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Vaccine effectiveness against anal HPV among men who have sex with men aged 18–45 years attending sexual health clinics in three United States cities, 2018–2023

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Abstract

Background: We assessed human papillomavirus (HPV) vaccine effectiveness (VE) against anal HPV among men who have sex with men (MSM) in 2018–2023.

Methods: Residual anal specimens from MSM without HIV ages 18–45 years were tested for HPV. We calculated adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) for associations between vaccination (≥ 1 dose) and quadrivalent vaccine (4vHPV)-type prevalence adjusting for city, race/ethnicity, and non-vaccine-type HPV prevalence, stratified by age group (18–26, 27–45). VE was calculated as $(1 - \text{aPR}) \times 100$.

Results: Among 2802 persons aged 18–26, 4vHPV-type prevalence was lower in those vaccinated at age < 18 (aPR=0.13, CI: 0.08–0.22, VE=87%) and those vaccinated ≥ 2 years before specimen collection (aPR=0.52, CI: 0.42–0.64, VE=48%), compared with unvaccinated persons. Among 3548 persons aged 27–45, 4vHPV-type prevalence was lower in those vaccinated at

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ages 18–26 (aPR=0.68, CI: 0.57–0.82, VE=32%) and those vaccinated ≥ 2 years before specimen collection (aPR=0.66, CI: 0.57–0.77, VE=33%), compared with unvaccinated persons. While we observed no VE in persons vaccinated at age >26 overall, 4vHPV-type prevalence was lower in the subgroup vaccinated ≥ 2 years before specimen collection (aPR=0.71, CI: 0.56–0.89, VE=29%).

Conclusions: We found high VE against anal 4vHPV-type prevalence among MSM aged 18–26 who were vaccinated at age <18 . Lower VE was observed among MSM ages 27–45 who were vaccinated at age 18–26 or ≥ 2 years before specimen collection. While ideally vaccination should be given at younger ages, vaccination can prevent some future infections in this population.

Summary:

In this analysis of HIV-negative men who have sex with men, we found effectiveness of HPV vaccination against anal HPV prevalence among persons aged 18–26 and 27–45 years. We also report vaccine effectiveness of 9-valent HPV vaccine specifically.

Keywords

papillomavirus vaccines; papillomavirus infections; sexual and gender minorities; vaccination

Background

Gay, bisexual, and other men who have sex with men (MSM) are disproportionately affected by human papillomavirus (HPV) infections and related diseases, many of which could be prevented by pre-exposure vaccination.¹ Quadrivalent HPV vaccine (4vHPV), which protects against four HPV types (6, 11, 16, and 18), was recommended by the Advisory Committee on Immunization Practices (ACIP) for routine immunization of girls and women in 2006 and of boys and men in 2011.^{2–4} The routine recommendation is for vaccination at age 11 or 12 years (can start at age 9 years). Initially, the routinely recommended upper age for men was through age 21 years, and through age 26 years for MSM.^{3,4} 9-valent HPV vaccine (9vHPV), which protects against the 4vHPV types and five additional types (31, 33, 45, 52, and 58), was licensed in late 2014;⁵ it has been the only HPV vaccine available for use in the United States since late 2016. In 2019, for those not vaccinated at the routine age, ACIP harmonized catch-up vaccination recommendations through age 26 years for all sexes and recommended shared clinical decision-making for adults aged 27–45 years.⁶

Data supporting 4vHPV licensure included one efficacy trial conducted among MSM with five or fewer lifetime sex partners. There was high efficacy in the per-protocol population.⁷ In the long-term follow-up study, men remained protected from anogenital disease related to 4vHPV types for up to 10 years after vaccination.⁸ No efficacy trial of 9vHPV was conducted among men, but efficacy was inferred from a trial in women and immunogenicity studies in men.^{5,9,10} Follow-up from a 9vHPV immunogenicity study conducted in 9–15-year-old boys and girls found sustained immunogenicity and effectiveness through at least 10 years after vaccination.¹¹

In post-licensure monitoring after introduction of 4vHPV among girls and women, strong herd effects such as reductions in anogenital warts among heterosexual men were observed, but these effects did not extend to MSM.^{12–15} After implementation of vaccination for males

in national programs, vaccine impact and effectiveness in MSM have been evaluated.^{16–20} In Australia, reductions in anal, penile, and oral 4vHPV-type prevalent infections occurred in repeated cross-sectional studies of MSM aged 16–20 years following the implementation of a school-based gender-neutral HPV vaccination program.²⁰ In the United States, an observational study of MSM and transgender women aged 18–26 years in three cities found that vaccine effectiveness (VE) against anal or oral 4vHPV-type prevalent infection was 59% for persons vaccinated at age ≤ 18 years.¹⁷ An additional analysis from that study found that VE against penile 4vHPV-type prevalent infection was 85% for persons vaccinated at age ≤ 18 years.¹⁸ A study in Canada among MSM aged 16–30 years found that VE against 12-month persistent infection with vaccine-preventable HPV types was 92% when vaccination was initiated by age 23 years.¹⁹

While HPV VE has been demonstrated among young adult MSM who were vaccinated at younger ages, there are limited data on VE among MSM aged >26 years.²¹ One study of HIV-negative MSM aged >26 years found that receipt of 4vHPV was associated with decreased risk of anal condyloma.²² There are limited data on VE of 9vHPV in MSM of any age group.

In this analysis, we assess VE against prevalent anal HPV infection among HIV-negative MSM, transgender, and non-binary persons assigned male at birth aged 18–26 and 27–45 years attending sexual health clinics in three U.S. cities. We use documented HPV vaccination history to assess VE for any HPV vaccine and for 9vHPV specifically.

