Research Article

Cancer Epidemiology, Biomarkers & Prevention

# Human Papillomavirus (HPV) 6, 11, 16, and 18 Seroprevalence Is Associated with Sexual Practice and Age: Results from the Multinational HPV Infection in Men Study (*HIM* Study)

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## Abstract

**Background:** Few human papillomavirus (HPV) serology studies have evaluated type-specific seroprevalence of vaccine HPV types in men. This study investigates seroprevalence of HPV 6, 11, 16, and 18, and associated risk factors in men residing in three countries (United States, Mexico, and Brazil).

**Methods:** Data from 1,477 men aged 18 to 70 enrolled in the HPV Infection in Men Study (HIM Study) were analyzed. Serum antibody testing was performed with virus-like particle-based ELISA. Potential risk factors were assessed for individual HPV types by the use of logistic regression.

**Results:** Overall, HPV-6, 11, 16, and 18 seroprevalence was 14.8%, 17.3%, 11.2%, and 5.8%, respectively. Thirty-four percent of men were seropositive to one or more HPV types. When examined by sexual practice, 31.2% of men who had sex with women, 65.6% of men who had sex with men (MSM), and 59.4% of men who had sex with both men and women (MSMW) were seropositive to one or more HPV types. Seroprevalence increased with age among young-to-middle-aged men with significant upward age trends observed for HPV 11, 16, and 18. Men with multiple lifetime male anal sex partners were 2 to 4 times more likely to be HPV 6 or 11 seropositive and 3 to 11 times more likely to be HPV 16 or 18 seropositive.

**Conclusion:** Our data indicate that exposures to vaccine HPV types were common in men and highly prevalent among MSM and MSMW.

**Impact:** Our study provides strong evidence that the practice of same-sex anal intercourse is an independent risk factor for seroprevalence of individual vaccine HPV types. Examination of antibody responses to HPV infections at various anatomic sites in future studies is needed to elaborate on the mechanism. *Cancer Epidemiol Biomarkers Prev; 20(5); 990–1002. ©2011 AACR.*

## Introduction

Human papillomavirus (HPV) infections cause approximately 85% of squamous cell anal cancer, 50% of penile cancer, 33% to 72% of oropharyngeal cancers, and 10% of laryngeal cancers (1–4). High prevalence of genital HPV infection has been reported in recent studies (5–7), with 25.8% to 72.9% of HIV-negative adult men testing positive for genital HPV. Anal and oral HPV, though less common, is present in 8.0% to 16.6% (8–10) and 2.9% to 7.6% (11) of HIV-negative adult men, respectively. Compared with men who have sex with women (MSW), men who have sex with men (MSM) and men who have sex with men and women (MSMW) were several times more likely to be infected with genital, anal, or oral HPV and hence at increased risk for HPV-associated diseases and cancers (12–17).

Serum antibodies elicited by natural HPV infection reflect cumulative exposures to HPV over time and across anatomic sites. Anti-HPV serum antibody immunoglobulin G detected by virus-like particles (VLP)-based assays are type specific (1, 18, 19). There is typically a 6- to 12-month latency for detection of antibodies following HPV DNA detection, as observed in women (20, 21). Antibodies seem to be stable over time and remain detectable even after a decade (22–25). Not all individuals challenged by natural exposure to HPV develop antibody responses detectable by current serology assays. Approximately

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30% to 40% of women with incident HPV 16 infection failed to show seropositivity in the months following DNA detection (20, 21). Similar data in men are not yet available. Although issues such as differential seroconversion rates following infection with different HPV types and unknown longevity of serum antibodies could limit faithful translation, HPV serology remains a useful means for estimating cumulative HPV exposures in a population. With the recent licensure of the quadrivalent HPV vaccine for use in males, information on seroprevalence of vaccine-type HPV in the general male population is needed to provide guidance for strategic planning of vaccination. To date, few studies have characterized seroprevalence of all HPV types targeted in current vaccines and investigated associated risk factors in men (26–35). Using baseline data from a large natural history study of HPV, we determined the seroprevalence of HPV 6, 11, 16, and 18, respectively, and identified demographic and behavioral factors that were independently associated with individual HPV seroprevalence in men.

## Methods

### Study population

This study included a subset of participants enrolled in the HPV Infection in Men Study (the HIM Study), a multinational longitudinal study of HPV infection in men. Details of the cohort have been reported elsewhere (36). In brief, 4,074 healthy men were recruited in São Paulo, Brazil; Cuernavaca, Mexico; and Tampa, FL, United States, between June 2005 and August 2009. Men were recruited from several population sources in Brazil including public health clinic attendees, partners of women participating in a natural history study of HPV, and the general population. In Mexico, men were recruited from employees and beneficiaries of a large government agency and military officials. In the United States, men were recruited from the University of South Florida and the greater Tampa metropolitan area. Men were considered eligible if the following criteria were met: (a) 18 to 70 years of age; (b) residents of 3 study sites; (c) no prior diagnosis of penile or anal cancers; (d) no prior diagnosis of genital or anal warts; (e) no symptoms of a sexually transmitted infection (STI) or current treatment of an STI; (f) no concurrent participation in an HPV vaccine study; (g) no history of HIV or AIDS; (h) no history of imprisonment, homelessness, or drug treatment during the past 6 months; and (i) willingness to comply with 10 scheduled visits every 6 months for 4 years with no plans to relocate in 4 years. The current analysis included 1,477 men with available serology, genital HPV DNA results, and survey information from the enrollment visit.

### Study protocol

At the enrollment visit, an extensive sexual history and health questionnaire was administered by using the Computer-Assisted Self-Interviewing (CASI) system to solicit information on participant sociodemographic characteristics, sexual history, condom use, alcohol and tobacco consumption, and history of abnormal pap smears in female partners. Ten milliliters of venous blood was collected for serum antibody testing, and participant external genitalia were sampled for HPV DNA testing.

### HPV serum antibody testing

Serum antibodies to HPV types 6, 11, 16, and 18 were measured by using VLP-based ELISA (37). HPV 6, 11, and 18 VLPs were produced in insect cells from recombinant baculoviruses expressing the L1 major capsid protein of individual HPV types (38), and HPV 16 VLPs were produced in mammalian cells from plasmids expressing the L1 and L2 capsid proteins (39). Specimens were tested in duplicate on separate plates, with retesting of specimens showing results exceeding a preset, acceptable coefficient of variation of 25%. Seropositivity was defined as an optical density (OD) value greater than the mean OD value plus 5 SDs, estimated by using serum samples from children of 1 to 10 years of age after exclusion of outliers. Quality control of the serology assays was assured by inclusion of laboratory-prepared positive and negative controls in each run of the assay. To ensure consistency in antibody measurements taken with HPV VLPs produced under 2 different protocols, testing of serum antibodies to HPV 16 was repeated for all 1,477 men using HPV 16 VLPs produced in insect cells, the same protocol adopted for production of HPV 6, 11, and 18 VLPs. Antibody measurements obtained from the second testing were found to be highly correlated with the measurements obtained from the original testing (correlation coefficient $= 0.78$, $P < 0.001$), suggesting that antibody measurements for HPV 16 were comparable despite protocol difference in VLP production.

