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Concurrent and Concordant Oral and Genital High-Risk Human Papillomavirus in the United States: Results from the National Health and Nutrition Examination Survey

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Background: Oropharyngeal cancers associated with high-risk human papillomavirus (HR-HPV) infection are increasing in the United States, especially among men. We evaluated the prevalence and predictors of concurrent (genital and oral) and concordant (same-type) HR-HPV infections in the United States.

Methods: We used the National Health and Nutrition Examination Survey from 2009 to 2016. Predictors were assessed via multivariable logistic regression.

Results: Among 10 334 respondents, 172 (2.1%) had concurrent infections (109 [3.5%] men and 63 [0.76%] women). Ninety-three (1.0%) had concordant infections (54 [1.6%] men and 39 [0.5%] women). Predictors of concurrence in men included the following: no longer married versus married (odds ratio [OR], 2.3; 95% confidence interval [CI], 1.3–4.9), living with a partner versus married (3.0; 1.2–7.5), and having 2–5 lifetime oral sex partners (3.0; 1.2–7.5). In women they included the following: no longer married versus married (3.6; 1.3–10.3), ≥2 recent sex partners (4.6; 1.4–15.6 for 2–5 partners and 3.9; 1.1–14.3 for ≥6 partners), and marijuana use (2.2; 1.0–4.5). The predictor of concordance in men and women was no longer married versus married (3.5; 1.2–9.9 in men and 3.2; 1.1–9.4 in women).

Conclusions: Concurrent and concordant HR-HPV infections occur at a high rate, especially among men, and are associated with behavioral factors. This underscores the importance of HPV vaccination, screening, and education in men.

Keywords. Concurrence; concordance; high-risk HPV infection; NHANES.

Human papillomavirus (HPV) is one of the most common sexually transmitted infections in the United States [1]. The most common anatomic sites for HPV infection are the anogenital and upper aerodigestive tracts. There are >100 types of HPV categorized either into high-risk HPV (HR-HPV) types with oncogenic potential or low-risk HPV (LR-HPV) types. Persistent HR-HPV infection is known to cause cancer at several anatomic sites such as cervix, vulva, vagina, oropharynx, anus, and penis [2]. The causal effect of HPV on cervical cancer is well known; 90%–99% of cervical cancer cases are attributable to HPV [3, 4]. Between 2004 and 2012 there was a decrease in yearly cervical cancer rates in the United States, likely owing to improved screening, vaccination, and testing in women; however, the overall rate of HPV-associated cancers has increased during the same time period [1].

The increase in HPV-associated cancers is partly attributed to the increasing incidence of HPV-positive oropharyngeal cancers (OPCs). The OPCs include "cancers of the base of the tongue, pharyngeal tonsils, anterior and posterior tonsillar pillars, and glossotonsillar sulci; anterior surface of soft palate and uvula; and lateral and posterior pharyngeal walls" [1]. Between 1988 and 2004, the incidence of HPV-positive OPCs increased by 225%, while the incidence of HPV-negative OPCs declined by 50% [5]. Approximately 70% of OPCs are associated with HPV [3, 5]. It was estimated that the annual number of HPV-associated OPCs would surpass the annual number of HPV-associated cervical cancers by 2020 if these trends continued; however, this happened earlier than expected, by 2012 [1, 5]. Studies from other countries have also reported increasing incidence of OPCs [6].

Although oral HPV infections are relatively rare, the rate of HPV-associated OPCs in men is about 4 times higher than that of women [1, 2, 6, 7]. Viens et al [1] reported the rates as 7.6 in men and 1.7 in women per 100 000 persons during 2008–2012 in the United States. These figures are concerning given a lack of Food and Drug Administration–approved screening tools for oral HR-HPV infection, which disproportionately affects men. In addition, the rate of HPV up-to-date vaccination coverage

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was lower among men (37.5%) than women (49.5%) in 2016 [8]. While no HPV vaccine trial (to our knowledge) has used oral HPV as an end point, some researchers have inferred a link between the vaccine and potential protection against oral HPV, in addition to genital HPV [9, 10]. Thus, it is possible that the higher rate of OPCs in men could be due to a lower vaccination rate among men.

There have been only a few studies to date focusing on both concurrent and concordant infections. Concurrent HPV infection is defined as simultaneous detection of any HR-HPV type in both the oral cavity and the cervix or penis of a person. Concordant HPV infection is defined as one or more of the same HR-HPV types detected in both the oral cavity and the cervix or penis of a person. Separate studies on men and women have estimated prevalence of concurrence from earlier cycles of the National Health and Nutrition Examination Survey (NHANES) [11, 12]. Limitations of these studies included small sample sizes and lack of sufficient power to analyze the HR-HPV subgroups responsible for the majority of cancers described above (eg, subgroup analyses of HPV types 16 and 18).

A study of men in rural China estimated the prevalence of concurrence and concordance but included LR-HPV subtypes. Results from that study are not generalizable to the US population [13]. Another study estimated prevalence of concurrent infections in the United States using NHANES, but its focus was comparative and it did not break down infections by HR-HPV versus LR-HPV [14]. We aimed to fill the gap in knowledge of concurrent and concordant HR-HPV infections by evaluating the prevalence and predictors of concurrent and concordant HR-HPV infections among US men and women using all available NHANES cycles, including the most recent to date.