Methods

Data are from the Surveillance of Anal HPV among MSM (SAM) project, which included patients who attended sexual health clinics during August 2018–July 2023 in three U.S. cities: Seattle, WA; New York City, NY; and Philadelphia, PA. We included patients aged 18–45 years who were assigned male at birth (regardless of present gender identity or expression), identified as gay or bisexual or reported ever having any type of sexual contact with a male partner, and submitted anal swab specimens for chlamydia and gonorrhea testing. Anal swab specimens were either self-collected or clinician-collected using the Aptima Multitest Swab Specimen Collection Kit (Hologic, Marlborough, MA). We have previously demonstrated that anal specimens remaining after Aptima chlamydia and gonorrhea testing are suitable for HPV testing.²³

After clinical testing, residual anal specimens were frozen and shipped on dry ice to the CDC HPV laboratory in Atlanta, GA. Long-term storage was at -80°C . A 400 μL aliquot of each sample was extracted with Chemagic Viral NA/gDNA kit (PerkinElmer Health Sciences, Shelton, CT) yielding 115 μL of extract. Extracts were tested using Novaplex II HPV28 Detection Assay (Seegene USA, Inc., Irvine, CA) according to manufacturer's protocol. The assay detects 28 types (HPV 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 66, 68, 69, 70, 73, or 82) and a human gene internal control to verify specimen adequacy. Any specimen negative for the internal control and all HPV types was considered inadequate.

Using a unique ID number, each specimen was linked with deidentified surveillance data, including demographic characteristics and chlamydia, gonorrhea, and HIV test results from clinic medical records. These data were also linked to documented HPV vaccination dates from clinic medical records, health system medical records, and/or immunization registry data. No personally identifiable information was shared beyond the clinic site.

This surveillance activity was reviewed and approved by the Centers for Disease Control and Prevention (CDC) and participating institutions as required, and was conducted consistent with applicable federal law and CDC and local policies.¹

Individuals were excluded from this analysis if they self-reported having HIV, had a positive HIV test result, or had unknown HIV status. We considered an individual to be vaccinated if they had received ≥ 1 documented dose of any HPV vaccine (i.e., 4vHPV, 9vHPV, a combination of these, or unknown HPV vaccine) ≥ 30 days before specimen collection; otherwise, they were considered unvaccinated. For a 9vHPV sub-analysis, we considered an individual vaccinated if they had received ≥ 1 documented 9vHPV dose ≥ 30 days before specimen collection. In this sub-analysis, individuals who received 4vHPV (alone or in combination with 9vHPV), any other, or an unknown HPV vaccine were excluded.

Analyses were stratified by age at specimen collection: 18–26 or 27–45 years. We compared demographic and clinical characteristics of unvaccinated and vaccinated persons using chi-square tests. We determined 4vHPV-type prevalence (HPV 6, 11, 16, 18), the additional 9vHPV-type prevalence (HPV 31, 33, 45, 52, 58), non-9vHPV-type prevalence (HPV 26, 35, 39, 40, 42, 43, 44, 51, 53, 54, 56, 59, 61, 66, 68, 69, 70, 73, 82), and prevalence of any of 28 HPV types, by demographic and clinical characteristics, vaccination status, age at first vaccination (<18 , 18–26, or >26 years), and time since first vaccination (<2 or ≥ 2 years). We also determined the prevalence of HPV 16 and HPV 18 by vaccination status, age at first vaccination, and time since first vaccination. In the 9vHPV sub-analysis, we additionally determined prevalence of 9vHPV-type prevalence (HPV 6, 11, 16, 18, 31, 33, 45, 52, 58) by the same variables. Non-9vHPV-type prevalence was used as a measure of sexual exposure because these HPV types are not expected to be prevented by any vaccine.

We used log-binomial regression to calculate prevalence ratios (PR) and 95% confidence intervals (CI) for associations between vaccination and HPV detection by age group. Models included city, race/ethnicity, and non-9vHPV-type prevalent infection to calculate adjusted PR (aPR). We assessed the joint and separate effects of age at first vaccination and time since first vaccination. Because few individuals aged 27–45 years had been vaccinated at age <18 years, these individuals were excluded from analyses of age at first vaccination. VE was calculated as $[(1 - aPR) \times 100]$.

P-values <0.05 were considered significant. All calculations were performed using SAS version 9.4 (SAS Institute, Cary, NC).

¹See e.g., 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

Results

A total of 6439 anal specimens from persons aged 18–45 years were collected. Of these, 6350 (98.6%) anal specimens were adequate for analysis. Among the specimens with adequate HPV typing results, 2802 were from persons aged 18–26 years and 3548 were from persons aged 27–45 years (Table 1). Of those with known gender identity, approximately 95% of persons in both age groups identified as men, with the remainder identifying as transgender or non-binary/gender queer/gender non-conforming. Within both age groups, the distribution of city, gender identity, race/ethnicity, and recent sex partners varied between unvaccinated and vaccinated persons. The prevalence of anal chlamydia or gonorrhea did not vary by vaccination status in either age group.

Ages 18–26 years

Among 2802 persons aged 18–26 years, ≥ 1 HPV vaccine dose ≥ 30 days before specimen collection was documented for 1249 (44.6%); 646 (23.1%) had received only 9vHPV (Table 1). Of those who had received any HPV vaccine, median age at first vaccination was 18 years and median time since first vaccination was 4.9 years (Table 2). Of those who received only 9vHPV, median age at first vaccination was 22 years and median time since first vaccination was 1.9 years.

4vHPV-type, additional 9vHPV-type, non-9vHPV-type, and any HPV-type prevalences were 18.1%, 19.2%, 68.2% and 72.3%, respectively (Table 3). Prevalences of these HPV type categories varied significantly by age at first vaccination and time since first vaccination (Table 4). Prevalence of HPV 16 was 7.1% and prevalence of HPV 18 was 2.9% (Supplemental Table 1). The 9vHPV sub-analysis included 2199 persons aged 18–26 years; prevalences for the 9vHPV sub-analysis are available in Supplemental Tables 2 and 3.