### HPV DNA sampling and testing

Three prewetted Dacron swabs were used to collect exfoliated skin cells from the penis and scrotum and later combined to form a single specimen. All specimens were stored at −70°C until PCR analyses and genotyping were conducted. DNA was extracted from exfoliated skin cell samples by using the QIAamp DNA Mini Kit (QIAGEN) and tested for HPV DNA by using PCR for amplification of a fragment of the *HPV L1* gene (40). HPV genotyping was conducted by using the LINEAR ARRAY HPV Genotyping Protocol (Roche Diagnostics) to detect 37 genital HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51 to 56, 58, 59, 61, 62, 64, 66 to 73, 81 to 84, IS39, and CP6108 (41).

### Statistical analysis

Overall seroprevalence and seroprevalence by sexual practice, age, country of residence, lifetime number of female partners, and male anal sex partners are presented in Figure 1. The $\chi^2$ test and the Cochran–Armitage test were used to compare seroprevalence and test for trends across levels of categorical variables, respectively. Serum

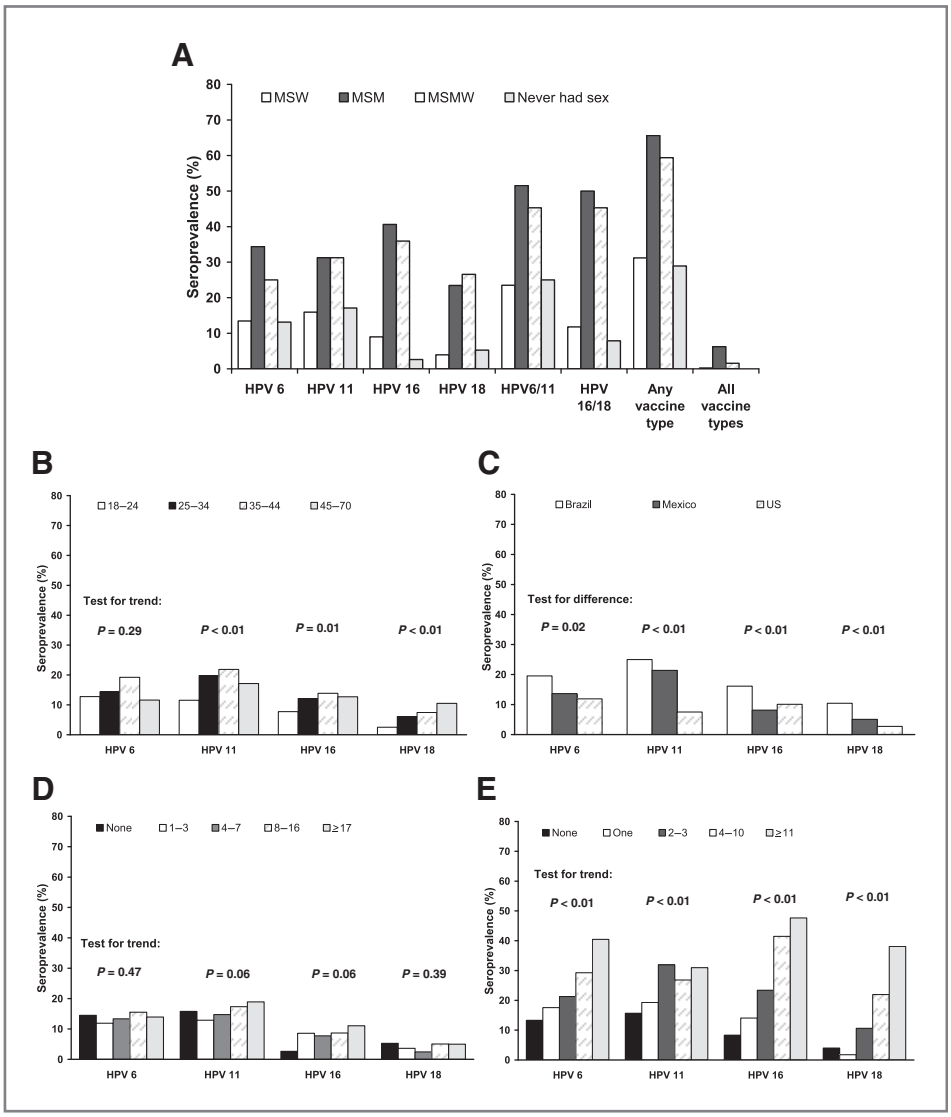


**Figure 1.** Seroprevalences of HPV 6, 11, 16, and 18 overall and by sexual practice, age, country, and lifetime number of female and male sex partners. A, seroprevalence overall and by sexual practice; B, seroprevalence by age; C, seroprevalence by country of residence; D, seroprevalence by lifetime number of female sex partners among MSW; E, seroprevalence by lifetime number of male anal sex partners.

antibody titer levels among seropositive men, as measured by OD values, were summarized by median and interquartile range (IQR). OD values were compared across levels of individual factors by using the Wilcoxon rank-sum and Kruskal–Wallis tests for each HPV type. The 95% CIs were calculated for all seroprevalence estimates on the basis of exact binomial probabilities. The association between potential risk factors and HPV 6, 11, 16, or 18 seroprevalence, treated as a dichotomous outcome, was evaluated on a type-specific basis by using unconditional logistic regression and measured by OR and its 95% CIs. Factors examined included (i) sociodemographic characteristics such as age, country of residence, race, ethnicity, marital status, and educational attainment; (ii) lifestyle and behavioral factors including alcohol consumption, smoking, circumcision, age at first sexual intercourse, sexual practice, the number of recent and lifetime sex partners, frequency of sexual intercourse, condom use, and history of other STIs; and (iii) corresponding HPV DNA status at the same visit. Variables that showed statistical significance at 0.1 level in the simple regression models were included in the multivariable regression models. Likelihood ratio tests and backward selection procedures were applied for variable selection. Factors were retained in the multivariable models if $P$ values of likelihood ratio test were 0.05 or less. Potential pair-wise interactions were explored. Because of the exploratory nature of this study, no adjustment for multiple testing was made.

