States, 86.0%; other, 39.1%).

HR-HPV penile prevalence was 24.5% overall. Prevalence was significantly associated with race/ethnicity, country of birth, poverty status, insurance status, number of lifetime partners, and new partner in the past year (all $P \leq 0.01$). (Table 1) Large absolute differences were seen by race/ethnicity (range: 13.6%–35.7%) and number of lifetime partners (range: 7.8%–38.8%).

HR-HPV penile prevalence was higher among circumcised (25.6%, 95% CI: 22.9–28.5) than uncircumcised (20.5%, 95% CI: 17.1–24.3) males prior to adjustment for sociodemographic or behavioral characteristics (PR: 1.25, 95% CI: 1.05–1.49). (Table 2) However, this association was attenuated after adjusting for race/ethnicity, country of birth, or number of lifetime partners alone or adjusting for either of the minimal sufficient sets (set 1: number

of lifetime partners and new partner in the past year, aPR (95% CI) = 1.10 (0.92–1.32); set 2: number of lifetime partners, age group, race/ethnicity, insurance status, and country of birth, aPR (95% CI) = 1.07 (0.88–1.30)). When considering HPV 16/18 and non-HR-HPV prevalence, point estimates were further from the null for HPV 16/18 and closer to the null for non-HR-HPV. However, after adjustment for race/ethnicity, lifetime partners, or either minimal sufficient set, prevalence did not statistically significantly differ between circumcised and uncircumcised males (data not shown).

To assess circumcision as a modifier of the effect of HPV acquisition through sex, HR-HPV penile prevalence was estimated by number of lifetime partners, stratified by circumcision status (Figure 2 and Table 3). Among circumcised and uncircumcised males, point estimates for HR-HPV prevalence were higher with increasing number of lifetime partners (Figure 2). Using prevalence among uncircumcised males reporting 1–2 lifetime sex partners as the reference, unadjusted PR point estimates were higher with higher numbers of lifetime partners from 3–5 to ≥ 16 partners for both circumcised (range of PRs: 1.31–4.04) and uncircumcised (range of PRs: 1.84–3.14) males. Prevalence was significantly higher among both circumcised and uncircumcised males with 6–9, 10–15, and ≥ 16 lifetime partners than uncircumcised males with 1–2 lifetime partners. Adjusted PRs followed a similar pattern to unadjusted results, but they were somewhat attenuated.

Among persons born in the United States, overall, HR-HPV prevalence was comparable between circumcised (26.2%, 95% CI: 23.2–29.4) and uncircumcised males (25.0%, 95% CI: 20.3–30.4; aPR: 1.02, 95% CI: 0.80–1.29). Results from the effect modification analysis were similar to the main analysis (Supplemental Table 3).

Discussion

In 2013–2016 in the United States, HR-HPV penile prevalence was not statistically associated with circumcision status among adult males after adjusting for number of lifetime partners and either new partner in the past year or demographic characteristics. Prior to adjustment, HR-HPV prevalence was 25% higher among circumcised males than uncircumcised males. However, there were substantial differences in prevalence of circumcision by race/ethnicity and country of birth, and we provide evidence these variables may have confounded the association between circumcision status and HR-HPV positivity. We also provide evidence circumcision may be an effect modifier on the relationship between number of lifetime partners and HR-HPV positivity. Among those with fewer lifetime partners, HR-HPV prevalence was lower among circumcised than uncircumcised males, but for those with more lifetime partners, prevalence was higher among circumcised males. However, HR-HPV prevalence was substantially higher in males with greater numbers of lifetime partners regardless of circumcision status.

In the United States, circumcision is most commonly performed as an elective procedure on neonates. Prevalence of circumcision has been declining among more recent birth cohorts but remains higher in the United States than any other developed country.(18, 19) Within the United States, prevalence varies substantially by race/ethnicity, socioeconomic status, and insurance status; this was seen in our study as well as others.(14, 19, 20) Although

circumcision has always ultimately been decided by parental preference, guidance from the American Academy of Pediatrics (AAP) has varied since the 1970s. Evidence and acknowledgment of potential medical benefits of circumcision has grown. In the 1970s, AAP concluded there was no medical benefit of circumcision; in 1989, there may be potential benefit; and in 1999, there was potential benefit.(21) In 2012, AAP convened a multiorganization task force to re-evaluate evidence regarding circumcision. Their evaluation determined there were health benefits for circumcision (e.g., HIV prevention) that outweighed risks associated with the procedure (e.g., bleeding, infection); parents had the right to factual information, physician counseling, and the ability to weigh the health benefits and risks relative to their own personal and cultural preferences; and there was enough evidence of benefit to justify the procedure should be covered by third-party reimbursement.(9) However, the benefits of circumcision were not deemed great enough to warrant a routine recommendation of circumcision for all male newborns.(22)