In the analysis of any HPV vaccination, compared with unvaccinated persons, 4vHPV-type prevalence was significantly lower in persons ever vaccinated (aPR=0.80, CI: 0.68–0.95, VE=20%), vaccinated at age <18 (aPR=0.13, CI: 0.08–0.22, VE=87%), and vaccinated ≥ 2 years before specimen collection (aPR=0.52, CI: 0.42–0.64, VE=48%) (Table 5). Regarding the additional 9vHPV-type prevalence, compared with unvaccinated persons, prevalence was significantly lower in persons ever vaccinated (aPR=0.73, CI: 0.62–0.85, VE=27%), vaccinated at age <18 (aPR=0.56, CI: 0.44–0.72, VE=44%), and vaccinated ≥ 2 years before specimen collection (aPR=0.63, CI: 0.52–0.75, VE=37%). HPV 16 and HPV 18 results were similar to results for 4vHPV-type prevalence (Supplemental Table 1).

In the 9vHPV sub-analysis, compared with unvaccinated persons, 4vHPV-type prevalence was lower in persons vaccinated at age <18 (Table 5). Compared with unvaccinated persons, additional 9vHPV-type prevalence was lower in persons ever vaccinated, vaccinated at age <18 , and vaccinated ≥ 2 years before specimen collection. Compared with unvaccinated persons, 9vHPV-type prevalence was lower in persons vaccinated at age <18 and vaccinated ≥ 2 years before specimen collection (Supplemental Table 4).

Ages 27–45 years

Among 3548 persons aged 27–45 years, ≥ 1 documented HPV vaccine dose ≥ 30 days before specimen collection was documented for 926 (26.1%); 690 (19.4%) had received only 9vHPV (Table 1). Of those who had received any HPV vaccine, median age at first vaccination was 29 years and median time since first vaccination was 2.7 years (Table 2). Of those who received only 9vHPV, median age at first vaccination was 32 years and median time since first vaccination was 1.8 years.

4vHPV-type, additional 9vHPV-type, non-9vHPV-type, and any HPV-type prevalences were 33.5%, 31.2%, 74.3% and 80.7%, respectively (Table 3). Prevalences of these HPV type categories varied significantly by vaccination status (Table 4). HPV 16 and HPV 18 were detected in 14.5% and 7.3% of specimens, respectively (Supplemental Table 1). The 9vHPV sub-analysis included 3312 persons aged 27–45 years (Supplemental Tables 2 and 3).

In the analysis of any HPV vaccination, compared with unvaccinated persons, 4vHPV-type prevalence was significantly lower in persons ever vaccinated (aPR=0.79, CI: 0.70–0.89, VE=21%), vaccinated at ages 18–26 (aPR=0.68, CI: 0.57–0.82, VE=32%), and vaccinated ≥ 2 years before specimen collection (aPR=0.66, CI: 0.57–0.77, VE=34%) (Table 5). While we observed no VE in persons vaccinated after age 26 years overall, 4vHPV-type prevalence was lower in those vaccinated at age >26 if time since first vaccination was ≥ 2 years (aPR=0.71, CI: 0.56–0.89, VE=29%). Regarding the additional 9vHPV types, compared with unvaccinated persons, prevalence was significantly lower among persons ever vaccinated (aPR=0.77, CI: 0.68–0.86, VE=23%), vaccinated at ages 18–26 (aPR=0.73, CI: 0.61–0.87, VE=27%), vaccinated at age >26 (aPR=0.79, CI: 0.68–0.91, VE=21%), and vaccinated ≥ 2 years before specimen collection (aPR=0.67, CI: 0.57–0.78, VE=33%). Among persons vaccinated after age 26 when time since vaccination was ≥ 2 years, VE was 44%. HPV 16 results were similar to the results for any 4vHPV type (Supplemental Table 1). We did not find any VE against HPV 18.

In the 9vHPV sub-analysis, compared with unvaccinated persons, 4vHPV-type prevalence was lower in persons ever vaccinated, vaccinated at ages 18–26, and vaccinated ≥ 2 years before specimen collection (Table 5). While we observed no VE in persons vaccinated after age 26 overall, 4vHPV-type prevalence was lower in those vaccinated at age >26 if time since first vaccination was ≥ 2 years. Compared with unvaccinated persons, additional 9vHPV-type (Table 5) and any 9vHPV-type (Supplemental Table 4) prevalences were lower in persons ever vaccinated, vaccinated at ages 18–26, vaccinated at age >26 , and vaccinated ≥ 2 years before specimen collection.

Discussion

In this analysis of HIV-negative MSM, transgender, and non-binary persons assigned male at birth attending sexual health clinics in three U.S. cities, we found effectiveness of HPV vaccination against anal HPV prevalence among 18–26 and 27–45-year-olds. Anal HPV infections were more common in the older age group, while vaccination coverage was higher in the younger age group. We observed the highest VE when vaccination occurred

at younger ages. This analysis offers two novel findings. First, we found significant VE in persons aged 27–45 years. Second, we report 9vHPV-specific VE.

As expected, most VE estimates observed in this analysis were lower than those found in per-protocol analyses in clinical trials among males.^{7,24} The high HPV vaccine efficacy found in the trials excluded participants with vaccine-type HPV at the time of vaccination. In observational VE studies, HPV infection status at the time of vaccination is unknown. Lower VE in this observational analysis compared to trials could also be due to differences in measuring prevalent (as opposed to incident) infection, number of vaccine doses (i.e., ≥ 1 versus 3 doses), and uncontrolled confounding due to the non-randomized population. Our VE estimates for prevention of 4vHPV-type prevalence in MSM ages 18–26 years are similar to what has been reported in previous observational studies.^{17,18}

Our analysis considered both age at first HPV vaccination and time since first vaccination to account for possible prevalent HPV at the time of vaccination. Studies have shown that VE is higher when vaccination occurs at younger ages, before exposure through sexual activity.²⁵ Time since vaccination also impacts observed estimates. For example, among persons aged 27–45 years, we found no VE in those vaccinated at age older than 26 years; however, VE against 4vHPV-type prevalence was 29% in the subgroup vaccinated at age >26 years and ≥ 2 years prior to specimen collection. Of note, VE for vaccination at ages 18–26 years was significant for persons aged 27–45 years but not for persons aged 18–26 years, likely because more time had passed since vaccination in the older age group. A pooled analysis of 34 studies found that about half of HPV 16 infections in HIV-negative MSM clear within two years.²⁶ By using lag periods between vaccination and specimen collection, some prevalent HPV infections at the time of vaccination may have cleared, allowing VE against newly detected infections to be observed.