METHODS

Study Design and Participants

We used data from NHANES, a nationally representative survey of the noninstitutionalized US population, collected by the National Center for Health Statistics and the Centers for Disease Control and Prevention [15]. During the informed consent process, survey participants were assured that collected data will be used only for study purposes and will not be released to others without consent of the individual or the establishment [16]. Participants included 18–59-year-old men who completed the survey in 2013–2016 and 18–59-year-old women who completed it in 2009–2016 and for whom oral and genital HPV test results were available.

Specimen Collection and Laboratory Methods

The NHANES procedure for sample collection and laboratory methods are outlined in detail elsewhere [17]. Briefly, oral samples were collected by having participants rinse and gargle with Scope mouthwash [17]. Genital samples were self-collected using vaginal and penile swab. These were analyzed for 37 types of HPV using a multiplex polymerase chain reaction assay [17]. Of 37 types, 18 are classified as HR-HPV—types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, and 82 [18].

Statistical Methods

First, we estimated the prevalence of HR-HPV concurrent and concordant infections for 4 clinically important subgroups: (1) all HR-HPV types, (2) the HR-HPV types covered in the 9-valent vaccine (HPV types 16, 18, 31, 33, 45, 52, and 58), (3) the most common types found in cervical cancers (HPV types 16, 18, or 45), and (4) the most common type found in HPV-associated cancers (HPV-16) [19, 20].

To estimate the prevalence of concurrent infections, we identified participants with simultaneous HR-HPV oral and genital infections. In the same manner, to estimate the prevalence of concordant infections, we identified participants with oral and genital infections who had at least one of the same HR-HPV types. The survey adjusted prevalence was calculated for total population, men and women.

We computed new NHANES sample weights by dividing Centers for Disease Control and Prevention weights by the number of cycles [15]. Thus, for men we used the 4-year sample weights by dividing by 2 (2013–2016). For women, we used 8-year sample weighs by dividing by 4 (2009–2016).

We also conducted Monte Carlo simulations for the 4 abovementioned HR-HPV groups to test whether concurrent and concordant HR-HPV infections occur more than expected from the population marginal prevalence of oral and genital infections. Ten thousand individuals were sampled with HR-HPV infection status based on the actual marginal oral and genital prevalence assuming a binomial distribution. The *P* value for each simulation was calculated by taking the proportion of simulated HR-HPV prevalence estimates (for concurrent or concordant infection) that were smaller than that observed in NHANES multiplied by 2. The 95% confidence interval (CI) was 2.5th and 97.5th percentiles of the simulated proportions.

Finally, we evaluated the predictors of concurrent and concordant HR-HPV infections using univariate and multivariable survey weighted logistic regression models in men and women separately. We computed adjusted χ^2 statistics for categorical predictors of concurrence and concordance. Variables included ethnicity (non-Hispanic white, non-Hispanic black, and other), age group (18–24, 25–39, or 40–59 years), marital status (married, no longer married [widowed, divorced, or separated], never married, living with partner, or missing), lifetime and recent number of sex (vaginal, oral, or anal) partners (0–1, 2–5, 6–10, ≥11, or data missing), and lifetime and recent number of oral sex partners (0–1, 2–5, 6–10, ≥11, or data missing), HPV vaccination (yes or no), smoking and marijuana use (never, ever, or data missing), and sexual orientation (heterosexual, homosexual/bisexual, or other). Multivariable models included any predictor with a *P* value <.15 on univariate analysis [14].

Statistical significance was set at a 2-sided type 1 error rate (α) of .05. We flagged all parameter estimates with a relative standard error >30%, because these are considered unstable and should be interpreted with caution. All the statistical analysis was performed using R Version 3.6.2.

RESULTS

Prevalence of Concurrent and Concordant HR-HPV Infections in the United States

Of 10 334 individuals (3241 men and 7093 women) tested for both oral and genital HPV infections, 172 (2.1%) had concurrent HR-HPV infection, while 93 (1.0%) had concordant HR-HPV infection (Tables 1 and 2). The prevalences of concurrent HR-HPV infection in the total population, in men, and in women were 2.1% (n = 172), 3.5% (n = 109), and 0.76% (n = 63), respectively. For the 9-valent vaccine types, they were 0.56% (n = 46), 0.86% (n = 27), and 0.27% (n = 19), respectively; for HPV types 16, 18, and 45, they were 0.34% (n = 32), 0.50% (n = 18), and 0.20% (n = 14); and for HPV-16, they were 0.15% (n = 18), 0.17% (n = 10), and 0.13% (n = 8) (Table 1). The odds ratios (OR) for oral HR-HPV infection for those with versus without an HPV genital infection for the total population, men, and women were as follows: for any HR-HPV: 3.44, 3.6, and 2.59, respectively; for the HR 9-valent vaccine types: 3.42, 2.96, and 5.33; for HPV types 16, 18, and 45: 4.77, 3.71, and 10.62; and for HPV-16: 5.4, 3.26, and 18.76. The χ^2 *P* value for each of the ORs was <.005 (Table 1).

The prevalences of concordant HR-HPV infection in the total population, in men, and in women were 1% (n = 93), 1.6% (n = 54), and 0.51% (n = 39), respectively. However, the prevalences of concordant HR-HPV infection in those who had concurrent infection were 48.5% (n = 93), 44.4% (n = 54), and 67.1% (n = 39), respectively (Table 2). HPV-16 was the most common concordant type in our study (Supplementary Table 1 enumerates the complete and partial type of HR-HPV concordances). This is important because HPV-16 is responsible for the majority of oral and cervical cancers [19, 20].

Monte Carlo simulations demonstrated that concurrence and concordance occurred significantly more than expected given the population marginal prevalence of oral and genital infections of the total population (Figure 1 for concurrence), men, and women (Supplementary Figures 1–5; all *P* values for the test of independence were <.001).