## Results

Characteristics of the 1,477 men included in the current analysis and the median and IQR of OD values among men seropositive to HPV 6, 11, 16, and 18 are summarized in Table 1. Of the 1,477 men, 546 (37.0%) were residents of

**Table 1.** Participant characteristics and the distribution of anti-HPV serum antibody titers for HPV 6, 11, 16, and 18 among seropositive men

| Characteristics | *n* (%) | HPV 6 antibody (OD, $10^{-3}$) Median (IQR) | HPV 11 antibody (OD, $10^{-3}$) Median (IQR) | HPV 16 antibody (OD, $10^{-3}$) Median (IQR) | HPV 18 antibody (OD, $10^{-3}$) Median (IQR) |
|---|---|---|---|---|---|
| Overall | 1,477 | 234 (187–312) | 244 (188–355) | 190 (121–427) | 172 (128–295) |
| Age (y) | | | | | |
| Median (range) | 30 (18–78) | | | | |
| 18–24 | 477 (32.3) | 233 (186–292) | 239 (182–307) | 134 (121–256) | 259 (162–337) |
| 25–34 | 444 (30.1) | 244 (186–308) | 244 (190–370) | 161 (112–382) | 164 (112–330) |
| 35–44 | 375 (25.4) | 221 (192–345) | 272 (187–370) | 260 (149–552) | 172 (133–263) |
| 45–70 | 181 (12.3) | 260 (186–324) | 230 (192–303) | 203 (115–464) | 154 (117–248) |
| *P*[a] | | 0.943 | 0.528 | 0.035 | 0.409 |
| Country of residence | | | | | |
| United States | 546 (37.0) | 218 (186–282) | 242 (195–312) | 177 (119–495) | 174 (114–348) |
| Brazil | 440 (29.8) | 244 (192–324) | 261 (192–423) | 241 (121–445) | 201 (133–326) |
| Mexico | 491 (33.2) | 242 (187–312) | 239 (184–303) | 195 (122–381) | 154 (117–222) |
| *P*[a] | | 0.338 | 0.154 | 0.849 | 0.363 |
| Marital status | | | | | |
| Single | 679 (46.0) | 242 (186–324) | 257 (192–368) | 193 (122–427) | 229 (128–421) |
| Cohabiting | 166 (11.2) | 245 (202–308) | 205 (174–340) | 160 (124–276) | 192 (111–275) |
| Married | 499 (33.8) | 211 (185–287) | 244 (188–340) | 146 (119–397) | 169 (137–242) |
| Divorced/separated/widowed | 119 (8.1) | 288 (217–364) | 264 (207–486) | 377 (130–544) | 131 (112–149) |
| *P*[a] | | 0.146 | 0.254 | 0.285 | 0.152 |
| Education | | | | | |
| <High school | 335 (22.7) | 245 (195–328) | 224 (184–366) | 155 (124–270) | 150 (128–255) |
| High school graduate | 357 (24.2) | 265 (210–368) | 255 (196–383) | 191 (121–382) | 153 (112–311) |
| ≥College/vocational school | 770 (52.1) | 212 (182–284) | 242 (191–308) | 224 (121–495) | 200 (136–302) |
| *P*[a] | | 0.002 | 0.460 | 0.515 | 0.413 |
| Circumcision[b] | | | | | |
| No | 861 (58.3) | 244 (192–317) | 246 (187–368) | 172 (119–382) | 175 (135–314) |
| Yes | 616 (41.7) | 222 (185–289) | 242 (195–317) | 241 (125–464) | 141 (112–205) |
| *P*[a] | | 0.077 | 0.999 | 0.304 | 0.031 |
| Sexual practice | | | | | |
| Sex with women | 1,247 (84.4) | 222 (186–294) | 230 (184–305) | 146 (116–362) | 161 (114–242) |
| Sex with men | 64 (4.3) | 318 (239–462) | 296 (259–436) | 368 (164–603) | 398 (154–515) |
| Sex with both men and women | 64 (4.3) | 255 (210–328) | 408 (249–626) | 347 (153–672) | 205 (133–255) |
| Never had sex | 76 (5.1) | 191 (169–306) | 307 (209–371) | 134 (122–145) | 143 (125–163) |
| *P*[a] | | 0.003 | 0.000 | 0.002 | 0.025 |
| Lifetime female sex partners among MSW, *n* | | | | | |
| None | 76 (5.1) | 188 (169–306) | 317 (208–374) | 134 (122–145) | 143 (125–163) |
| 1–3 | 303 (20.5) | 236 (186–301) | 230 (189–301) | 124 (109–165) | 161 (113–295) |
| 4–7 | 285 (19.3) | 250 (197–317) | 223 (182–293) | 139 (120–292) | 114 (112–192) |
| 8–16 | 277 (18.8) | 222 (186–282) | 221 (180–292) | 149 (122–313) | 174 (152–271) |
| ≥17 | 280 (19.0) | 211 (185–297) | 258 (187–373) | 269 (130–587) | 123 (111–198) |
| *p*[a] | | 0.587 | 0.280 | 0.018 | 0.096 |
| Lifetime male anal sex partners, *n* | | | | | |
| None | 1,226 (83.0) | 222 (186–299) | 230 (187–310) | 145 (116–338) | 152 (114–222) |
| 1 | 57 (3.9) | 230 (186–268) | 293 (184–450) | 179 (122–390) | 139 (139–139) |
| 2–3 | 47 (3.2) | 199 (182–292) | 340 (258–671) | 317 (155–479) | 205 (169–271) |
| 4–10 | 41 (2.8) | 277 (218–503) | 329 (261–563) | 407 (241–603) | 255 (136–435) |
| ≥11 | 42 (2.8) | 324 (222–376) | 273 (241–449) | 396 (160–737) | 274 (125–409) |
| *p*[a] | | 0.024 | 0.006 | 0.001 | 0.280 |

*(Continued on the following page)*

Table 1. Participant characteristics and the distribution of anti-HPV serum antibody titers for HPV 6, 11, 16, and 18 among seropositive men (Cont'd)

| Characteristics | *n* (%) | HPV 6 antibody (OD, $10^{-3}$) Median (IQR) | HPV 11 antibody (OD, $10^{-3}$) Median (IQR) | HPV 16 antibody (OD, $10^{-3}$) Median (IQR) | HPV 18 antibody (OD, $10^{-3}$) Median (IQR) |
|---|---|---|---|---|---|
| Recent new sex partners (either sex), *n* | | | | | |
| None | 972 (65.8) | 217 (186–287) | 240 (185–306) | 159 (122–383) | 157 (114–225) |
| 1 | 318 (21.5) | 266 (200–350) | 258 (197–368) | 214 (115–427) | 198 (114–295) |
| ≥2 | 165 (11.2) | 261 (209–376) | 302 (205–449) | 224 (142–607) | 309 (146–422) |
| *P*[a] | | 0.011 | 0.155 | 0.465 | 0.055 |

NOTE: Cells that do not add up to 100% are due to missing values. OD used as measurement of serum antibody levels.
[a]*P* values were derived from Wilcoxon rank-sum or Kruskal–Wallis test statistics.
[b]Circumcision status was assessed by study clinician.