Although 9vHPV efficacy data are available from clinical trials, to date there are no published data on 9vHPV VE from observational studies.²¹ We were able to estimate 9vHPV VE in our analysis because 52% of vaccinated persons aged 18–26 years and 75% of vaccinated persons aged 27–45 years received only 9vHPV. In persons aged 18–26 years, 9vHPV VE against the five additional 9vHPV types was 65% when vaccination occurred before age 18 years. In persons aged 27–45 years, 9vHPV VE against the five additional 9vHPV types was 46% when vaccination occurred at ages 18–26 years. We also examined 9vHPV VE against 4vHPV types and found that estimates for 9vHPV and any HPV vaccine were similar.

We report HPV 16 and HPV 18 prevalence and VE specifically against these types. HPV 16 is the most carcinogenic type and is responsible for most anal cancers, and HPV 18 is the second most carcinogenic HPV type in the anus.²⁷ In our analyses, VE estimates against HPV 16 were similar or higher than against any 4vHPV types. In persons aged 18–26 years, VE estimates against HPV 18 were similar to those against any 4vHPV type. However, in persons aged 27–45 years, we did not find VE against HPV 18. Further examination of VE against HPV 18 in this population is warranted.

We were not able to control for all possible confounders in our analyses due to limited data collected in this project. However, prevalence of anal chlamydia or gonorrhea did not vary by vaccination status and non-9vHPV-type HPV prevalence was higher among vaccinated compared with unvaccinated persons in both age groups, suggesting that the VE observed was not due to lower sexual exposure to HPV among the vaccinated population. Persons aged 18–26 years had higher 4vHPV-type as well as non-9HPV-type prevalence if they were vaccinated at ages 18–26 years or <2 before specimen collection, relative to unvaccinated persons, perhaps illustrating efforts to vaccinate persons with high-risk behaviors in sexual health clinics.

A strength of this analysis is the inclusion of documented HPV vaccination status, whereas previous observational studies have often relied on self-report.^{17–19} An analysis of MSM aged 18–26 years in Seattle found that sensitivity of self-report was 83.2% but varied by time since first vaccine dose.²⁸ Using documented vaccination status also allowed us to carefully examine age at first vaccination, time since first vaccination, and HPV vaccine product received, all of which are subject to recall bias in self-reported data. HPV vaccination coverage varied by city in this project. In the United States, coverage is known to vary widely by jurisdiction.²⁹ In this analysis, coverage reflects vaccination at routine and catch-up ages, and vaccination that might have occurred at the sexual health clinic during a previous visit. Of note, the sexual health clinics included in this project offer HPV vaccination.

This cross-sectional analysis is subject to at least four limitations. First, participants attended sexual health clinics in three U.S. cities and results may not be generalizable to persons who do not attend sexual health clinics and/or live in other geographic regions. Related to this, there may be selection bias of persons with greater sexual exposure risk due to recruitment from sexual health clinics. Second, it is possible that some vaccination records were under-ascertained because of limited access to external clinic or health system vaccination records, potential immunization registry incompleteness, and limited sharing between jurisdictional immunization registries. If some vaccinated individuals were misclassified as unvaccinated, we would expect our results to be biased towards the null. Third, we were unable to account for within-individual clustering in our models because this information was not available from one city. However, we conducted a post-hoc sensitivity analysis in which we excluded specimens (n=697) from individuals who were known to contribute >1 specimen to this analysis from the other two cities, and the results of our models did not substantially change. Fourth, we were unable to assess other potentially important variables, including age at first sex and lifetime number of sex partners, because this information was not available from all three cities. Although we adjusted for non-9vHPV-type prevalent infection, our results may still have residual confounding. We did not examine VE by number of vaccine doses because of the small number of persons who received <3 doses.

Findings from this analysis confirm previous reports that HPV vaccination is effective against anal HPV among persons vaccinated at younger ages, and provide new evidence of effectiveness, although lower, with vaccination at ages >26 years. These results support the current ACIP recommendation for HPV vaccination for all adolescents in the United States. While highest effectiveness is expected with vaccination before exposure through sexual

contact, vaccination even at older ages can prevent future HPV infections in sexually active populations. MSM and other sexual and gender minority groups bear a disproportionate burden of HPV infection and disease.¹ Surveillance data, such as these from the SAM project, can be used to monitor changes in HPV prevalence, vaccination coverage, and VE in this population over time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic and clinical characteristics of 6350 men who have sex with men and other persons assigned male at birth attending sexual health clinics in three U.S. cities, by human papillomavirus (HPV) vaccination status and age group — 2018–2023