Multiple clinical trials have shown circumcision reduces risk of HR-HPV acquisition by 30–40% and increases the rate of clearance of infection by 35–75%.(6, 8, 23) Our analysis of circumcision as an effect modifier found HR-HPV prevalence was 33% lower (nonsignificant) in circumcised than uncircumcised males among those with 1–2 lifetime sex partners. However, HR-HPV prevalence was higher among circumcised than uncircumcised males for those with >5 lifetime partners. There are several reasons our results may have differed from the results of these clinical trials. First, the trials primarily focused on HPV acquisition rather than prevalent infection. Second, in the trials, circumcision was performed on adult males as an intervention. Third, HPV prevalence varies by sampling site in the anogenital area, particularly among males.(24) In the clinical trials, the glans was sampled, whereas the entire penis was sampled in NHANES. One trial that sampled the glans and shaft separately found that circumcision was protective against HR-HPV at the glans, but not the shaft.(6)

Several systematic reviews have concluded circumcision is protective against prevalent HPV infection.(25–27) A recent review demonstrated that HR-HPV prevalence was statistically significantly lower among circumcised males than uncircumcised males when the glans was the anatomic site sampled. However, when the sample was from the shaft only or a combination of sites (e.g., glans and shaft in one sample), there is more ambiguity in the association between circumcision status and HR-HPV prevalence among studies included in the review. Among studies that reported an odds ratio, the odds ratios were less than one but had confidence intervals that included the null, suggesting HR-HPV prevalence was non-statistically significantly lower among circumcised than uncircumcised males. However, among studies that reported prevalence ratios, there was no difference in prevalence between circumcised and uncircumcised males, similar to our findings. (27) The strength and consistency of the association between circumcision status and HR-HPV prevalence at the glans may be due to differences in prevalence at that site by circumcision status. There is evidence that HR-HPV prevalence is higher at the glans/corona among uncircumcised than circumcised males, while prevalence at the shaft is similar.(12) About 60% of penile cancers are caused by HPV, and the glans is the most common subsite of penile cancer.(28) Lower HR-HPV prevalence at the glans among circumcised males may explain the lower rates of penile cancer among circumcised compared to uncircumcised males.

The biological mechanism for circumcision as an HPV prevention tool is unclear. It is theorized that HPV is less likely to infect the more keratinized glans of a circumcised penis than the less keratinized epithelium of the preputial space. However, the difference in thickness of keratin has not been conclusively shown. Current theories on the biologic mechanism of circumcision as a prevention tool are largely based on HIV transmission research and include differences in the microbiome and immune environment, which may also be affected by behavioral practices such as hygienic practices, between circumcised and uncircumcised penises.(29, 30)

This analysis has some limitations. First, NHANES participants are asked to sample the entire penis (including shaft, glans, and, if uncircumcised, prepuce) using one swab. It is not possible to determine whether the association between circumcision and HR-HPV status varies by sampling site in our study. Second, circumcision status was self-reported using medical illustrations and was not medically confirmed. Third, some groups had smaller sample sizes limiting our ability to perform stratified analyses, such as analyses by race/ethnicity, which could have provided some information on the presence of residual confounding as there are substantial differences between circumcised and uncircumcised males that may not be fully accounted for through model adjustment. Fourth, NHANES does not collect information on age at circumcision. Age at circumcision is infrequently collected in studies and likely varies across studies assessing the association between circumcision status and HPV, limiting the ability to compare findings. As a proxy for controlling for age at circumcision, we performed a sensitivity analysis restricted to participants born in the United States; results were similar when restricted to this population.

In this cross-sectional U.S. study, male circumcision was not statistically associated with lower HR-HPV prevalence among adult, sexually experienced male NHANES participants. While circumcision as an HPV prevention tool may be useful in some settings, national HPV prevention measures should continue to focus on vaccinating young males and females at the recommended ages.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

We thank Mariela Scarbrough and Juanita Onyekwuluje, Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases, CDC, for their exceptional work in the HPV laboratory.