Tampa, FL, 440 (29.8%) residents of São Paulo, Brazil, and 491 (33.2%) residents of Cuernavaca, Mexico. These men were predominantly younger than 35 years (62.4%), single (unmarried), or cohabiting (57.2%), had college or higher education (52.1%), and uncircumcised (58.3%). A total of 1,247 (84.4%) men were identified as MSW, 64 (4.3%) as MSM, 64 (4.3%) as MSMW, and 76 (5.1%) as men who reported never having any type of sex, based on their responses to multiple survey questions concerning their recent and lifetime sexual behaviors (Table 1).

Overall, HPV 6, 11, 16, and 18 seroprevalence was 14.8% (95% CI, 13.1–16.7), 17.3% (95% CI, 15.4–19.4), 11.2% (95% CI, 9.6–12.9), and 5.8% (95% CI, 4.7–7.1), respectively (Fig. 1A). A total of 499 men (33.8%, 95% CI, 31.4–36.3) were seropositive to 1 or more HPV type, and only 8 men (0.5%, 95% CI, 0.2–1.1) were seropositive to all 4 HPV types. Seroprevalence of HPV 6/11 was 25.7% (95% CI, 23.5–28.0), and seroprevalence of HPV 16/18 was 14.8% (95% CI, 13.1–16.7) for the entire cohort.

When examined by sexual practice, 31.2% (95% CI, 28.6–33.8) of MSW, 65.6% (95% CI, 52.7–77.1) of MSM, 59.4% (95% CI, 46.4–71.5) of MSMW, and 29.0% (95% CI, 19.1–40.5) of men who never had sex were seropositive to 1 or more HPV type; and 0.2% (95% CI, 0.02–0.6) of MSW, 6.3% (95% CI, 1.7–15.2) of MSM, 1.6% (95% CI, 0.04–8.4) of MSMW, and 0% (95% CI, 0–4.7) of men who never had sex were seropositive to all 4 HPV types. Seroprevalence of HPV 6/11 was 23.5% (95% CI, 21.2–26.0) for MSW, 51.6% (95% CI, 38.7–64.2) for MSM, 45.3% (95% CI, 32.8–58.3) for MSMW, and 25.0% (95% CI, 15.8–36.3) for men who reported never having sex; whereas seroprevalence of HPV 16/18 was 11.8% (95% CI, 10.1–13.7) for MSW, 50.0% (95% CI, 37.2–62.8) for MSM, 45.3% (95% CI, 32.8–58.3) for MSMW, and 7.9% (95% CI, 3.0–16.4) for men who never had sex (Fig. 1A).

The seroprevalence of HPV 6, 11, 16, and 18 increased with age among young-to-middle-aged men (Fig. 1B), with significant upward age trends observed for HPV 11, 16, and 18 seroprevalence. HPV 6 and 11 seroprevalence peaked at ages 35 to 44 and declined in older age, whereas HPV 16 seroprevalence plateaued after peaking at ages 35 to 44 and HPV 18 seroprevalence continued to increase in older men. Seroprevalence also varied significantly by country of residence (Fig. 1C). Brazilian men had the highest seroprevalence for all HPV types among the 3 countries, reaching 19.5% (95% CI, 15.9–23.6), 25.0% (95% CI, 21.0–29.3), 16.1% (95% CI, 12.8–19.9), and 10.5% (95% CI, 7.8–13.7), respectively. Type-specific seroprevalence did not differ significantly by the number of lifetime female sex partners among MSW (Fig. 1D). In contrast, there was a statistically significant, strong positive trend of seroprevalence associated with the number of lifetime male anal sex partners for each HPV type (Fig. 1E).

The median and IQR of serum antibody levels among seropositive men, as measured by OD values, were 0.234 (IQR, 0.187–0.312) for HPV 6, 0.244 (IQR, 0.188–0.355) for HPV 11, 0.190 (IQR, 0.121–0.427) for HPV 16, and 0.172 (IQR, 0.128–0.295) for HPV 18 (Table 1). Serum antibody levels differed significantly by sexual practice for all HPV types and by lifetime number of male anal sex partners for HPV 6, 11, and 16. In addition, HPV 6 antibody levels differed significantly by the number of recent new sex partners; HPV 16 antibody levels differed by age and lifetime number of female sex partners; and HPV 18 antibody levels differed by circumcision status.

In univariate analyses, common risk factors for seroprevalence of all 4 HPV types were age, country of residence, sexual practice, the number of lifetime male anal sex partners, and recent new sex partners of either sex (Table 2). Additional factors significantly associated with seroprevalence in univariate analyses included education and cigarette smoking for HPV 6 seroprevalence; ethnicity, race, marital status, education, cigarette smoking, circumcision, age at first sex, the number of lifetime female sex partners among MSW, frequency of recent vaginal sex, and concurrent detection of HPV 11 DNA for