	Total n (%)	Unvaccinated n (%)	Any HPV vaccine ^a n (%)	p-value ^b	9vHPV ^c n (%)	p-value ^d
Ages 18–26 years						
Total	2802	1553	1249		646	
City				<0.0001		<0.0001
Seattle	1083 (38.7)	458 (29.5)	625 (50.0)		371 (57.4)	
Philadelphia	853 (30.4)	543 (35.0)	310 (24.8)		92 (14.2)	
New York City	866 (30.9)	552 (35.5)	314 (25.1)		183 (28.3)	
Gender identity				0.0001		<0.0001
Male	2150 (76.7)	1146 (73.8)	1004 (80.4)		538 (83.3)	
Female/transgender female	42 (1.5)	23 (1.5)	19 (1.5)		8 (1.2)	
Non-binary/gender-queer/ gender non-conforming/other	104 (3.7)	58 (3.7)	46 (3.7)		29 (4.5)	
Unknown	506 (18.1)	326 (21.0)	180 (14.4)		71 (11.0)	
Race/ethnicity				<0.0001		<0.0001
Non-Hispanic Black	545 (19.5)	222 (14.3)	323 (25.9)		117 (18.1)	
Non-Hispanic White	1015 (36.2)	652 (42.0)	363 (29.1)		235 (36.4)	
Non-Hispanic Asian/Pacific Islander	282 (10.1)	143 (9.2)	139 (11.1)		96 (14.9)	
Hispanic	655 (23.4)	339 (21.8)	316 (25.3)		152 (23.5)	
Another race, non-Hispanic	192 (6.9)	117 (7.5)	75 (6.0)		32 (5.0)	
Unknown	113 (4.0)	80 (5.2)	33 (2.6)		14 (2.2)	
Recent sex partner(s) ^e				<0.0001		<0.0001
Male	2334 (83.3)	1299 (83.6)	1035 (82.9)		533 (82.5)	
Female	6 (0.2)	3 (0.2)	3 (0.2)		2 (0.3)	
Both	118 (4.2)	85 (5.5)	33 (2.6)		14 (2.2)	
Other ^f	18 (0.6)	10 (0.6)	8 (0.6)		5 (0.8)	
No recent sex partners	64 (2.3)	40 (2.6)	24 (1.9)		9 (1.4)	
Unknown	262 (9.4)	116 (7.5)	146 (11.7)		83 (12.8)	
CT/GC test result				0.9468		0.7573
Negative	2280 (81.4)	1263 (81.3)	1017 (81.4)		529 (81.9)	
Positive	522 (18.6)	290 (18.7)	232 (18.6)		117 (18.1)	
Ages 27–45 years						
Total	3548	2622	926		690	
City				<0.0001		<0.0001
Seattle	1317 (37.1)	690 (26.3)	627 (67.7)		488 (70.7)	
Philadelphia	1066 (30.0)	929 (35.4)	137 (14.8)		54 (7.8)	

	Total n (%)	Unvaccinated n (%)	Any HPV vaccine ^a n (%)	p-value ^b	9vHPV ^c n (%)	p-value ^d
New York City	1165 (32.8)	1003 (38.3)	162 (17.5)		148 (21.4)	
Gender identity				0.0019		0.0009
Male	2862 (80.7)	2091 (79.7)	771 (83.3)		585 (84.8)	
Female/transgender female	29 (0.8)	18 (0.7)	11 (1.2)		8 (1.2)	
Non-binary/gender-queer/ gender non-conforming/other	53 (1.5)	34 (1.3)	19 (2.1)		13 (1.9)	
Unknown	604 (17.0)	479 (18.3)	125 (13.5)		84 (12.2)	
Race/ethnicity				<0.0001		<0.0001
Non-Hispanic Black	535 (15.1)	451 (17.2)	84 (9.1)		43 (6.2)	
Non-Hispanic White	1439 (40.6)	1056 (40.3)	383 (41.4)		298 (43.2)	
Non-Hispanic Asian/Pacific Islander	324 (9.1)	203 (7.7)	121 (13.1)		93 (13.5)	
Hispanic	904 (25.5)	661 (25.2)	243 (26.2)		189 (27.4)	
Another race, non-Hispanic	232 (6.5)	173 (6.6)	59 (6.4)		40 (5.8)	
Unknown	114 (3.2)	78 (3.0)	36 (3.9)		27 (3.9)	
Recent sex partner(s)^e				<0.0001		<0.0001
Male	2956 (83.3)	2205 (84.1)	751 (81.1)		555 (80.4)	
Female	23 (0.6)	22 (0.8)	1 (0.1)		1 (0.1)	
Both	158 (4.5)	136 (5.2)	22 (2.4)		13 (1.9)	
Other ^f	25 (0.7)	20 (0.8)	5 (0.5)		5 (0.7)	
No recent sex partners	102 (2.9)	77 (2.9)	25 (2.7)		20 (2.9)	
Unknown	284 (8.0)	162 (6.2)	122 (13.2)		96 (13.9)	
CT/GC test result				0.2141		0.2155
Negative	3013 (84.9)	2215 (84.5)	798 (86.2)		596 (86.4)	
Positive	535 (15.1)	407 (15.5)	128 (13.8)		94 (13.6)	

CT, chlamydia; GC, gonorrhea; 9vHPV, 9-valent HPV vaccine

^aAny documented HPV vaccination (i.e., 4vHPV, 9vHPV, a combination of these, or unknown HPV vaccine) $\geq$ 30 days before specimen collection

^bChi-square test comparing persons who received any HPV vaccine to unvaccinated persons

^cDocumented 9vHPV vaccination $\geq$ 30 days before specimen collection; individuals who received 4vHPV (alone or in combination with 9vHPV) or who had another or unknown HPV vaccine product were excluded

^dChi-square test comparing persons who received 9vHPV vaccine to unvaccinated persons

^e“Recent” was defined as the previous 2 months in Seattle or the previous 3 months in Philadelphia and New York City

^fOther includes transgender woman, transgender man, non-binary, genderqueer, and gender non-conforming

Table 2.