Demographic and Behavioral Predictors of Concurrent HR-HPV Infections in Men and Women

Tables 3 and 4 display the prevalence by demographic and behavioral predictors and logistic regression results for concurrent and concordant infection among men and women, respectively. In univariate analysis for men, ethnicity, marital status, number of lifetime and recent sex partners, number of lifetime and recent oral sex partners, cigarette use, marijuana use, and sexual orientation were associated with concurrence. In multivariable analysis, men who were no longer married had higher odds of having a concurrent HR-HPV infection than married men (OR, 2.5; 95% CI, 1.2–5.2). Men who were living with a partner had higher odds of a concurrent infection than married men (OR, 3.0; 95% CI, 1.2–7.5). Men with 2–5 lifetime oral sex partners had higher odds of having concurrent infection than men with or ≤1 partner (OR, 3.0; 95% CI, 1.2–7.5).

In univariate analysis for women, marital status, number of lifetime and recent sex partners, number of lifetime and recent oral sex partners, cigarette use, and marijuana use were associated with concurrence. In multivariable analysis, only marital status, number of recent sex partners, and marijuana use remained associated. Women who were no longer married had higher odds of having a concurrent infection than married women (OR, 3.6, 95% CI, 1.3–10.3). Women with 2–5 or 6–10 recent sex partners had higher odds of having a concurrent infection than women with ≤1 partner (OR, 4.6; 95% CI, 1.4–15.6) and (OR, 3.9; 95% CI, 1.1–14.3), respectively. Women who ever used marijuana had higher odds of having concurrent infection than never-users (OR, 2.2; 95% CI, 1.0–4.5).

Demographic and Behavioral Predictors of Concordant HR-HPV Infections in Men and Women

Univariate logistic regression results were similar to that for concurrence. For men, marital status, number of lifetime and recent sex partners, number of lifetime and recent oral sex partners, and sexual orientation were associated with concordance (Table 3). For women, marital status, number of lifetime and recent sex partners, number of lifetime and recent oral sex partners, and marijuana use were associated with concordance (Table 4).

Moreover, for multivariable regression, both men and women who were no longer married had >3 times the odds of having a concordant infection compared with married men and women, after adjustment for other variables (OR in men, 3.5 [95% CI, 1.2–9.9]; OR in women, 3.2 [95% CI, 1.1–9.4]) (Tables 3 and 4).

DISCUSSION

The literature on concurrent and concordant HR-HPV infections is limited. We believe ours is the largest and latest nationally representative US study to focus solely on estimating prevalence and determining predictors of concurrent and concordant HR-HPV infections. This study showed that 2.1% of the US population had concurrent and 1% had concordant HR-HPV infection from 2009 to 2016. Aligning with the 2010 US census, this roughly equates to 6.4 million Americans living with concurrent and 3.1 million with concordant HR-HPV infections. The burden is particularly large for men, equating to roughly 5.3 million (3.5%) and 2.4 million (1.6%) men as compared with roughly 1.2 million (0.76%) and 0.8 million (0.51%) women with concurrent and concordant HR-HPV infections, respectively.

Table 1. Prevalence of Concurrent Oral and Genital High-Risk Human Papillomavirus (HR-HPV) Infections Among 4 Groups of HR-HPV for the Total Population, for Men, and for Women[a]