**Table 2.** Factors associated with seroprevalence of HPV 6, 11, 16, and 18 among 1,477 men in univariate analyses

| Risk factors | HPV 6 | | HPV 11 | | HPV 16 | | HPV 18 | |
|---|---|---|---|---|---|---|---|---|
| | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) |
| Age (y) | | | | | | | | |
| 18–24 | 12.8 | 1.00 | 11.5 | 1.00 | 7.8 | 1.00 | 2.5 | 1.00 |
| 25–34 | 14.4 | 1.15 (0.79–1.68) | 19.8 | 1.90 (1.32–2.73)[e] | 12.2 | 1.65 (1.06–2.56)[e] | 6.1 | 2.51 (1.26–5.01)[e] |
| 35–44 | 19.2 | 1.62 (1.12–2.35)[e] | 21.9 | 2.15 (1.48–3.12)[e] | 13.9 | 1.91 (1.23–2.99)[e] | 7.5 | 3.13 (1.57–6.23)[e] |
| 45–70 | 11.6 | 0.90 (0.53–1.52) | 17.1 | 1.59 (0.98–2.56) | 12.7 | 1.73 (0.99–3.00) | 10.5 | 4.54 (2.16–9.56)[e] |
| Country of residence | | | | | | | | |
| United States | 11.9 | 1.00 | 7.5 | 1.00 | 10.1 | 1.00 | 2.7 | 1.00 |
| Brazil | 19.5 | 1.80 (1.27–2.55)[e] | 25.0 | 4.10 (2.79–6.03)[e] | 16.1 | 1.72 (1.18–2.50)[e] | 10.5 | 4.13 (2.27–7.51)[e] |
| Mexico | 13.6 | 1.17 (0.81–1.69) | 21.4 | 3.35 (2.28–4.92)[e] | 8.1 | 0.79 (0.52–1.21) | 5.1 | 1.90 (0.99–3.64) |
| Hispanic | | | | | | | | |
| No | 15.2 | 1.00 | 15.5 | 1.00 | 12.0 | 1.00 | 5.5 | 1.00 |
| Yes | 14.5 | 0.95 (0.71–1.27) | 19.7 | 1.34 (1.02–1.76)[e] | 10.0 | 0.81 (0.58–1.13) | 6.0 | 1.09 (0.70–1.70) |
| Race | | | | | | | | |
| White | 15.8 | 1.00 | 13.6 | 1.00 | 12.4 | 1.00 | 6.6 | 1.00 |
| Black/African American | 15.7 | 1.00 (0.65–1.53) | 21.4 | 1.73 (1.16–2.58)[e] | 14.8 | 1.23 (0.78–1.92) | 6.7 | 1.00 (0.54–1.87) |
| Other | 13.7 | 0.85 (0.62–1.17) | 20.0 | 1.59 (1.17–2.15)[e] | 8.6 | 0.67 (0.46–0.97)[e] | 4.4 | 0.65 (0.39–1.07) |
| Marital status | | | | | | | | |
| Single | 14.9 | 1.00 | 15.0 | 1.00 | 11.6 | 1.00 | 5.0 | 1.00 |
| Cohabiting | 16.9 | 1.16 (0.73–1.84) | 21.7 | 1.57 (1.02–2.40)[e] | 14.5 | 1.28 (0.78–2.10) | 6.6 | 1.35 (0.67–2.72) |
| Married | 14.6 | 0.98 (0.71–1.36) | 20.2 | 1.44 (1.06–1.94)[e] | 7.8 | 0.64 (0.43–0.96)[e] | 6.6 | 1.34 (0.82–2.20) |
| Divorced/separated/ widowed | 11.8 | 0.76 (0.42–1.39) | 11.8 | 0.75 (0.42–1.37) | 18.5 | 1.72 (1.03–2.89)[e] | 5.0 | 1.01 (0.41–2.45) |
| Education | | | | | | | | |
| <High school | 20.3 | 1.00 | 23.9 | 1.00 | 9.6 | 1.00 | 8.7 | 1.00 |
| High school graduate | 13.7 | 0.62 (0.42–0.93)[e] | 19.9 | 0.79 (0.55–1.14) | 9.5 | 1.00 (0.60–1.66) | 5.0 | 0.56 (0.31–1.03) |
| ≥College/vocational school | 13.0 | 0.59 (0.42–0.82)[e] | 13.4 | 0.49 (0.36–0.68)[e] | 12.7 | 1.38 (0.91–2.10) | 4.9 | 0.55 (0.33–0.90)[e] |
| Alcohol drinking[a] | | | | | | | | |
| Light drinking | 16.6 | 1.00 | 18.7 | 1.00 | 10.3 | 1.00 | 5.2 | 1.00 |
| Moderate drinking | 14.0 | 0.82 (0.56–1.21) | 17.6 | 0.93 (0.65–1.33) | 12.1 | 1.20 (0.78–1.86) | 3.6 | 0.67 (0.34–1.33) |
| Heavy drinking | 15.1 | 0.90 (0.59–1.37) | 14.7 | 0.75 (0.49–1.15) | 11.0 | 1.08 (0.66–1.78) | 7.3 | 1.43 (0.77–2.68) |
| Cigarette smoking[b] | | | | | | | | |
| Never | 12.5 | 1.00 | 14.5 | 1.00 | 9.5 | 1.00 | 3.7 | 1.00 |
| Current, light-moderate | 15.6 | 1.30 (0.74–2.28) | 21.8 | 1.64 (0.99–2.72) | 7.5 | 0.77 (0.37–1.60) | 3.4 | 0.91 (0.31–2.68) |

*(Continued on the following page)*

Table 2. Factors associated with seroprevalence of HPV 6, 11, 16, and 18 among 1,477 men in univariate analyses (Cont'd)

| Risk factors | HPV 6 | | HPV 11 | | HPV 16 | | HPV 18 | |
|---|---|---|---|---|---|---|---|---|
| | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) |
| Current, heavy | 20.4 | 1.79 (1.10–2.92)[e] | 21.4 | 1.60 (1.00–2.56)[e] | 12.9 | 1.42 (0.81–2.51) | 7.0 | 1.94 (0.86–4.36) |
| Former, light-moderate | 12.2 | 0.97 (0.51–1.85) | 17.1 | 1.21 (0.69–2.14) | 11.4 | 1.23 (0.62–2.42) | 2.4 | 0.65 (0.18–2.36) |
| Former, heavy | 16.2 | 1.36 (0.74–2.50) | 13.5 | 0.92 (0.49–1.73) | 13.5 | 1.50 (0.77–2.92) | 9.0 | 2.57 (1.06–6.22)[e] |
| Circumcision[c] | | | | | | | | |
| No | 16.0 | 1.00 | 21.5 | 1.00 | 11.3 | 1.00 | 7.0 | 1.00 |
| Yes | 13.0 | 0.78 (0.58–1.05) | 11.5 | 0.48 (0.35–0.64)[e] | 11.2 | 0.99 (0.72–1.38) | 4.2 | 0.59 (0.37–0.94)[e] |
| Sexual practice | | | | | | | | |
| Sex with women | 13.5 | 1.00 | 16.0 | 1.00 | 9.0 | 1.00 | 3.9 | 1.00 |
| Sex with men | 34.4 | 3.36 (1.96–5.78)[e] | 31.3 | 2.39 (1.38–4.15)[e] | 40.6 | 6.93 (4.06–11.84)[e] | 23.4 | 7.48 (3.93–14.27)[e] |
| Sex with both men and women | 25.0 | 2.14 (1.19–3.86)[e] | 31.3 | 2.39 (1.38–4.15)[e] | 35.9 | 5.69 (3.29–9.82)[e] | 26.6 | 8.84 (4.74–16.50)[e] |
| Never had sex | 13.2 | 0.97 (0.49–1.93) | 17.1 | 1.09 (0.59–2.01) | 2.6 | 0.27 (0.07–1.13) | 5.3 | 1.36 (0.48–3.87) |
| Age at first sexual intercourse (y) | | | | | | | | |
| Never had sex | 13.1 | 0.96 (0.46–2.00) | 20.8 | 2.12 (1.04–4.33)[e] | 12.3 | 0.78 (0.38–1.61) | 7.7 | 1.32 (0.49–3.59) |
| ≤15 | 14.3 | 1.06 (0.58–1.93) | 20.6 | 2.09 (1.12–3.90)[e] | 12.8 | 0.81 (0.46–1.46) | 7.3 | 1.24 (0.53–2.91) |
| 16–17 | 14.9 | 1.12 (0.62–2.01) | 14.9 | 1.41 (0.75–2.66) | 10.0 | 0.62 (0.34–1.11) | 4.7 | 0.78 (0.32–1.87) |
| 18–20 | 17.6 | 1.36 (0.75–2.48) | 17.6 | 1.73 (0.91–3.29) | 9.4 | 0.58 (0.31–1.08) | 5.5 | 0.92 (0.37–2.26) |
| ≥21 | 13.6 | 1.00 | 11.0 | 1.00 | 15.3 | 1.00 | 5.9 | 1.00 |
| Lifetime female sex partners among MSW, *n* | | | | | | | | |
| None | 14.5 | 1.26 (0.61–2.60) | 15.8 | 1.27 (0.63–2.56) | 2.6 | 0.29 (0.07–1.24) | 5.3 | 1.47 (0.46–4.77) |
| 1–3 | 11.9 | 1.00 | 12.9 | 1.00 | 8.6 | 1.00 | 3.6 | 1.00 |
| 4–7 | 13.3 | 1.14 (0.70–1.86) | 14.7 | 1.17 (0.73–1.87) | 7.7 | 0.89 (0.49–1.61) | 2.5 | 0.67 (0.26–1.75) |
| 8–16 | 15.5 | 1.36 (0.85–2.19) | 17.3 | 1.42 (0.90–2.24) | 8.7 | 1.01 (0.57–1.81) | 5.1 | 1.41 (0.63–3.17) |
| ≥17 | 13.9 | 1.20 (0.74–1.95) | 18.9 | 1.58 (1.01–2.48)[e] | 11.0 | 1.33 (0.77–2.30) | 5.0 | 1.40 (0.62–3.13) |
| Lifetime male anal sex partners, *n* | | | | | | | | |
| None | 13.3 | 1.00 | 15.7 | 1.00 | 8.3 | 1.00 | 4.0 | 1.00 |
| 1 | 17.5 | 1.39 (0.69–2.80) | 19.3 | 1.29 (0.66–2.53) | 14.0 | 1.80 (0.83–3.90) | 1.8 | 0.43 (0.06–3.16) |
| 2–3 | 21.3 | 1.76 (0.86–3.61) | 31.9 | 2.52 (1.34–4.75)[e] | 23.4 | 3.37 (1.66–6.81)[e] | 10.6 | 2.86 (1.08–7.55)[e] |
| 4–10 | 29.3 | 2.70 (1.35–5.39)[e] | 26.8 | 1.97 (0.97–4.01) | 41.5 | 7.81 (4.06–15.00)[e] | 22.0 | 6.76 (3.06–14.93)[e] |
| ≥11 | 40.5 | 4.43 (2.34–8.39)[e] | 31.0 | 2.41 (1.23–4.73)[e] | 47.6 | 10.02 (5.29–18.97)[e] | 38.1 | 14.78 (7.45–29.33)[e] |
| Recent new sex partners (either sex), *n* | | | | | | | | |
| None | 13.4 | 1.00 | 15.6 | 1.00 | 9.6 | 1.00 | 4.5 | 1.00 |
| 1 | 18.2 | 1.45 (1.03–2.03)[e] | 21.7 | 1.50 (1.09–2.05)[e] | 12.3 | 1.32 (0.89–1.97) | 6.0 | 1.34 (0.77–2.33) |
| ≥2 | 16.4 | 1.27 (0.81–1.99) | 18.2 | 1.20 (0.78–1.85) | 17.0 | 1.93 (1.22–3.06)[e] | 12.1 | 2.91 (1.67–5.08)[e] |