Human papillomavirus (HPV) vaccination characteristics of men who have sex with men and other persons assigned male at birth attending sexual health clinics in three U.S. cities, by age group — 2018–2023

	Any HPV vaccine ^a n (%)	9vHPV ^b n (%)
Ages 18–26 years		
Total	1249	646
Age at first vaccination, years		
< 18	573 (45.9)	95 (14.7)
18–26	676 (54.1)	551 (85.3)
Median (IQR)	18 (15–22)	22 (20–24)
Time since first vaccination, years		
≥ 2	917 (73.4)	317 (49.1)
< 2	332 (26.6)	329 (50.9)
Median (IQR)	4.9 (1.8–8.0)	1.9 (0.8–3.5)
Median time since first vaccination (years) among those vaccinated at age < 18 years (IQR)	8.2 (6.6–9.5)	5.5 (4.2–6.7)
Median time since first vaccination (years) among those vaccinated at age 18–26 years (IQR)	2.1 (0.8–3.8)	1.5 (0.6–2.8)
HPV vaccine		
4vHPV	383 (30.7)	n/a
9vHPV	646 (51.7)	646 (100)
Combination of 4vHPV and 9vHPV	208 (16.7)	n/a
Other or unknown	12 (1.0)	n/a
Number of documented HPV vaccine doses		
1	168 (13.5)	112 (17.3)
2	253 (20.3)	176 (27.2)
3 or more	828 (66.3)	358 (55.4)
Ages 27–45 years		
Total	926	690
Age at first vaccination, years		
< 18	19 (2.1)	1 (0.1)
18–26	362 (39.1)	175 (25.4)
> 26	545 (58.9)	514 (74.5)
Median (IQR)	29 (25–35)	32 (26–37)
Time since first vaccination, years		
≥ 2	543 (58.6)	315 (45.7)
< 2	383 (41.4)	375 (54.4)
Median (IQR)	2.7 (1.1–5.1)	1.8 (0.9–3.2)
Median time since first vaccination (years) among those vaccinated at age 18–26 years (IQR)	5.5 (3.4–7.6)	3.4 (2.4–4.9)

	Any HPV vaccine ^a n (%)	9vHPV ^b n (%)
Median time since first vaccination (years) among those vaccinated at age > 26 years (IQR)	1.5 (0.7–2.7)	1.4 (0.7–2.6)
HPV vaccine		
4vHPV	155 (16.7)	n/a
9vHPV	690 (74.5)	690 (100)
Combination of 4vHPV and 9vHPV	62 (6.7)	n/a
Other or unknown	19 (2.0)	n/a
Number of documented HPV vaccine doses		
1	159 (17.2)	110 (15.9)
2	234 (25.3)	186 (27.0)
3 or more	533 (57.6)	394 (57.1)

4vHPV, quadrivalent HPV vaccine; 9vHPV, 9-valent HPV vaccine; IQR, interquartile range

^aAny documented HPV vaccination (i.e., 4vHPV, 9vHPV, a combination of these, or unknown HPV vaccine) ≥ 30 days before specimen collection

^bDocumented 9vHPV vaccination ≥ 30 days before specimen collection; individuals who received 4vHPV (alone or in combination with 9vHPV) or who had another or unknown HPV vaccine product were excluded

Table 3.

Prevalence of anal human papillomavirus (HPV) among men who have sex with men and other persons assigned male at birth attending sexual health clinics in three U.S. cities, by demographic and clinical characteristics — 2018–2023

		Prevalence, n (%)			
	N	Any 4vHPV type	Any additional 9vHPV type	Any non-9vHPV type	Any HPV type
Ages 18–26 years					
Total	2802	508 (18.1)	538 (19.2)	1912 (68.2)	2026 (72.3)
City		<i>a</i>		<i>a</i>	<i>a</i>
Seattle	1083	236 (21.8)	221 (20.4)	801 (74.0)	845 (78.0)
Philadelphia	853	119 (14.0)	152 (17.8)	560 (65.7)	594 (69.6)
New York City	866	153 (17.7)	165 (19.1)	551 (63.6)	587 (67.8)
Gender identity		<i>a</i>			
Male	2150	415 (19.3)	429 (20.0)	1485 (69.1)	1575 (73.3)
Female/transgender female	42	8 (19.0)	6 (14.3)	30 (71.4)	31 (73.8)
Non-binary/gender-queer/gender non-conforming/other	104	17 (16.3)	14 (13.5)	75 (72.1)	78 (75.0)
Unknown	506	68 (13.4)	89 (17.6)	322 (63.6)	342 (67.6)
Race/ethnicity		<i>a</i>		<i>a</i>	<i>a</i>
Non-Hispanic Black	545	77 (14.1)	92 (16.9)	380 (69.7)	398 (73.0)
Non-Hispanic White	1015	193 (19.0)	187 (18.4)	681 (67.1)	715 (70.4)
Non-Hispanic Asian/Pacific Islander	282	42 (14.9)	51 (18.1)	181 (64.2)	194 (68.8)
Hispanic	655	137 (20.9)	151 (23.1)	476 (72.7)	505 (77.1)
Another race, non-Hispanic	192	35 (18.2)	34 (17.7)	124 (64.6)	136 (70.8)
Unknown	113	24 (21.2)	23 (20.4)	70 (61.9)	78 (69.0)
CT/GC test result				<i>a</i>	<i>a</i>
Negative	2280	413 (18.1)	434 (19.0)	1507 (66.1)	1605 (70.4)
Positive	522	95 (18.2)	104 (19.9)	405 (77.6)	421 (80.7)
Ages 27–45 years					
Total	3548	1190 (33.5)	1106 (31.2)	2636 (74.3)	2864 (80.7)
City		<i>a</i>		<i>a</i>	<i>a</i>
Seattle	1317	484 (36.8)	436 (33.1)	1038 (78.8)	1120 (85.0)
Philadelphia	1066	343 (32.2)	336 (31.5)	789 (74.0)	866 (81.2)
New York City	1165	363 (31.2)	334 (28.7)	809 (69.4)	878 (75.4)
Gender identity					
Male	2862	964 (33.7)	910 (31.8)	2128 (74.4)	2315 (80.9)
Female/transgender female	29	9 (31.0)	9 (31.0)	23 (79.3)	23 (79.3)
Non-binary/gender-queer/gender non-conforming/other	53	17 (32.1)	17 (32.1)	43 (81.1)	44 (83.0)
Unknown	604	200 (33.1)	170 (28.1)	442 (73.2)	482 (79.8)