	Oral HR-HPV Infection in Persons With Genital Infection					
	Yes		No		Total	
HR-HPV Group	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Total Population						
HR-HPV[b]	OR, 3.44; χ^2 = 162.81; P < .005					
Yes	172	2.1 (1.7–2.7)	2649	24.3 (22.8–25.9)	2821	26.4 (24.8–28.2)
No	158	1.8 (1.4–2.3)	7355	71.8 (69.9–73.5)	7513	73.6 (71.8–75.2)
Total	330	3.9 (3.3–4.6)	10004	96.1 (95.4–96.7)	10334	
9V HR-HPV types[c]	OR, 3.42; χ^2 = 65.51; P < .005					
Yes	46	0.56 (0.37–.84)	1231	11.2 (10.3–12.1)	1277	11.7 (10.8–12.7)
No	85	1.3 (.93–1.7)	8972	87.0 (85.9–88.0)	9057	88.3 (87.3–89.2)
Total	131	1.8 (1.5–2.2)	10203	98.2 (97.8–98.5)	10334	
HPV type 16, 18, or 45[d]	OR, 4.77; χ^2 = 75.60; P < .005					
Yes	32	0.34 (0.22–.55)	676	6.5 (5.8–7.2)	708	6.8 (6.2–7.6)
No	64	1.0 (.78–1.3)	9562	92.1 (91.4–92.8)	9626	93.2 (92.4–93.8)
Total	96	1.4 (1.1–1.7)	10238	98.6 (98.3–98.9)	10334	
HPV-16[e]	OR, 5.4; χ^2 = 44.70; P < .005					
Yes	18	0.15 (.09–.25)	336	3.6 (3.1–4.2)	354	3.7 (3.2–4.3)
No	46	0.75 (.55–1.0)	9934	95.5 (94.9–96.1)	9980	96.3(95.7–96.8)
Total	64	0.90 (.70–1.1)	10270	99.1 (98.9–99.3)	10334	
Men						
HR-HPV[b]	OR, 3.6; χ^2 = 84.16; P < .005					
Yes	109	3.5 (2.7–4.6)	808	24.6 (22.4–26.9)	917	28.1 (25.5–30.8)
No	92	2.7 (2.0–3.7)	2232	69.2 (66.2–72.0)	2324	71.9 (69.2–74.5)
Total	201	6.3 (5.2–7.6)	3040	93.7 (92.4–94.8)	3241	
9V HR-HPV types[c]	OR, 2.96; χ^2 = 24.21; P < .005					
Yes	27	0.86 (.52–1.4)	378	11.5 (10.0–13.0)	405	12.3 (10.8–14.0)
No	53	2.2 (1.5–3.1)	2783	85.5 (83.6–87.2)	2836	87.7(86.0–89.2)
Total	80	3.0 (2.3–3.9)	3161	97.0 (96.1–97.7)	3241	
HPV type 16, 18, or 45[d]	OR, 3.71; χ^2 = 23.36; P < .005					
Yes	18	0.50 (.27–.91)	210	6.8 (5.7–8.0)	228	7.3 (6.3–8.4)
No	42	1.8 (1.3–2.4)	2971	90.9 (89.7–92.0)	3013	92.7 (91.6–93.7)
Total	60	2.3 (1.8–3.0)	3181	97.7 (97.0–98.2)	3241	
HPV-16[e]	OR, 3.26; χ^2 = 7.41; P < .05					
Yes	10	0.17 (.09–.34)[f]	109	3.8 (3.0–4.8)	119	4.0 (3.2–4.9)
No	32	1.3 (.93–1.9)	3090	94.7 (93.6–95.6)	3122	96.0 (95.1–96.8)
Total	42	1.5 (1.1–2.0)	3199	98.5 (98.0–98.9)	3241	
Women						
HR-HPV[b]	OR, 2.59; χ^2 = 27.68; P < .005					
Yes	63	0.76 (.56–1.0)	1841	24.1 (22.6–25.7)	1904	24.8 (23.3–26.5)
No	66	0.90 (.65–1.2)	5123	74.3 (72.7–75.8)	5189	75.2 (73.5–76.7)
Total	129	1.7 (1.3–2.1)	6964	98.3 (97.9–98.7)	7093	
9V HR-HPV types[c]	OR, 5.33; χ^2 = 39.15; P < .005					
Yes	19	0.27 (.15–.46)	853	10.9 (9.9–11.9)	872	11.1 (10.2–12.2)
No	32	0.41 (.26–.64)	6189	88.5 (87.4–89.5)	6221	88.9 (87.8–89.8)
Total	51	0.67 (.45–.99)	7042	99.3 (99.0–99.5)	7093	
HPV type 16, 18, or 45[d]	OR = 10.62; χ^2 = 69.37; P < .005					
Yes	14	0.20 (.10–.40)[f]	466	6.2 (5.5–7.1)	480	6.4 (5.7–7.3)
No	22	0.28 (.16–.49)	6591	93.3 (92.4–94.1)	6613	93.6 (92.7–94.3)
Total	36	0.48 (.28–.80)	7057	99.5 (99.2–99.7)	7093	
HPV-16[e]	OR, 18.76; χ^2 = 90.90; P < .005					
Yes	8	0.13 (.06–.30)[f]	227	3.4 (2.8–4.0)	235	3.5 (2.9–4.2)
No	14	0.20 (.10–.40)[f]	6844	96.3 (95.6–96.9)	6858	96.5 (95.8–97.1)
Total	22	0.33 (.19–.59)	7071	99.7 (99.4–99.8)	7093	

Abbreviations: 9V, 9-valent (vaccine); CI, confidence interval; HPV, Human papillomavirus; HR-HPV, high-risk HPV; OR, odds ratio.

[a]National Health and Nutrition Examination Survey data (2013–2016 for men, 2009–2016 for women).

[b]All 18 HR-HPV types.

[c]HR-HPV types covered in the 9V HPV vaccine (types 16, 18, 31, 33, 45, 52, and 58).

[d]HPV types 16, 18, and 45 are the most common types found in cervical cancers.

[e]HPV-16: The most common type found in HPV-associated cancers.

[f]The relative standard error of the weighted prevalence estimate was >30%.

Table 2. Prevalence of Concordant Oral and Genital High-Risk Human Papillomavirus Infections for Total Population, Men, and Women[a]

	Total Population		Men		Women	
Infection Type	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
Total population	10 334		3241		7093	
Concordant	93	1.0 (.77–1.4)	54	1.6 (1.1–2.2)	39	0.51 (.36–.72)
Nonconcordant	79	1.1 (.79– 1.5)	55	2.0 (1.4–2.8)	24	0.25 (.16–.39)
No concurrent	10 162	97.9 (97.3– 98.3)	3132	96.5 (95.4– 97.3)	7030	99.2 (99.0–99.4)
Individuals with concurrent infections	172		109		63	
Concordant	93	48.5 (38.9–58.3)	54	44.4 (33.1–56.3)	39	67.1 (53.8–78.1)
Nonconcordant	79	51.5 (41.7–61.1)	55	55.6 (43.7–66.9)	24	32.9 (21.9–46.2)

Abbreviation: CI, confidence interval.

[a]National Health and Nutrition Examination Survey data (2013–2016 for men, 2009–2016 for women).

Our study findings on difference in the burden are consistent with results from other studies, which have typically included both LR-HPV and HR-HPV types. Kedarisetty et al [11] showed that for any HPV type, 7% of women with genital HPV infection also had oral HPV infection compared with only 1% of women with no genital HPV infection. Patel et al [13] found similar results for any HPV in men: 19% of men with penile HPV infection had oral HPV infection, compared with 4% of men with no penile HPV infection. Sonawane et al [14] showed similar associations for oral HPV infections between both men and women with or without genital HPV infections. Moreover, a study for both and LR-HPV and HR-HPV in a geographically distinct rural Chinese sample also found overall greater concurrence and concordance than expected [12], using the same simulation-based approach as our study.

