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Determinants of Type-Specific HPV Concordance Across Anatomic Sites in Young Men Who Have Sex with Men and Transgender Women, 3 U.S. Cities, 2016–2018

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Abstract

Background: Among men who have sex with men (MSM) and transgender women (TGW), the dynamics of HPV infections at different anatomical sites are not well understood. Information on HPV concordance between anatomic sites can inform the extent of auto-inoculation, and susceptibility of different anatomic areas to HPV infection. We described and assessed correlates of HPV concordance across anal, oral, and genital samples.

Methods: We enrolled 1876 MSM and TGW aged 18-26 years in three US cities. Oral, genital, and anal samples were self-collected for type-specific HPV DNA testing (37 types). Demographics, sexual behaviors, and health history were self-reported. Kappa statistics based on

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percent positive agreement (kappa+) and generalized estimating equations were used to describe and identify correlates of HPV type-specific concordance between anatomic sample pairs.

Results: Any HPV was detected in 69.9%, 48.6%, and 7.4% of anal, genital, and oral samples, respectively. Detection of any HPV (concurrence) was most common in anal-genital pairs (40.9%) and uncommon in oral-genital and oral-anal pairs (3.4% and 6.5% respectively). Type-specific concordance was poor across all sample pairs (kappa+ <0.20). Younger age and older age at first sex were positively associated with type-concordant anal-genital infections. Sexual behaviors were unassociated with concordance.

Conclusions: Poor oral/anogenital concordance suggests the oral mucosa has different susceptibility to HPV infection, differential clearance and/or auto-inoculation between oral and anogenital sites is unlikely. There was some observed concurrence and concordance between anal and genital sites, unassociated with sexual behavior, suggesting auto-inoculation. Longitudinal studies are necessary to further elucidate mechanisms of multi-site infections.

Short Summary:

Among MSM aged 18–26-years, HPV was detected in both anal and genital specimens from 41% (11% with type-specific concordance). Concordance was rare in oral-anal or oral-genital pairs.

INTRODUCTION

In men, human papillomavirus (HPV) infections cause anogenital warts and cancers of the genitals, anus, and oropharynx[1]. Men who have sex with men (MSM) and transgender women (TGW) are at disproportionately high risk for HPV infections and HPV-associated diseases. HPV seroprevalence is approximately 2-6 times higher among MSM compared to men who have sex exclusively with women (MSW)[2]. Among MSM, anal HPV prevalence ranges from 65%-93%[3], and anal cancer incidence is estimated to be 37 cases per 100,000 person-years[3] (and higher in MSM living with versus without human immunodeficiency virus (HIV) infection)[3]. There are limited data on HPV-related health outcomes among TGW, with many reports not disaggregating results from MSM and TGW. Nevertheless, multiple studies have reported an even higher burden of HPV infections in TGW than in MSM[4], with HPV-related cancers therefore expected to occur more frequently in TGW[5]. Furthermore, despite the availability of effective vaccines to prevent HPV infections, HPV vaccine coverage in MSM in the US is suboptimal and data on vaccine coverage in TGW are lacking[4].

Epidemiology and risk factors for HPV infections among MSM and TGW are not fully understood. Limited data are available about the relationship between HPV infections at different anatomical sites. Information on HPV concordance across anatomical sites can provide information on sources of infection, the extent of auto-inoculation between sites, and susceptibility of different anatomic areas to HPV infection. In MSM and TGW a limited number of studies have evaluated the presence and positive concordance of HPV DNA at anal, genital, and/or oropharyngeal sites. Most of these studies showed low concordance, with a wide range of estimates across studies that may be due to variability in sampling methods, differences in sensitivity of detection methods, and differences in anatomic sites included [6-14]. To enhance our understanding of HPV transmission and risk for HPV-

related cancers in MSM and TGW, additional studies are needed to accurately describe concordance and associated risk factors across anatomic sites.