		Prevalence, n (%)			
	N	Any 4vHPV type	Any additional 9vHPV type	Any non-9vHPV type	Any HPV type
Race/ethnicity				<i>a</i>	<i>a</i>
Non-Hispanic Black	535	169 (31.6)	166 (31.0)	370 (69.2)	413 (77.2)
Non-Hispanic White	1439	516 (35.9)	446 (31.0)	1105 (76.8)	1191 (82.8)
Non-Hispanic Asian/Pacific Islander	324	88 (27.2)	99 (30.6)	225 (69.4)	238 (73.5)
Hispanic	904	308 (34.1)	296 (32.7)	677 (74.9)	741 (82.0)
Another race, non-Hispanic	232	73 (31.5)	66 (28.4)	171 (73.7)	187 (80.6)
Unknown	114	36 (31.6)	33 (28.9)	88 (77.2)	94 (82.5)
CT/GC test result		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>
Negative	3013	988 (32.8)	917 (30.4)	2205 (73.2)	2398 (79.6)
Positive	535	202 (37.8)	189 (35.3)	431 (80.6)	466 (87.1)

CT, chlamydia; GC, gonorrhea; 4vHPV, quadrivalent HPV vaccine; 9vHPV, 9-valent HPV vaccine

4vHPV types, HPV 6, 11, 16, 18

Additional 9vHPV types, HPV 31, 33, 45, 52, 58

Non-9vHPV types, HPV 26, 35, 39, 40, 42, 43, 44, 51, 53, 54, 56, 59, 61, 66, 68, 69, 70, 73, 82

^a Chi-square p-value < 0.05

Note: Prevalences specific for the 9vHPV sub-analysis are available in Supplemental Table 2.

Table 4.

Prevalence of anal human papillomavirus (HPV) among men who have sex with men and other persons assigned male at birth attending sexual health clinics in three U.S. cities, by vaccination characteristics — 2018–2023

		Prevalence, n (%)			
	N	Any 4vHPV type	Any additional 9vHPV type	Any non-9vHPV type	Any HPV type
Ages 18–26 years					
HPV vaccination			<i>a</i>	<i>a</i>	<i>a</i>
No	1553	299 (19.3)	328 (21.1)	1010 (65.0)	1084 (69.8)
Yes	1249	209 (16.7)	210 (16.8)	902 (72.2)	942 (75.4)
Age at first vaccination, years		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>
< 18	573	15 (2.6)	70 (12.2)	383 (66.8)	390 (68.1)
18–26	676	194 (28.7)	140 (20.7)	519 (76.8)	552 (81.7)
Time since first vaccination, years		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>
≥ 2	917	97 (10.6)	130 (14.2)	646 (70.5)	668 (72.9)
< 2	332	112 (33.7)	80 (24.1)	256 (77.1)	274 (82.5)
Time since first vaccination (years) among those vaccinated at age 18–26 years		<i>a</i>	<i>a</i>		
≥ 2	348	83 (23.9)	61 (17.5)	267 (76.7)	282 (81.0)
< 2	328	111 (33.8)	79 (24.1)	252 (76.8)	270 (82.3)
HPV vaccine		<i>a</i>			<i>a</i>
4vHPV	383	20 (5.2)	63 (16.5)	258 (67.4)	268 (70.0)
9vHPV	646	169 (26.2)	117 (18.1)	488 (75.5)	515 (79.7)
Combination of 4vHPV and 9vHPV	208	20 (9.6)	28 (13.5)	149 (71.6)	151 (72.6)
Ages 27–45 years					
HPV vaccination		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>
No	2622	912 (34.8)	850 (32.4)	1906 (72.7)	2091 (79.8)
Yes	926	278 (30.0)	256 (27.7)	730 (78.8)	773 (83.5)
Age at first vaccination, years		<i>a</i>			
< 18	19	2 (10.5)	6 (31.6)	14 (73.7)	14 (73.7)
18–26	362	92 (25.4)	95 (26.2)	289 (79.8)	298 (82.3)
> 26	545	184 (33.8)	155 (28.4)	427 (78.4)	461 (84.6)
Time since first vaccination, years		<i>a</i>	<i>a</i>	<i>a</i>	
≥ 2	543	138 (25.4)	133 (24.5)	441 (81.2)	457 (84.2)
< 2	383	140 (36.6)	123 (32.1)	289 (75.5)	316 (82.5)
Time since first vaccination (years) among those vaccinated at age 18–26 years					
≥ 2	324	80 (24.7)	85 (26.2)	260 (80.3)	267 (82.4)
< 2	38	12 (31.6)	10 (26.3)	29 (76.3)	31 (81.6)

		Prevalence, n (%)			
	N	Any 4vHPV type	Any additional 9vHPV type	Any non-9vHPV type	Any HPV type
Time since vaccination (years) among those first vaccinated at age > 26 years		<i>a</i>	<i>a</i>	<i>a</i>	
≥ 2	200	56 (28.0)	42 (21.0)	167 (83.5)	176 (88.0)
< 2	345	128 (37.1)	113 (32.8)	260 (75.4)	285 (82.6)
HPV vaccine					
4vHPV	155	38 (24.5)	51 (32.9)	128 (82.6)	132 (85.2)
9vHPV	690	220 (31.9)	184 (26.7)	534 (77.4)	570 (82.6)
Combination of 4vHPV and 9vHPV	62	13 (21.0)	14 (22.6)	52 (83.9)	54 (87.1)

4vHPV, quadrivalent HPV vaccine; 9vHPV, 9-valent HPV vaccine; vaccination defined as documented receipt of HPV vaccination (i.e., 4vHPV, 9vHPV, a combination of these, or unknown HPV vaccine) ≥ 30 days before specimen collection

4vHPV types, HPV 6, 11, 16, 18

Additional 9vHPV types, HPV 31, 33, 45, 52, 58

Non-9vHPV types, HPV 26, 35, 39, 40, 42, 43, 44, 51, 53, 54, 56, 59, 61, 66, 68, 69, 70, 73, 82

^aChi-square p-value < 0.05

Note: Prevalences specific for the 9vHPV sub-analysis are available in Supplemental Table 3.