Another noteworthy finding of our study was the prevalence of concurrent infections with HR-HPV types covered by the 9-valent HPV vaccine among men (0.86%) and women (0.27%), reflecting roughly 1.3 million men and just over 400 000 women who have infections amenable to prevention by the HPV 9-valent

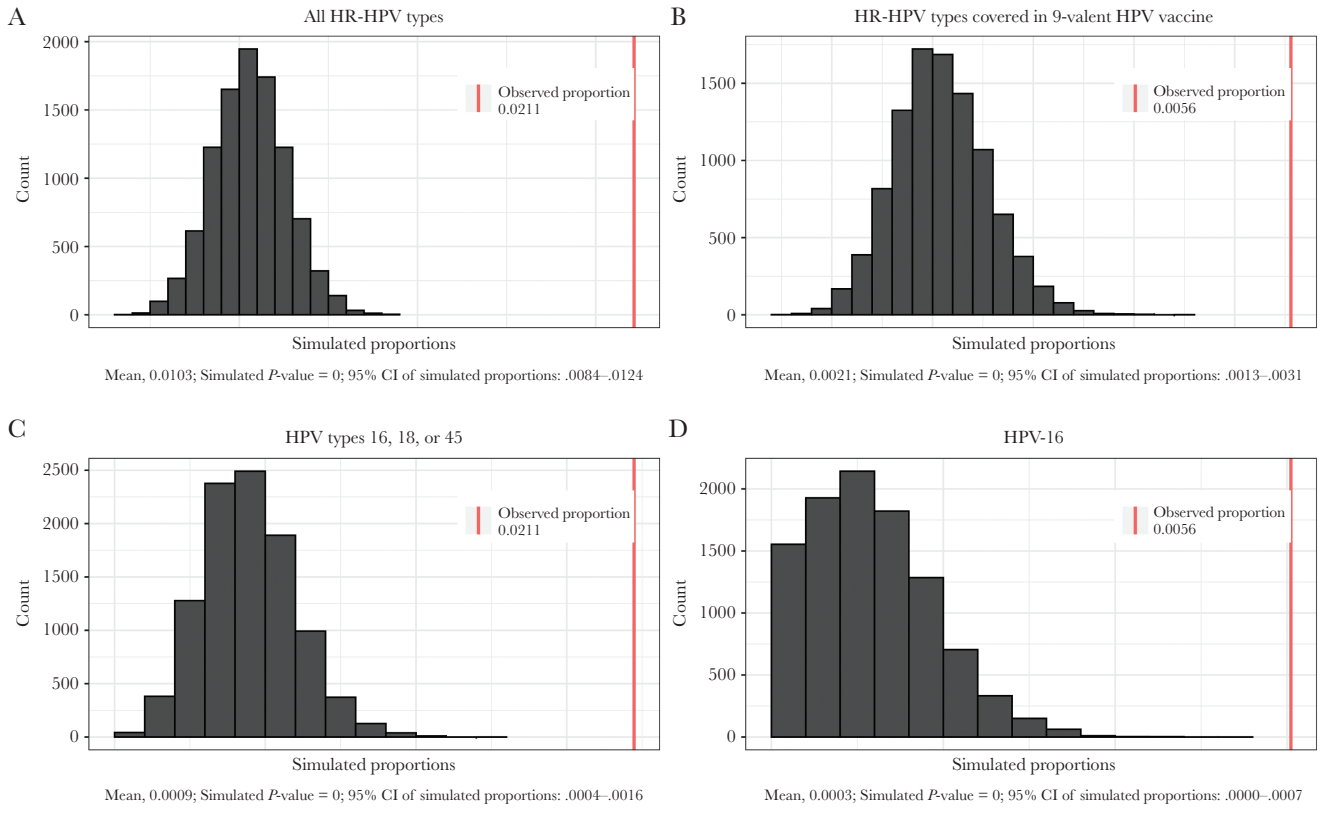

Figure 1. Histograms of simulated proportions of concurrent high-risk human papillomavirus (HR-HPV) infection for total population by 4 HR-HPV groups (National Health and Nutrition Examination Survey, 2013–2016 for men and 2009–2016 for women). *A,* All HR-HPV types. *B,* HR-HPV types covered in 9-valent HPV vaccine. *C,* HPV types 16, 18, or 45. *D,* HPV-16. Abbreviation: CI, confidence interval.

Table 3. Prevalence and Predictors of the Concurrent and Concordant High-Risk Human Papillomavirus Infections Among Men[a]