METHODS

Study design

To describe the concordance of HPV types and associated risk factors across anatomic sites, we conducted a cross-sectional analysis using data from the HPV Vaccine Impact in Men (VIM) study conducted among young MSM and TGW in three US cities, as described previously[15, 16].

Study population

During 2016-2018, the study enrolled participants at a sexual health clinic and community STD/HIV testing site in Seattle, WA a community center serving lesbian, gay, bisexual, and transgender (LGBT) persons in Chicago, IL and an LGBT clinic in Los Angeles, CA. Individuals aged 18-26 years were eligible if they reported having been assigned male sex at birth and reported a history of anal or oral sex with a male partner, identified as gay/homosexual or bisexual, or intended to have sex with a male partner in the future.

Ethical considerations

After providing written informed consent, participants were enrolled and completed all study elements on the same day. Study procedures were reviewed and approved by the institutional review boards at all participating institutions. This study was reviewed by CDC and was conducted consistent with federal law and CDC policy.

Study procedures

Study participants completed a survey which included questions on demographics, sexual behaviors, and health information including HIV status and HPV vaccination history. Additional data were extracted from clinic records for subjects enrolled in Seattle.

Each participant was invited to self-collect and submit at least two specimens for HPV DNA testing: an anal swab and an oral rinse specimen. Additionally, Seattle participants were invited to self-collect and submit a genital swab. Participants were provided with verbal and written instructions on how to self-collect clinical specimens.[15-17] Specimens were shipped frozen to the CDC research laboratory in Atlanta, Georgia, for batch processing as previously described.[17] Briefly, DNA extracts were assayed for HPV using the Roche Linear Array (Roche Diagnostics, Pleasanton, CA) to detect any of 37 HPV DNA types (6/11/16/18/26/31/33/35/39/40/42/45/51/52/53/54/55/56/58/59/61/62/64/66/67/68/69/70/71/72/73/81/82/83/84/89/IS39). Specimens were considered inadequate if test results were negative for the human β-globin gene and all 37 HPV types.

Prevalence was calculated for the following categories of HPV types: any type (37 HPV types), any high-risk type (16/18/31/33/35/39/45/51/52/56/58/59/66/68), any 4-valent HPV vaccine-type (6/11/16/18), and any 9-valent HPV vaccine-type (6/11/16/18/31/33/45/52/58). We determined prevalence estimates for each anatomic site separately (anal, genital or oral),

and for concurrent detection at two anatomic sites (oral/anal, oral/genital, or anal/genital), or all three anatomic sites (anal, genital and oral). For each set of anatomic sites, we also described the proportion with full, partial, and no agreement in the HPV types detected between sites. Anatomic site-specific analyses were restricted to those with an adequate specimen at the specific site(s).

Data analysis

Type-specific HPV concordance was determined by comparing detection between paired anatomic sites. We defined complete concordance as detection of all of the same HPV types in both anatomic sites, while partial concordance was defined as only some of the same HPV types detected in both sites. Pooled positive type-specific concordance was calculated for any HPV, any high-risk HPV, any 9-valent HPV vaccine-type, and any 4-valent HPV vaccine-type, HPV 6 and/or 11, and HPV 16 and/or 18. The observed proportion positive agreement (PPA) between sites was calculated by obtaining the paired samples positive in both sites divided by the number of paired samples with any positive test at either site. The expected PPA between these sites was calculated based on the product of the marginal probabilities of obtaining positive samples at both sites divided by the probability of obtaining a positive at either site. To adjust for the PPA caused by chance for each pair, the unweighted PPA kappa statistic (kappa+) and 95% confidence interval (CI) was calculated using percentile bootstraps (where the bootstrap resampled individuals to account for the correlation between samples within an individual).