Table 5.

Adjusted prevalence ratios for associations between documented receipt of human papillomavirus (HPV) vaccine and anal HPV types among men who have sex with men and other persons assigned male at birth attending sexual health clinics in three U.S. cities, stratified by age group — 2018–2023

	Any 4vHPV type		Any additional 9vHPV type	
	Any HPV vaccine Adjusted PR ^{a,b} (95% CI)	Restricted to 9vHPV Adjusted PR ^{a,c} (95% CI)	Any HPV vaccine Adjusted PR ^{a,b} (95% CI)	Restricted to 9vHPV Adjusted PR ^{a,c} (95% CI)
Ages 18–26 years^d				
HPV vaccination				
No	Ref	Ref	Ref	Ref
Yes	0.80 (0.68, 0.95)	1.22 (1.03, 1.44)	0.73 (0.62, 0.85)	0.75 (0.62, 0.91)
Age at first vaccination, years				
Unvaccinated	Ref	Ref	Ref	Ref
< 18	0.13 (0.08, 0.22)	0.16 (0.05, 0.50)	0.56 (0.44, 0.72)	0.35 (0.17, 0.72)
18–26	1.31 (1.11, 1.54)	1.39 (1.17, 1.65)	0.85 (0.71, 1.02)	0.82 (0.67, 0.99)
Time since first vaccination, years				
Unvaccinated	Ref	Ref	Ref	Ref
≥ 2	0.52 (0.42, 0.64)	0.89 (0.69, 1.14)	0.63 (0.52, 0.75)	0.54 (0.40, 0.73)
< 2	1.50 (1.25, 1.80)	1.52 (1.26, 1.84)	0.98 (0.79, 1.21)	0.95 (0.76, 1.19)
Time since first vaccination (years) among those vaccinated at age 18–26 years				
Unvaccinated	Ref	Ref	Ref	Ref
≥ 2	1.10 (0.88, 1.36)	1.17 (0.91, 1.49)	0.72 (0.56, 0.92)	0.62 (0.45, 0.85)
< 2	1.57 (1.30, 1.89)	1.56 (1.29, 1.88)	0.98 (0.79, 1.22)	0.96 (0.77, 1.19)
Ages 27–45 years^e				
HPV vaccination				
No	Ref	Ref	Ref	Ref
Yes	0.79 (0.70, 0.89)	0.85 (0.75, 0.97)	0.77 (0.68, 0.86)	0.75 (0.65, 0.86)
Age at first vaccination, years^f				
Unvaccinated	Ref	Ref	Ref	Ref
18–26	0.68 (0.57, 0.82)	0.62 (0.47, 0.82)	0.73 (0.61, 0.87)	0.54 (0.39, 0.74)
>26	0.88 (0.77, 1.01)	0.93 (0.81, 1.06)	0.79 (0.68, 0.91)	0.82 (0.71, 0.96)
Time since first vaccination, years				
Unvaccinated	Ref	Ref	Ref	Ref
≥ 2	0.66 (0.57, 0.77)	0.69 (0.56, 0.83)	0.67 (0.57, 0.78)	0.57 (0.45, 0.71)
< 2	0.98 (0.85, 1.13)	1.00 (0.87, 1.16)	0.91 (0.78, 1.07)	0.91 (0.78, 1.07)
Time since first vaccination (years) among those vaccinated at age 18–26 years				

	Any 4vHPV type		Any additional 9vHPV type	
	Any HPV vaccine Adjusted PR ^{a,b} (95% CI)	Restricted to 9vHPV Adjusted PR ^{a,c} (95% CI)	Any HPV vaccine Adjusted PR ^{a,b} (95% CI)	Restricted to 9vHPV Adjusted PR ^{a,c} (95% CI)
Unvaccinated	Ref	Ref	Ref	Ref
≥ 2	0.67 (0.55, 0.82)	0.57 (0.41, 0.80)	0.73 (0.61, 0.89)	0.50 (0.34, 0.72)
< 2	0.88 (0.56, 1.39)	0.86 (0.53, 1.40)	0.73 (0.43, 1.23)	0.71 (0.40, 1.24)
Time since first vaccination (years) among those vaccinated at age >26 years				
Unvaccinated	Ref	Ref	Ref	Ref
≥ 2	0.71 (0.56, 0.89)	0.77 (0.61, 0.97)	0.56 (0.42, 0.73)	0.62 (0.47, 0.82)
< 2	1.02 (0.88, 1.18)	1.03 (0.89, 1.19)	0.94 (0.80, 1.11)	0.94 (0.80, 1.10)

9vHPV, 9-valent HPV vaccine

4vHPV types, HPV 6, 11, 16, 18

Additional 9vHPV types, HPV 31, 33, 45, 52, 58

Non-9vHPV types, HPV 26, 35, 39, 40, 42, 43, 44, 51, 53, 54, 56, 59, 61, 66, 68, 69, 70, 73, 82

^a Adjusted for city, race/ethnicity, and non-9vHPV-type prevalent infection

^b Comparing persons with any documented HPV vaccination (i.e., 4vHPV, 9vHPV, a combination of these, or unknown HPV vaccine) ≥ 30 days before specimen collection to unvaccinated persons

^c Comparing persons with documented 9vHPV vaccination ≥ 30 days before specimen collection to unvaccinated persons; individuals who received 4vHPV (alone or in combination with 9vHPV) or who had another or unknown HPV vaccine product were excluded

^d Any HPV vaccine: N= 2802; restricted to 9vHPV: N=2199

^e Any HPV vaccine: N= 3548; restricted to 9vHPV: N=3312

^f Because few individuals aged 27–45 years had been vaccinated at age <18 years, these individuals were excluded from analyses of age at first vaccination.

Bold text indicates statistical significance at $p < 0.05$