	Concurrent Infection				Concordant Infection			
	Prevalence		Logistic Regression		Prevalence		Logistic Regression	
Variables[b]	No.	% (95% CI)	Univariate OR	Adjusted OR	No.	% (95% CI)	Univariate OR	Adjusted OR
Marital status[c,d]								
Married	30	1.7 (0.83–2.5)	Reference	Reference	14	0.68 (.25–1.1)[g]	Reference	Reference
No longer married	21	9.5 (5.9–13.1)	5.4 (2.9–10.1)[e]	2.5 (1.2–5.2)[f,g]	10	4.1 (1.5–6.8)[g]	6.9 (2.5–18.6)[e]	3.5 (1.2–9.9)[f,g]
Never married	34	4.5 (2.8–6.2)	2.9 (1.7–5.0)[e]	2.3 (1.0–4.9)[g]	18	2.1 (.99–3.1)	3.2 (1.5–7.0)[g,h]	1.4 (0.41–4.9)[g]
Living with partner	21	5.8 (2.6–9.0)	3.7 (1.6–8.4)[e,g]	3.0 (1.2–7.5)[f,g]	10	2.7 (.79–4.6)[g]	4.3 (1.5–12.5)[f,g]	2.6 (0.71–9.7)[g]
Missing	3	0.94 (–0.28 to 2.2)[g]	0.58 (0.13–2.6)	1.5 (0.17–13.5)[g]	2	0.77 (–.39 to 1.9)[g]	1.2 (0.21–7.0)	1.2 (0.07–20.9)[g]
Lifetime sex partners[c,d]								
0–5	13	0.87 (0.21–1.5)[g]	Reference	Reference	11	0.62 (.11–1.1)[g]	Reference	Reference
6–10	18	2.1 (0.90–3.3)	2.5 (1.1–5.7)[f,g]	1.1 (0.38–3.4)[g]	8	1.3 (.30–2.3)[g]	2.1 (0.71–6.2)[g]	1.2 (0.31–5.0)[g]
≥11	71	7.0 (4.8–9.3)	8.6 (3.7–20.1)[e]	3.3 (1.0–10.6)[g]	33	2.8 (1.6–4.0)	4.7 (1.9–12.0)[e,g]	2.4 (0.60–9.4)[g]
Missing	7	4.7 (0.54–8.8)[g]	…	…	2	0.94 (–.30 to 2.2)[g]	…	…
Recent sex partners[c,d]								
0–1	56	2.2 (1.4–2.9)	Reference	Reference	26	0.89 (.53–1.2)	Reference	Reference
2–5	36	9.3 (5.8–12.8)	4.6 (2.9–7.4)[e]	2.7 (1.0–7.3)[g]	19	4.3 (2.2–6.3)	5.0 (3.1–8.1)[e]	1.5 (0.65–3.6)[g]
≥6	10	6.6 (1.7–11.6)[g]	3.2 (1.3–8.1)[f,g]	1.3 (0.33–5.2)[g]	7	5.1 (.39–9.8)[g]	6.0 (2.0–18.0)[e,g]	1.4 (0.27–6.8)[g]
Missing	7	4.7 (0.54–8.8)[g]	…	…	2	0.94 (–.30 to 2.2)[g]	…	…
Lifetime oral sex partners[c,d]								
0–1	10	0.53 (.12–.94)[g]	Reference	Reference	8	0.44 (.07–.82)[g]	Reference	Reference
2–5	33	3.2 (2.1–4.2)	6.1 (2.7–13.5)[e]	3.0 (1.2–7.5)[f,g]	16	1.6 (.54–2.6)[g]	3.5 (1.2–10.1)[f,g]	1.6 (0.53–5.1)[g]
≥6	59	6.6 (4.5–8.8)	13.2 (5.9–29.6)[e]	2.7 (1.1–6.7)[g]	28	2.7 (1.4–4.1)	6.3 (2.5–15.7)[e]	1.2 (0.31–4.3)[g]
Missing	7	4.7 (0.54–8.8)[g]	…	…	2	0.94 (–.30 to 2.2)[g]	…	…
Recent oral sex partners[c,d]								
0–1	68	2.6 (1.8–3.5)	Reference	Reference	30	0.99 (.58–1.4)	Reference	Reference
2–5	27	9.1 (5.4–12.7)	3.7 (2.3–6.0)[e,g]	0.92 (0.41–2.1)	17	5.6 (2.6–8.6)	5.9 (3.2–11.1)[e]	2.5 (0.81–7.5)[g]
≥6	7	9.7 (1.4–17.9)[g]	4.0 (1.5–11.0)[f,g]	1.3 (0.25–6.5)[g]	5	6.7 (.61–12.8)[g]	7.2 (2.4–21.6)[e]	2.1 (0.27–16.9)[g]
Missing	7	4.7 (0.54–8.8)[g]	…	…	2	0.94 (–.30 to 2.2)[g]	…	…
Marijuana use[c]								
Never	21	1.5 (0.72–2.3)	Reference	Reference	15	1.2 (.48–2.0)[g]	Reference	…
Ever	81	4.5 (3.1–5.9)	3.1 (1.6–5.8)[e]	1.3 (0.63–2.5)[g]	37	1.8 (1.1–2.5)	1.4 (0.72–2.9)[g]	…
Missing	7	4.5 (0.53–8.5)[g]	…	…	2	0.92 (–.29 to 2.1)[g]	…	…

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]National Health and Nutrition Examination Survey data from 2013–2016.

[b]Additional adjusted covariates included ethnicity, age group, human papillomavirus vaccine, cigarette use, and sexual orientation.

[c]$P < .005$ for concurrent infection (χ^2 test).

[d]$P < .005$ for concordant infection (χ^2 test).

[e]$P < .005$ for logistic regression OR.

[f]$P < .05$ for logistic regression OR.

[g]The relative standard error of the weighted prevalence estimate was >30%.

[h]$P < .01$ for logistic regression OR.