We then conducted generalized estimating equations logistic regression to measure the effect of individual risk factors associated with type-specific concordance of HPV infections across oral-anal and genital-anal sample pairings (separate models). We did not assess for factors associated with concordance across oral-genital sample pairs due to the low number of concordant pairs. We estimated odds ratios (OR) and 95% CI based on robust variance estimates using a generalized estimating equation approach, clustering on the individual. Variables assessed included: age, sexual orientation, race/ethnicity, smoking status, self-reported HIV status, history of ever taking HIV pre-exposure prophylaxis (PrEP), self-reported HPV vaccination status, age at first HPV vaccine dose, age at first sex with any partner, lifetime number of sex partners (any gender), male sex partners in the last 12 months, male sex partners in the last 2 months, new male sex partner in the last 2 months, gave oral sex to male partners in the last 2 months, received oral sex from male partners in the last 2 months, was a bottom (receptive) in anal sex in the last 12 months, engaged in condomless anal sex as a bottom in the last 12 months, was a top (insertive) in anal sex in the last 12 months, engaged in condomless anal sex as a top in the last 12 months, history of anogenital warts, history of genital herpes, gonorrhea or chlamydia in the last 12 months, and syphilis in the last 12 months. The following variables were not collected from one of the Seattle clinics: received oral sex from male partners in the last 2 months, history of anogenital warts and history of genital herpes. Variables found to be statistically significant in the univariate analysis ($P<0.10$) were entered into multivariate logistic regression models. When a variable found significant in the univariate analysis had >5% missing data, we added a category for the missing data and performed the multivariate analysis with the missing

category included for the particular variable. All calculations were performed in RStudio 2022.07.2+576.

RESULTS

A total of 1881 participants were enrolled, of whom 1876 had ≥1 adequate biologic specimen result and were included in this analysis. Adequate results were available for 1779 oral-anal pairs, 700 oral-genital pairs, 668 anal-genital pairs, and 667 at all three sites.

Demographics, sexual behavior, and health history characteristics

The median age of participants was 23 years (interquartile range [IQR] 21-25 years) and the median age of first sex with any partner was 16 years (IQR 15-18 years) (Table 1). The majority of participants identified as male (94.5%) and self-reported being gay or homosexual (72.4%). The most commonly self-reported race and/or ethnicity was non-Hispanic White (31.2%), followed by Hispanic (31.2%), non-Hispanic Black (14.1%) and Asian/Pacific Islander (7.8%). Having tested positive for HIV was reported by 143 (7.6%) participants. 742 (39.6%) participants reported receipt of ≥1 HPV vaccine dose, with the median age at first HPV vaccination being 19 (IQR 16-22) years. More than half of participants reported a lifetime number of >20 sex partners (any gender) and 72.3% reported a new male sex partner in the prior two months.

Prevalence and concordance of HPV detection among study participants

Most participants (71.2%) had HPV detected from ≥1 anatomic site, with more than half (52.5%) having a high-risk type (Table 2). HPV was most commonly detected from anal specimens (69.9%; 1250/1787), followed by genital specimens (48.6%; 341/701), and oral specimens (7.4%; 138/1868). This pattern was similar across the different HPV type groups evaluated, including high-risk HPV, 4-valent HPV vaccine types, and 9-valent HPV vaccine types. Among participants who had HPV detected in anal samples, the mean (standard deviation [SD]) and median (IQR) number of HPV types detected was 3.1 (2.3) and 2 (1-4) respectively. The mean (SD) and median (IQR) number of HPV types detected was 2.0 (1.5) and 1 (1-3) for genital samples, and 1.3 (0.6) and 1 (1-1) for oral samples.

Concurrent detection of any HPV at more than one anatomic site was most common in anal-genital sample pairs (40.9%) followed by oral-anal sample pairs (6.5%) and oral-genital samples (3.4%) (Table 2). Among participants with samples from all three sites, 3.0% had at least one HPV type detected at all three sites, and 1.2% had at least one high-risk type detected in all three sites. Of participants with concurrent anal and genital infections, 10.6% had complete concordance of the HPV types detected at both sites. The proportion of concurrently positive pairs with complete concordance was lower at both the oral and anal sites and at the oral and genital sites at 5.2% and 8.3% respectively. Similarly, partial concordance was highest in anal-genital samples compared to oral-anal samples and oral-genital samples at 61.2%, 31.0% and 25.0% respectively. Of the 20 participants with concurrent HPV detection at all three sites, only one had complete concordance, while 4 had partial concordance.