*(Continued on the following page)*

Table 2. Factors associated with seroprevalence of HPV 6, 11, 16, and 18 among 1,477 men in univariate analyses (Cont'd)

| Risk factors | HPV 6 | | HPV 11 | | HPV 16 | | HPV 18 | |
|---|---|---|---|---|---|---|---|---|
| | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) | Seroprevalence (%) | OR (95% CI) |
| Frequency of recent vaginal sex (times/wk) | | | | | | | | |
| <1 | 14.5 | 1.00 | 14.9 | 1.00 | 9.4 | 1.00 | 4.4 | 1.00 |
| 1–2 | 14.2 | 0.98 (0.65–1.49) | 21.2 | 1.54 (1.05–2.24)[e] | 6.9 | 0.72 (0.41–1.24) | 5.6 | 1.28 (0.66–2.49) |
| ≥3 | 16.1 | 1.13 (0.77–1.68) | 19.5 | 1.39 (0.95–2.01) | 10.5 | 1.13 (0.71–1.81) | 4.0 | 0.91 (0.45–1.85) |
| Recent condom use in vaginal sex | | | | | | | | |
| Always | 11.8 | 1.00 | 16.7 | 1.00 | 9.4 | 1.00 | 3.5 | 1.00 |
| Frequently | 13.6 | 1.17 (0.71–1.92) | 18.6 | 1.14 (0.74–1.76) | 7.9 | 0.82 (0.46–1.49) | 3.9 | 1.14 (0.48–2.72) |
| Sometimes | 17.6 | 1.60 (0.92–2.77) | 15.0 | 0.88 (0.52–1.52) | 11.8 | 1.29 (0.69–2.42) | 4.6 | 1.33 (0.50–3.57) |
| Never | 16.0 | 1.43 (0.92–2.20) | 18.8 | 1.16 (0.79–1.70) | 10.1 | 1.09 (0.66–1.79) | 6.5 | 1.95 (0.94–4.03) |
| Recent condom use in anal sex | | | | | | | | |
| Always | 26.4 | 1.00 | 27.8 | 1.00 | 23.6 | 1.00 | 12.5 | 1.00 |
| Frequently | 21.5 | 0.76 (0.40–1.47) | 22.8 | 0.77 (0.40–1.45) | 15.2 | 0.58 (0.28–1.20) | 10.1 | 0.79 (0.33–1.91) |
| Sometimes | 23.8 | 0.87 (0.39–1.94) | 28.6 | 1.04 (0.49–2.23) | 19.0 | 0.76 (0.32–1.80) | 9.5 | 0.74 (0.24–2.31) |
| Never | 23.7 | 0.87 (0.53–1.41) | 23.2 | 0.78 (0.48–1.28) | 10.6 | 0.38 (0.21–0.69)[e] | 8.2 | 0.63 (0.31–1.26) |
| History of other STIs[d] | | | | | | | | |
| No | 14.1 | 1.00 | 16.5 | 1.00 | 9.8 | 1.00 | 4.9 | 1.00 |
| Yes | 18.3 | 1.36 (0.95–1.96) | 21.5 | 1.39 (0.99–1.96) | 18.3 | 2.07 (1.42–3.01)[e] | 10.2 | 2.19 (1.34–3.56)[e] |
| Corresponding genital HPV DNA status | | | | | | | | |
| Negative | 14.5 | 1.00 | 17.0 | 1.00 | 11.0 | 1.00 | 5.8 | 1.00 |
| Positive | 18.8 | 1.37 (0.81–2.31) | 36.4 | 2.78 (1.15–6.70)[e] | 15.2 | 1.46 (0.80–2.64) | 7.4 | 1.30 (0.30–5.59) |

[a]Light drinking was defined as less than half a drink per day; moderate drinking as one half to 2 drinks per day; and heavy drinking as more than 2 drinks per day on average.
[b]Heavy exposure was defined as 913 or more pack-years, and light-moderate exposure as less than 913 pack-years, equivalent to 10 cigarettes per day for 5 years.
[c]Circumcision status was assessed by study clinician.
[d]Other STIs: *Chlamydia* infection, HSV infection, genital warts, gonorrhea, hepatitis B, hepatitis C, nongonococcal urethratitis, syphilis.
[e]Denote statistical significance ($P < 0.05$).