Table 4. Prevalence and Predictors of the Concurrent and Concordant High-Risk Human Papillomavirus Infections Among Women[a]

	Concurrent Infection				Concordant Infection			
	Prevalence		Logistic Regression		Prevalence		Logistic Regression	
Variables[b]	No.	% (95% CI)	Univariate OR	Adjusted OR	No.	% (95% CI)	Univariate OR	Adjusted OR
Marital status[c,d]								
Married	11	0.28 (0.10–.46)[e]	Reference	Reference	9	0.24 (0.07–0.42)[e]	Reference	Reference
No longer married	16	1.7 (0.75–2.6)	5.8 (2.2–15.7)[f]	3.6 (1.3–10.3)[e,g]	11	1.3 (0.44–2.2)[e]	5.3 (1.8–15.8)[e,f]	3.2 (1.1–9.4)[e,g]
Never married	21	0.95 (0.49–1.4)	3.2 (1.4–7.5)[e,h]	2.6 (0.88–7.9)[e]	9	0.45 (0.15–0.75)[e]	1.8 (0.67–5.1)[e]	1.5 (0.40–5.4)[e]
Living with partner	6	0.86 (0.17–1.6)[e]	2.7 (0.90–8.1)[e]	2.3 (0.72–7.4)[e]	2	0.27 (−0.11 to 0.64)[e]	1.1 (0.22–5.5)[e]	0.96 (0.21–4.5)
Missing	9	1.8 (0.38–3.1)[e]	6.2 (2.2–17.4)[f]	6.7 (1.4–32.2)[e,g]	8	1.6 (0.25–3.0)[e]	6.6 (2.2–20.1)[e,f]	6.0 (0.99–35.9)[e]
Lifetime sex partners[i]								
0–1	8	0.28 (.07–.49)[e]	Reference	Reference	7	0.21 (0.05–.38)[e]	Reference	Reference
2–5	17	0.66 (0.15–1.2)[e]	2.3 (0.71–7.3)[e]	1.2 (0.24–6.0)[e]	10	0.41 (0.05–.77)[e]	1.9 (0.52–6.8)[e]	0.77 (0.13–4.5)
6–10	18	0.96 (0.45–1.5)	3.3 (1.3–8.7)[e,g]	1.0 (0.29–3.7)[e]	11	0.61 (0.19–1.0)[e]	2.8 (1.0–7.7)[e]	0.80 (0.19–3.3)
≥11	17	1.3 (0.56–2.1)	4.5 (1.7–12.0)[e,f]	0.92 (0.22–3.9)	11	1.0 (0.27–1.8)[e]	4.7 (1.6–13.7)[e,h]	1.0 (0.24–4.6)[e]
Missing	3	0.32 (−0.05 to 0.70)[e]	…	…	0	…	…	…
Recent sex partners[c,d]								
0–1	34	0.51 (.31–.71)	Reference	Reference	24	0.35 (0.21–0.49)	Reference	Reference
2–5	23	2.4 (1.2–3.6)	4.7 (2.4–9.1)[f]	4.6 (1.4–15.6)[e,g]	13	1.6 (0.53–2.6)[e]	4.5 (2.0–10.3)[f]	4.2 (0.83–21.0)[e]
≥6	3	4.6 (−2.03 to 11.3)[e]	9.4 (1.8–47.5)[e,h]	3.9 (1.1–14.3)[e,g]	2	3.8 (−2.74 to 10.3)[e]	10.9 (1.7–69.1)[e,g]	3.8 (0.77–18.4)[e]
Missing	3	0.32 (−0.05 to 0.70)[e]	…	…	0	…	…	…
Lifetime oral sex partners[i,j]								
0–1	17	0.46 (0.18–0.74)[e]	Reference	Reference	11	0.24 (0.06–.42)[e]	Reference	Reference
2–5	27	0.84 (0.47–1.2)	1.8 (0.94–3.5)[e]	1.1 (0.43–2.9)[e]	19	0.69 (0.35–1.0)	2.9 (1.1–7.6)[e,g]	1.8 (0.42–7.4)[e]
≥6	16	1.3 (0.61–2.1)	2.9 (1.2–6.6)[e,g]	1.1 (0.28–4.7)[e]	9	0.83 (0.16–1.5)[e]	3.4 (1.1–10.6)[e,g]	0.94 (0.15–5.9)
Missing	3	0.33 (−0.05 to 0.70)[e]	…	…	0	…	…	…
Recent oral sex partners[c,d]								
0–1	45	0.67 (0.45–0.89)	Reference	Reference	28	0.44 (0.27–0.62)	Reference	Reference
2–5	12	1.6 (0.54–2.6)[e]	2.4 (1.2–4.8)[e,g]	0.50 (0.14–1.8)	9	1.2 (0.35–2.1)[e]	2.8 (1.2–6.6)[e,g]	0.71 (0.14–3.5)
≥6	3	7.1 (−3.07 to 17.4)[e]	11.1 (2.2–57.3)[e,h]	2.8 (0.65–12.3)[e]	2	5.8 (−4.16 to 15.8)[e]	13.4 (2.0–88.1)[e,h]	3.9 (0.69–22.2)[e]
Missing	3	0.33 (−0.05 to 0.70)[e]	…	…	0	…	…	…
Marijuana use[c,d]								
Never	14	0.37 (0.14–.61)[e]	Reference	Reference	9	0.25 (0.04–0.45)[e]	Reference	Reference
Ever	46	1.1 (0.77–1.5)	3.0 (1.5–6.0)[e,f]	2.2 (1.0–4.5)[e,g]	30	0.80 (0.49–1.1)	3.2 (1.3–8.4)[e,g]	2.0 (0.70–5.5)[e]
Missing	3	0.32 (.05 to 0.69)[e]	…	…	0	…	…	…

Abbreviations: CI, confidence interval; OR, odds ratio.

[a]National Health and Nutrition Examination Survey data from 2009–2016.

[b]Additional adjusted covariates included ethnicity, age group, human papillomavirus vaccine, cigarette use, and sexual orientation.