Type-specific HPV concordance was highest for genital/anal sample pairs (PPA=16.7%, kappa+=0.15, 95% CI:0.13–0.17) (Table 3). The PPA among both oral/anal sample pairs and oral/genital sample pairs was considerably lower at 1.2% (kappa+=0.01, 95% CI:0.01–0.01) and 1.4% (kappa+=0.01, 95% CI:0.00–0.02) respectively. Similar patterns for comparisons of agreement across sample pairs were observed for all HPV type groups evaluated.

Factors associated with type-specific HPV concordance across oral-anal sample pairings

In univariate analyses, the likelihood of detecting the same HPV type in paired oral and anal samples was significantly higher among participants who had ever smoked compared to those who had never smoked (OR=2.30; 95% CI:1.19–4.47). Participants who were aged ≥16 years at sexual debut were less likely to have a concordant oral-anal infection than those who were aged ≤15 years (OR=0.48, 95% CI:0.26–0.91) (Table 4). Borderline statistically significant associations were observed for lifetime number of sex partners and reporting being a top in anal sex in the past 12 months.

In the multivariate model including smoking status, age of sexual debut, lifetime number of sex partners and being a top in anal sex in the last 12 months, younger age at sexual debut remained significantly associated with type-specific HPV concordance (adjusted OR (aOR)=0.50, 95% CI:0.27–0.93). The association between smoking status and concordance was attenuated and borderline statistically significant (aOR=1.91, 95% CI:0.96–3.77). Associations for lifetime number of sex partners and being a top in anal sex in the last 12 months were not statistically significant in the multivariate model (Table 4).

Factors associated with type specific HPV concordance across anal-genital sample pairs

In the univariate analysis, odds of having a concordant anal-genital HPV infection were significantly lower in participants aged 22-26 years versus 18-21 years (OR=0.66, 95% CI:0.47–0.93) (Table 5). On the other hand, the odds of detecting the same HPV type in paired anal-genital samples were higher among participants who reported that their age at first sex was ≥16 years than in those who reported a younger age at first sex (OR=1.43, 95% CI:1.02–2.01). Self-reporting testing HIV-positive also trended towards having a significant association with concordant anal-genital HPV infections (OR=2.02, 95% CI:0.92–4.44).

After including age at enrolment, age at first sex and HIV status in the multivariate model, the likelihood of a concordant HPV infection was even lower in participants aged 22-26 years versus <22 years (adjusted odds ratio (aOR)=0.62; 95% CI:0.44–0.87). Older age at first sex also continued to be significantly associated with having a higher odds of same-type HPV detection across paired anal and genital samples (aOR=1.48; 95% CI:1.06–2.08). Moreover, the magnitude of association between concordance and HIV status was slightly larger in the multivariate model, but only borderline significant (aOR=2.21, 95% CI:0.99–4.89) (Table 5).

DISCUSSION

In this population of young MSM and TGW, concurrent detection of any HPV at multiple anatomic sites was highest for paired anal-genital sample pairs (over 40%). This is higher than reported in other studies among MSM in which the prevalence of concurrent

anal-genital HPV infection ranged between 15%-23%[12, 18]. This difference could be due to sampling techniques or participant characteristics, since our study population was younger, with a higher likelihood of more recently acquired infections. Nonetheless, the high prevalence of concurrent infections highlights the importance of early HPV vaccination to prevent HPV infections and HPV-related cancers in MSM and TGW.