**Table 3.** Factors associated with seroprevalence of HPV 6, 11, 16, and 18 among 1,477 men in multivariable analyses

| Risk factors | HPV 6 AOR (95% CI) | HPV 11 AOR (95% CI) | HPV 16 AOR (95% CI) | HPV 18 AOR (95% CI) |
|---|---|---|---|---|
| Age (y) | | | | |
| 18–24 | 1.00 | 1.00 | 1.00 | 1.00 |
| 25–34 | 0.95 (0.64–1.41) | 1.50 (1.03–2.23)[b] | 1.81 (1.09–3.01)[b] | 1.62 (0.75–3.46) |
| 35–44 | 1.31 (0.88–1.93) | 1.58 (1.06–2.37)[b] | 2.22 (1.26–3.92)[b] | 2.13 (1.00–4.52)[b] |
| 45–70 | 0.76 (0.44–1.31) | 1.44 (0.87–2.39) | 2.23 (1.13–4.40)[b] | 3.21 (1.41–7.33)[b] |
| Country of residence | | | | |
| United States | – | – | | 1.00 |
| Brazil | – | – | – | 2.09 (1.04–4.19)[b] |
| Mexico | – | – | – | 1.63 (0.81–3.33) |
| Marital status | | | | |
| Single | – | – | 1.00 | – |
| Cohabiting | – | – | 1.19 (0.68–2.08) | – |
| Married | – | – | 0.54 (0.33–0.90)[b] | – |
| Divorced/separated/widowed | – | – | 1.20 (0.64–2.25) | – |
| Education | | | | |
| <High school | 1.00 | 1.00 | – | – |
| High school graduate | 0.67 (0.44–1.02) | 0.89 (0.61–1.31) | – | – |
| ≥College/vocational school | 0.59 (0.41–0.85)[b] | 0.61 (0.43–0.88)[b] | – | – |
| Circumcision[a] | | | | |
| No | – | 1.00 | – | – |
| Yes | – | 0.67 (0.48–0.94)[b] | – | – |
| Lifetime male anal sex partners, *n* | | | | |
| None | 1.00 | 1.00 | 1.00 | 1.00 |
| 1 | 1.32 (0.65–2.67) | 1.24 (0.62–2.47) | 1.61 (0.74–3.54) | 0.35 (0.05–2.57) |
| 2–3 | 1.68 (0.82–3.47) | 2.14 (1.13–4.09)[b] | 3.34 (1.63–6.85)[b] | 2.21 (0.81–6.03) |
| 4–10 | 2.68 (1.33–5.41)[b] | 1.99 (0.96–4.15) | 7.19 (3.68–14.05)[b] | 6.10 (2.67–13.94)[b] |
| ≥11 | 4.34 (2.28–8.29)[b] | 2.32 (1.12–4.84)[b] | 7.74 (3.96–15.12)[b] | 11.46 (5.40–24.34)[b] |
| Recent new sex partners (either sex), *n* | | | | |
| None | – | 1.00 | – | – |
| 1 | – | 1.64 (1.17–2.30)[b] | – | – |
| ≥2 | – | 1.01 (0.61–1.66) | – | – |

[a]Circumcision status was assessed by study clinician.
[b]Denote statistical significance ($P < 0.05$).

HPV 11 seroprevalence; race, marital status, recent condom use in anal sex, and the history of other STIs for HPV 16 seroprevalence; and education, cigarette smoking, circumcision, and the history of other STIs for HPV 18 seroprevalence.

In multivariable analyses, the number of lifetime male anal sex partners was independently associated with seroprevalence of HPV 6, 11, 16, and 18, respectively (Table 3). Men with multiple lifetime male anal sex partners were more likely to be seropositive to HPV 6, 11, 16, or 18 [adjusted OR (AOR) for ≥11 partners: 4.34 (95% CI, 2.28–8.29) for HPV 6; 2.32 (95% CI, 1.12–4.84) for HPV 11; 7.74 (95% CI, 3.96–15.12) for HPV 16; and 11.46 (95% CI, 5.40–24.34) for HPV 18]. Increasing age was significantly associated with higher seroprevalence of HPV 11, 16, and 18, with an AOR of 1.50 to 1.58 for HPV 11, 1.81 to 2.23 for HPV 16, and 1.62 to 3.21 for HPV 18. In addition, for HPV 6, men with college or higher education had a significantly lower seroprevalence [AOR, 0.59 (95% CI, 0.41–0.85)]. For HPV 11, men with a recent new sex partner were significantly more likely to test seropositive [AOR, 1.64 (95% CI, 1.17–2.30)], whereas college-educated [AOR, 0.61 (95% CI, 0.43–0.88)] and circumcised men [AOR, 0.67 (95% CI, 0.48–0.94)] were less likely to test seropositive. For HPV 16, married men had significantly lower seroprevalence [AOR, 0.54 (95% CI, 0.33–0.90)]. For HPV 18, Brazilian residency was significantly associated with higher seroprevalence [AOR, 2.09 (95% CI, 1.04–4.19)].

## Discussion

This study characterized the seroprevalence of 4 HPV types targeted in the currently licensed HPV vaccines and determined factors associated with individual HPV seroprevalence in 1,477 men residing in the United States, Mexico, and Brazil. Our findings show that approximately one third of cohort participants were exposed to 1 or more vaccine HPV types and the risk of exposure was twice as high among MSM and MSMW. Age was significantly associated with seroprevalence of all vaccine HPV types except for HPV 6, and anal sex with men was significantly associated with a higher risk of seropositivity to individual HPV types.