[c]$P < .005$ for concurrent infection (χ^2 test).

[d]$P < .005$ for concordant infection (χ^2 test).

[e]The relative standard error of the weighted prevalence estimate was >30%.w

[f]$P < .005$ for logistic regression OR.

[g]$P < .05$ for logistic regression OR.

[h]$P < .05$ for logistic regression OR.

[i]$P < .05$ for concordant infection (χ^2 test).

[j]$P < .05$ for concurrent infection (χ^2 test).

vaccine. Such difference is alarming considering low HPV vaccine uptake, especially in men. The Advisory Committee on Immunization Practices has recommended vaccination for girls aged 11 or 12 years since 2006, and for boys since 2011 [21]. HPV-16 and HPV-18 are the 2 most common types found in HPV-associated cancers, causing 63% of cases [1].

All HPV vaccines (bivalent, quadrivalent, and 9-valent) protect against HPV types 16 and 18. Vaccination against types 16 and 18 could prevent almost 25 000 cancer cases annually in the United States [3]. Of adolescent girls aged 13–17 years in the United States, 65.1% received ≥1, 55.0% received ≥2, and 43.0% received ≥3 doses in 2016; for adolescent boys, the rates were 56.0%, 43.6%, and 31.5%, respectively [8]. This is in stark contrast to the hepatitis B vaccine, for which 94.1% of adolescent boys received ≥3 doses [8]. In general, our study underscores the importance of the HPV vaccine, and for providing support for its continued recommendation for boys and men, who have much lower vaccination rates than girls and women [8]. The role of HPV vaccine in protecting against certain types of HPV that can cause OPCs may contribute in preventing OPCs overall [9, 10]. Moreover, among groups of people at high risk, such as men who have sex with men, for whom oral sex is common, it is also important to use a condom or dental dam to prevent transmission of infection via oral sex.

Although concurrent HR-HPV infections are relatively rare, the rates of concordant infection among those with concurrent infections were very high, particularly among women (67.1% in women vs 44.4% in men). In this case, HR-HPV genital infection can flag the potential for HR-HPV oral infection. Conversely, individuals with diagnosed HR-HPV oral infection could be more closely monitored for genital infections and cancer. This is more important for men because they are not screened for genital infections at all. Just as an anal Papanicolaou test is recommended for a group of men at high risk [22], a penile swab sample could be used in practice to test HPV DNA based on personal medical history and presence of risk factors. Selective screening guidelines should be developed to risk stratify people and recommend additional screening in those known to have a positive HR-HPV result at one anatomic site, as also suggested by Kedarisetty et al [11]. Moreover, OPCs are increasing among young US men, and there is no existing protocol for HPV-positive OPC screening.

In the United States, the rates of any HPV oral infections (LR-HPV or HR-HPV) are higher in men than in women [11, 13, 14]. Current results are similar with respect to HR-HPV infections. Although the exact reason is unknown, possible explanations include that men have more sexual partners than women, that transmission of HPV is more efficient when performing oral sex on infected women compared with infected men, and/or that women may have partial immunity from cervical infections that protect them against oral HPV infections [2]. One risk factor associated with both concurrence and concordance in men and women was marital status.

Our finding of a greater risk among women who are no longer married is supported by findings of a major population-based study in Italy that found a higher prevalence of HPV infection among single women [23]. Compared with married people, those who are no longer married may become involved with a greater number of sex (oral or any sex) partners, which can ultimately put them at risk of HR-HPV infections. In addition, sexual behavior associated with concurrence included 2–5 lifetime oral sex partners in men and ≥2 recent sex partners in women. Association with these sexual behaviors is clinically unsurprising and well supported by the literature [13, 14, 24, 25].

Marijuana use was a risk factor for the concurrence among women. Although it is not related to the natural history of oral or genital HPV infection [26, 27], it may cause oral infection through sharing of smoking apparatus [27]. In addition, marijuana users may also indulge in other substance use and risky sexual behavior because of impulsivity [28, 29].

Our study should be considered in light of some limitations. First, some adjusted model estimates had a relative standard error >30%; therefore, we suggest the results to be considered for hypothesis generating only. Second, we could not demonstrate temporality owing to the cross-sectional nature of the study; however, our study is backed by well-established associations that have been vastly reported in the literature. Third, self-reported sexual behaviors can lead to misclassification of the exposure; however, this is the nature of the data collection procedures specific to NHANES. Fourth, NHANES does not collect data on marriage between 2 men or 2 women; such data could be helpful in evaluating the number of lifetime oral sex partners, especially among men, to identify possible differences in transmission between oral sex with a woman versus with a man. Moreover, NHANES data do not differentiate between receptive and insertive oral sex partners for men, which could be important for evaluating the prevalence by specific site (oral vs penile) of HPV infection.

Major strengths of this study are that it is the largest nationally representative survey data, well known for its comprehensively detailed data on infections. In addition, our study adds clarity and urgency about HR-HPV, a greater public health concern than LR-HPV, which is often lumped in with HR-HPV for the sake of epidemiologic analyses [11–13].

In conclusion, the prevalence of concurrent and concordant HR-HPV infection was relatively higher among men as than along women in the United States, and marital status and certain behaviors were associated with concurrence and concordance in the US population. Therefore, we hypothesize that oral screening of people with genital HR-HPV infection, as well as increasing HPV vaccination uptake, particularly among men, can be central to reducing HR-HPV infections, OPCs and other HPV-associated cancers in the United States.

Supplementary Data

Supplementary materials are available at The *Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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