Concurrent HPV detection in oral-genital and oral-anal sample pairs was uncommon, likely related to the low oral HPV prevalence in our study. Among the 7.4% of participants with oral HPV, concurrent HPV detection was much more common with an anal sample (84%) than a genital sample (17%), possibly attributable to both the high prevalence of anal HPV infection and multiple-type HPV in anal samples. In the 2012-2014 Young Men's HPV Study of MSM and TGW, a similarly low level of concurrent oral-anal HPV detection (8.0%) was observed, and among the 9.8% of participants with oral HPV, 82.2% had concurrent HPV detection from anal samples [9]. Although other studies among MSM have reported a slightly higher prevalence of concurrent HPV in oral-genital samples (6%-9%)[6, 19], the prevalence of concordant oral-genital HPV was low[6, 10].

Similar to other studies in men[6, 7, 9-12], we noted little type-specific agreement between the various sample pairs analyzed. The observed HPV type-specific agreement in the current study was low for anal-genital sample pairs, and there was little to no agreement in pairs involving an oral sample.

Younger age was positively associated with anal-genital concordance. In contrast, other studies in MSM and the general male population have not reported any association of age with concordant HPV across anatomic sites[8, 9, 11, 20, 21]. However, as in our study, some studies in women demonstrated increasing age to be associated with lower likelihood of detecting type-concordant HPV in anal-genital[22] and oral-genital samples[23]. Conversely, we did not observe any association of age with oral-anal concordance in our study, possibly due to the low prevalence of oral HPV infections.

Smoking was associated with a twofold higher likelihood of HPV type-concordant oral-anal infection, although this association was attenuated and not statistically significant in the adjusted model. Other studies in both MSM and MSW have reported smoking to be associated with concordant oral and anogenital infections[8, 9]. Smoking is generally thought to increase the persistence and reactivation of HPV infections in the oral cavity and is therefore associated with higher oral HPV prevalence[24]. The higher prevalence of concordant oral-anal HPV infections among smokers is probably related to higher oral HPV prevalence in this group. In contrast, smoking was not associated with anal-genital type concordance in our study.

The only sexual behavior characteristic that was significantly associated with type-specific concordance was age at first sex. Oral-anal type-specific HPV concordance was significantly lower among participants who reported an older versus younger age at first sex. In contrast, the inverse was observed for anal-genital samples. Potential explanations include different dynamics in HPV acquisition at the oral and anogenital sites, or variances in time to HPV clearance and persistence in the oral site compared to anal and genital sites[25]. In the only

other study among MSM that reported on the association of age of first sex with HPV concordance, those who reported an older age more often had a concordant infection at both sites, compared to those who reported a younger age, but this was not statistically significant[20]. On the other hand, studies among women have observed that those reporting a younger age of sexual debut were more likely to have a concordant oral-genital HPV infection[22, 23] but the findings in these studies failed to achieve statistical significance in multivariate models.

The lack of type-concordance between oral and anogenital HPV infections in our study and other similar studies suggest that oral HPV infections may be acquired independently of anogenital infections or may be less likely to reactivate from latency compared to anogenital infections[6]. In addition, auto-inoculation between oral and anogenital sites may be uncommon, and there are likely different pathways or timing of infection at the oral site compared to the anogenital sites[25]. Faster clearance from oral epithelia and latent infections remaining undetected due to limitations of exfoliated cell sampling might also explain the low prevalence of concordant infections involving the oral site. Moreover, the lack of observed concordance might also be explained by differences in the duration of infection at the different anatomic sites[26], varying limitations of specimen collection from the three anatomic sites, and difference in tissue structure and virus tropism between the different anatomic sites[12]. Given the rise in HPV-related oropharyngeal cancers in men, additional studies to understand the epidemiology and natural history of oral versus anogenital HPV infections are warranted.

Of note, we observed some type-concordance between genital and anal HPV infections in our population of young MSM and TGW, and this was not associated with sexual behaviors. This suggests that other factors such as nonpenetrative sexual behaviors or auto-inoculation between different anatomic sites might have a role in the transmission of HPV infections. This theory is also supported by the high prevalence of anal HPV in the absence of anal sex in studies of both men and women[22, 27]. Although the mechanism of transport between these anatomic sites is unclear, some data suggest that HPV at either site can serve as a reservoir for infection at the other site[28] and there is potential for transmission of HPV via hand carriage[29] and objects[30], which may facilitate HPV inoculation between the anal canal and genitals. Our study was cross-sectional which limited the ability to distinguish between newly acquired versus persistent infections; longitudinal studies are needed to elucidate HPV transmission dynamics.