Funding source:

Centers for Disease Control and Prevention funded this study.

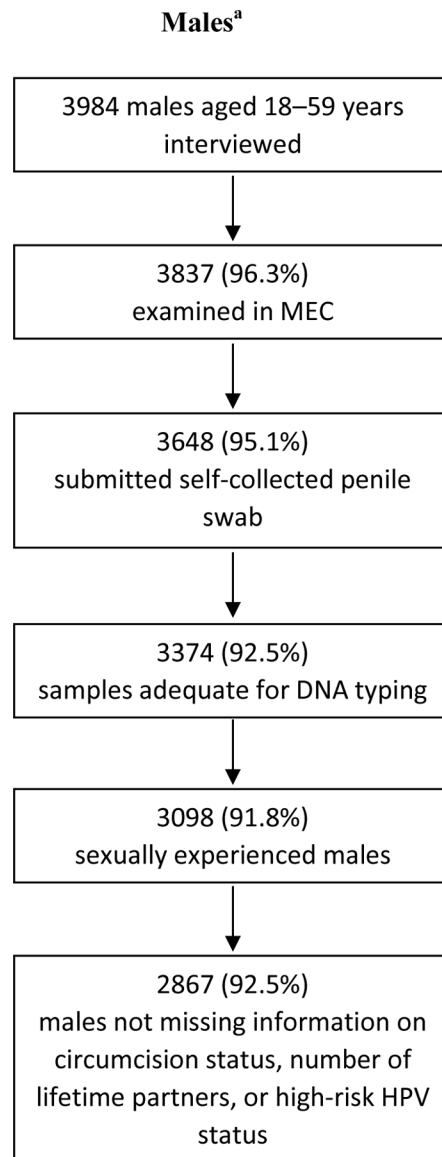
Data availability:

All data are publicly available on the NHANES website.

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**Figure 1:**

Participation and sample collection among males, NHANES, United States, 2013–2016
 HPV, human papillomavirus; MEC, Mobile Examination Center; NHANES, National Health and Nutrition Examination Survey

^a2013–2014 NHANES cycle: overall response rates were 70.6% for the interview and 68.1% for the examination; 2015–2016 NHANES cycle: overall response rates were 60.1% for the interview and 57.4% for the examination.

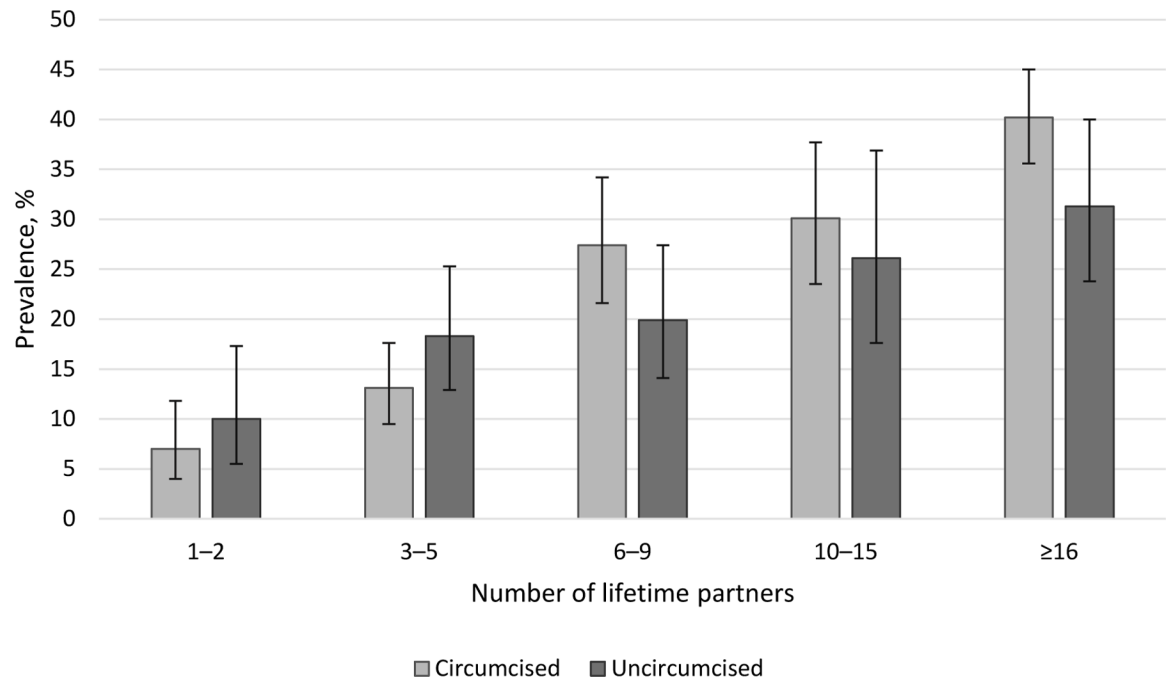


Figure 2:

High-risk HPV penile prevalence by number of lifetime partners and circumcision status among sexually experienced 18–59-year-old males, NHANES, United States, 2013–2016

Error bars represent 95% confidence intervals.

HPV, human papillomavirus; NHANES, National Health and Nutrition Examination Survey

Table 1:
Participant characteristics and behaviors by high-risk penile HPV status and circumcision status among sexually experienced 18–59-year-old males, NHANES, United States, 2013–2016

Characteristic/behavior	N	Column % (95% CI)			Row % (95% CI)	
		Circumcision Status		<i>p</i> ^a	HR-HPV Status	
		Circumcised	Uncircumcised		Positive	<i>p</i> ^b
Overall	2867	-	-		24.5 (22.0–27.1)	
Age group, years						
18–29	823	26.0 (23.6–28.4)	33.3 (29.7–37.2)	0.01	26.0 (22.0–30.4)	0.11
30–39	739	24.0 (21.5–26.8)	25.1 (21.4–29.3)		25.7 (22.6–29.1)	
40–49	649	24.4 (22.2–26.9)	21.1 (17.8–24.7)		19.9 (16.7–23.7)	
50–59	656	25.5 (23.0–28.3)	20.5 (17.3–24.1)		25.9 (21.1–31.3)	
Missing	0					
Race/ethnicity						
Non-Hispanic White	1083	73.1 (67.8–77.9)	26.4 (20.0–34.0)	<0.01	23.9 (20.5–27.7)	<0.01
Non-Hispanic Black	606	10.9 (8.3–14.1)	12.5 (9.7–16.0)		35.7 (32.4–39.3)	
Mexican American	445	5.2 (3.7–7.3)	30.3 (22.8–39.1)		19.3 (15.8–23.2)	
Other Hispanic	290	4.2 (3.0–5.9)	16.1 (12.5–20.4)		25.1 (19.8–31.2)	
Non-Hispanic Asian	315	2.6 (1.8–3.8)	11.5 (8.3–15.8)		13.6 (10.7–17.1)	
Other non-Hispanic	128	4.0 (2.8–5.7)	3.1 (1.9–5.1)		27.3 (19.4–36.9)	
Missing	0					
Country of birth						
United States	2056	91.1 (89.1–92.8)	51.9 (45.4–58.4)	<0.01	26.0 (23.1–29.1)	<0.01
Other	810	8.9 (7.2–10.9)	48.1 (41.6–54.6)		17.2 (14.4–20.3)	
Missing	1					
Poverty status						
Below poverty	560	11.8 (9.6–14.5)	21.1 (17.1–25.9)	<0.01	32.6 (28.2–37.3)	0.01
At or above poverty	2092	88.2 (85.5–90.4)	78.9 (74.1–82.9)		23.5 (20.7–26.6)	
Missing	215					
Insurance status						
Private insurance	1526	66.6 (62.2–70.8)	51.8 (46.3–57.3)	<0.01	21.4 (18.3–24.8)	<0.01
Other insurance	530	14.1 (12.1–16.4)	15.9 (13.2–19.1)		29.1 (23.5–35.3)	
Uninsured	808	19.3 (16.1–22.9)	32.2 (27.7–37.1)		30.3 (27.6–33.1)	
Missing	3					
Number of lifetime partners						
1–2	534	16.0 (13.9–18.4)	22.8 (19.7–26.2)	<0.01	7.8 (5.1–11.9)	<0.01
3–5	616	19.5 (17.2–22.0)	26.6 (23.1–30.3)		14.5 (11.0–18.9)	
6–9	463	16.6 (14.6–18.9)	15.2 (12.8–17.9)		25.9 (20.9–31.6)	
10–15	472	18.5 (16.6–20.6)	15.9 (12.0–20.8)		29.3 (23.5–36.0)	
≥16	782	29.3 (26.5–32.3)	19.6 (16.5–23.1)		38.8 (34.4–43.4)	
Missing	0					
New partner in the past year						