Age has been consistently associated with HPV seroprevalence in previous serology studies in men using VLP-based ELISA (26–35, 42). The upward age trends associated with HPV 16 and 18 seroprevalences observed in this study are consistent with those reported in population-based (30), community-based (26, 42), or clinic-based studies (31, 33–35). Only 3 studies have evaluated HPV 6 and/or 11 seroprevalence in men (27, 28, 31) and their findings on age have been mixed. The study of Hariri and colleagues showed a significant, increasing age trend for HPV 11 seroprevalence for males 6- to 49-year-olds, followed by an insignificant decline through age 59 in a population-based study of 3,589 men (28), similar to the age pattern observed for HPV 11 seroprevalence in the current study. In the remaining 2 studies, HPV 6 seroprevalence was significantly associated with older age (>35; OR, 2.2; 95% CI, 1.0–4.8) in the study of Hagensee and colleagues (27), whereas no age association with HPV 6/11 seroprevalence was detected by Slavinsky and colleagues (31). The age patterns observed in the current study as well as previous studies likely reflect complex changes in individual immune capacity and the balance between HPV acquisition and clearance over their life span. The lack of age association in the study of Slavinsky and colleagues (31) may be explained by the exclusive enrollment of highly sexually active STI clinic attendees who had multiple sex partners and a history of STI in the past year, as it is suggested that concomitant infection with other sexually transmitted agents may facilitate persistence of HPV infection, eliciting a stronger immune response and longer-lasting immune memory (32, 34, 35) and resulting in less variation in seroprevalence across age groups. Seroprevalence estimates for U.S. males in the present study were higher than what were reported for U.S. National Health and Nutrition Survey (NHANES) populations (28, 30, 32), likely in part due to differences in age composition between the present study and the NHANES studies. Only adult men aged 18 to 70 were enrolled in the present study, whereas males as young as 6 years old were enrolled in the NHANES studies with young males 19 or younger accounting for 24% to 37% of the total male cohorts. The inclusion of a large proportion of young males 19 or younger who were at lower risk for HPV exposure and thus for developing seropositivity may partially explain the lower seroprevalence estimates for U.S. males observed in the NHANES studies.

Our data showed that seroprevalence of vaccine HPV types differed significantly between MSW, MSM, and MSMW. To our knowledge, this study is the first to compare vaccine-type HPV seroprevalence between men with different sexual practices. Overall, MSM and MSMW exhibited approximately 2 to 6 times higher seroprevalence compared with MSW. Furthermore, no statistically significant trend or association of HPV seroprevalence with the number of lifetime female sex partners was observed among MSW for any vaccine HPV type examined. In contrast, seroprevalence increased significantly with increasing number of lifetime male anal sex partners for individual HPV types, and significant independent associations were detected for men reporting multiple male anal sex partners. The higher seroprevalence associated with the practice of same-sex anal sex among MSM and MSMW is consistent with the previous findings (28–30, 32) and is likely explained by the increased risk of simultaneous HPV infections (oral, genital, and anal) at multiple anatomic sites among MSM and MSMW. It probably also implies that HPV infection at keratinized epithelium is less likely to induce an immune response than infection of mucosal epithelium. However, as the significant associations between seroprevalence and the number of male anal sex partner were primarily derived from a relatively small group of men who reported multiple male anal sex partner in their lifetime, 8.8% (130) of the total cohort, these associations need to be further confirmed in future studies. In addition, it is noteworthy that seroprevalence of vaccine HPV types among men who reported never having any type of sex was comparable with that reported for MSW, except for HPV 16 seroprevalence which was much lower among those with no sex. It is possible that besides sexual intercourse, HPV transmission may have occurred through other forms of contact such as skin contact and use of sex toys, or through vertical transmission, although less likely.

In this study, circumcision was independently associated with lower HPV 11 seroprevalence but not with any other vaccine HPV types. A statistically significant association with circumcision was also observed in univariate analysis of HPV 18 seroprevalence. However, it was not retained in multivariate analyses. An approximately 30% reduction in acquisition and 30% increase in clearance of oncogenic HPV infection was shown in a recent randomized controlled trials of circumcision (43, 44). In addition, 2 to 3 times higher likelihood of clearance for both oncogenic and nononcogenic HPV infections was shown in longitudinal epidemiologic studies (45, 46). It is possible that the lower incidence and shorter duration of HPV 11 infection due to circumcision may have contributed to the lower HPV 11 seroprevalence observed among circumcised men.

It was noted that in this study the detection of anti-HPV serum antibodies was not significantly associated with simultaneous presence of HPV DNA for any vaccine-type HPV, indicating a possible lag time between HPV DNA detection and detection of serum antibodies, and the limited value of serum antibodies as a marker of current infection, consistent with what has been reported previously (21, 23, 47). Our data also showed substantial gaps between HPV DNA prevalence and seroprevalence. The gap was most prominent for HPV 11 (seroprevalence: DNA prevalence ratio = 11.6) and least prominent for HPV 16 (seroprevalence: DNA prevalence ratio = 1.8). It was suggested that longer presence of HPV DNA is associated with higher likelihood of seroconversion (20, 23). With a longer duration of infection for HPV 16 than HPV 11 in this cohort of men (15), a smaller gap between HPV 16 DNA prevalence and seroprevalence was counterintuitive. However, HPV 16 and other oncogenic HPV were shown to have evolved an immune evasion mechanism inhibiting host detection of virus (48). It was likely that the lack of immune evasion mechanism for HPV 11 and frequent presence of HPV 11–positive warts may have contributed to a higher seroconversion rate for HPV 11 than for HPV 16. In addition, HPV 11 seroprevalence was associated with the presence of new sex partner in past 6 months, which may indicate a shorter latency period for HPV 11 serum antibody detection. The combination of a shorter latency and a higher seroconversion may have led to the great discrepancy observed between HPV 11 DNA prevalence and seroprevalence. Unique to HPV 6 and 11, a higher level of education was significantly associated with lower seroprevalence, which was also observed in the study of Hariri and colleagues (28). We hypothesize that education is likely a marker of lifestyle characteristics which may impact potential HPV transmission.

The major strengths of this study are the inclusion of men of a wide age range (18–70), especially those 60 and older, the age group that was rarely evaluated in previous studies, and the availability of detailed and extensive participant sexual behavioral information that has been previously validated (49). However, several limitations must be addressed. First, this study is a cross-sectional analysis utilizing serology measured at the baseline of a large natural history study in men. With our limited understanding of seroconversion rates following natural infection and the longevity of type-specific serum antibodies, baseline serostatus may underestimate the true proportion of cumulative HPV exposure and thus making it less informative for estimating population exposure. Second, differences in serologic assays used and the choice of control population and cutoff points for determining seropositivity between the present study and the previous studies may limit a direct comparison of our results with those published previously. Finally, because of the recruitment method used in the present study, the cohort presented may not be a representative sample of the general male population of the participating country, which limits the generalizability of our findings.

Despite the aforementioned limitations, this study provided important data on the distribution of vaccine-type HPV exposure in community-based male populations from 3 countries and epidemiologic factors associated with seroprevalence of individual HPV types targeted in the current vaccines. Our results indicated exposure to vaccine HPV types is common in men and increased from young to middle-aged men. Our data also showed that MSM and MSMW had greatly elevated risk of exposure to vaccine HPV types compared with MSW, and their engagement in same-sex intercourse was a strong determinant of seroprevalence for all vaccine HPV types.

## Disclosure of Potential Conflicts of Interest

The authors have no commercial or other association that might pose a conflict of interest for the work submitted.

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