Characteristic/behavior	N	Column % (95% CI)			Row % (95% CI)	
		Circumcision Status			HR-HPV Status	
		Circumcised	Uncircumcised	<i>p</i> ^a	Positive	<i>p</i> ^b
Yes	589	19.2 (16.4–22.2)	21.5 (18.5–24.7)	0.26	37.4 (32.1–43.0)	<0.01
No	2262	80.8 (77.8–83.6)	78.5 (75.3–81.5)		21.4 (18.8–24.1)	
Missing	16					

CI, confidence interval; HPV, human papillomavirus; HR-HPV, high-risk HPV; NHANES, National Health and Nutrition Examination Survey

^a*P* from Wald F test assessing the association between the characteristic of interest and circumcision status (excluding persons missing on the characteristic)

^b*P* from Wald F test assessing the association between the characteristic of interest and HR-HPV status (excluding persons missing on the characteristic)

Table 2:

Adjusted prevalence ratios comparing high-risk HPV penile prevalence among circumcised males to uncircumcised males among sexually experienced 18–59-year-old males, NHANES, United States, 2013–2016

Adjustment variable	aPR (95% CI) Reference group: Uncircumcised males
None (unadjusted estimate)	1.25 (1.05–1.49)
Individual characteristics	
Age group	1.26 (1.07–1.50)
Race/ethnicity	1.21 (0.98–1.49)
Country of birth	1.09 (0.92–1.30)
Poverty status	1.36 (1.12–1.64)
Insurance	1.33 (1.13–1.57)
Number of lifetime partners	1.08 (0.91–1.29)
New partner in the past year	1.26 (1.06–1.51)
Minimal sufficient sets	
Lifetime partners, new partner in past year	1.10 (0.92–1.32)
Lifetime partners, age group, race/ethnicity, insurance status, country of birth	1.07 (0.88–1.30)

aPR, adjusted prevalence ratio comparing high-risk HPV prevalence in circumcised males to uncircumcised males; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey

Table 3:

High-risk HPV penile prevalence and prevalence ratios by number of lifetime partners and circumcision status among sexually experienced 18–59-year-old males, NHANES, United States, 2013–2016

No. of lifetime partners	N		Prevalence, % (95% CI)		PR (95% CI)		aPR (95% CI) ^a	
	Circumcised N = 1967	Uncircumcised N = 900	Circumcised N = 1967	Uncircumcised N = 900	Circumcised N = 1967	Uncircumcised N = 900	Circumcised N = 1959 ^b	Uncircumcised N = 888 ^c
1–2	310	224	7.0 (4.0–11.8)	10.0 (5.5–17.3)	0.70 (0.34–1.46)	Reference	0.67 (0.30–1.52)	Reference
3–5	384	232	13.1 (9.5–17.6)	18.3 (12.9–25.3)	1.31 (0.70–2.47)	1.84 (0.95–3.56)	1.24 (0.60–2.56)	1.72 (0.87–3.42)
6–9	334	129	27.4 (21.6–34.2)	19.9 (14.1–27.4)	2.75 (1.62–4.67)	2.00 (1.04–3.85)	2.38 (1.22–4.62)	1.85 (0.90–3.81)
10–15	340	132	30.1 (23.5–37.7)	26.1 (17.6–36.9)	3.02 (1.67–5.47)	2.62 (1.31–5.24)	2.74 (1.33–5.66)	2.35 (1.10–5.00)
≥16	599	183	40.2 (35.6–45.0)	31.3 (23.8–40.0)	4.04 (2.27–7.19)	3.14 (1.70–5.80)	3.45 (1.65–7.18)	2.62 (1.21–5.66)

aPR, adjusted prevalence ratio; CI, confidence interval; HPV, human papillomavirus; NHANES, National Health and Nutrition Examination Survey; PR, prevalence ratio

^a aPR adjusted for age group, race/ethnicity, country of birth, insurance, new partner in the past year

^b 8 participants excluded due to missing information on country of birth (n = 1), new partner in the past year (n = 5), or insurance status (n = 2)

^c 12 participants excluded due to missing information on new partner in the past year (n = 11), insurance status (n = 1), or both (n = 1)