A strength of our study was that it was conducted in three cities with access to a large source population which allowed us to conduct the largest study to date evaluating HPV concordance at three anatomic sites in young racially and ethnically diverse MSM and TGW. Another strength is that we used the gold standard method of collecting HPV specimens from the various anatomic sites and all samples were tested by PCR at the same laboratory at CDC using a validated assay for type-specific detection. Lastly, we had access to a rich array of demographic data, medical information and sexual behavior data, allowing us to study a wide range of potential covariates.

This analysis is subject to at least three limitations. First, our convenience sample may not be representative of MSM or TGW in general. Second, some self-reported characteristics may have been overreported or underreported due to social desirability and recall biases. Third, the sensitivity of HPV DNA testing across anatomic sample types may vary.

In summary, our results show that MSM and TGW are likely to harbor concurrent HPV infections at multiple anatomic sites, highlighting the need for increased efforts to promote HPV vaccination in early adolescence to prevent HPV-related cancers in MSM and TGW. We observed some concordance between type-specific anal and genital HPV infections that was unassociated with sexual behaviors, suggesting that non-sexual transmission such as auto-inoculation plays an important role in HPV infections at anogenital sites. Conversely, concordant HPV detection between oral and anogenital sites was rare, suggesting that oral HPV infections are more likely to be acquired independently of anogenital infection or at a different point in time. To better understand HPV transmission dynamics and HPV-related cancer risk in MSM and TGW, additional studies that consider both the timing and clearance of oral versus anogenital HPV infections and characterize factors associated with HPV persistence and concordance across sites are warranted.

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Table 1 -

Baseline demographics and sexual characteristics of young MSM and transgender women enrolled in the VIM study, 3 U.S. cities, 2016-2018

Characteristic		No. (%)[†] (N = 1876) [¤]
City	Chicago, IL	664 (35.4%)
	Los Angeles, LA	462 (24.6%)
	Seattle, WA	750 (40%)
Age, years	Mean (SD), N = 1876	22.5 (2.4)
	Median (IQR), N = 1876	23 (21 – 25)
	18 – 21	661 (35.2%)
	22 – 26	1215 (64.8%)
Gender identity	Male	1772 (94.5)
	Female/transgender female	55 (2.9%)
	Other/unknown [¤]	49 (2.6%)
Sexual orientation	Gay/homosexual	1358 (72.4%)
	Straight/heterosexual	32 (1.7%)
	Other/unknown [¤]	486 (25.9%)
Race and ethnicity	Non-Hispanic White	585 (31.2%)
	Non-Hispanic Black	265 (14.1%)
	Asian/Pacific Islander	147 (7.8%)
	Hispanic	585 (31.2%)
	Other [*]/unknown [¤]	294 (15.7%)
Smoking status	Ever smoked	789 (42.1%)
	Never smoked or unknown [¤]	1087 (57.9%)
Most recent HIV test result	Positive	143 (7.6%)
	Negative or unknown [¤]	1733 (92.4%)
History of PrEP for HIV prevention	Yes	397 (21.2)
	No or unknown [¤]	1479 (78.8%)
Ever received any HPV vaccine	No, none	741 (39.5%)
	Yes, any	742 (39.6%)
	Don’t know/Unknown	393 (20.9%)
Age at first HPV vaccination (restricted to 742 participants self-reporting HPV vaccination) missing = 52	Mean (SD), N = 690	18.7 (4.5)
	Median (IQR), N = 690	19 (16 – 22)
	≤18 years	311 (45.1%)
	>18 years	379 (54.9%)
Age at first sex with any partner missing = 13	Mean (SD), N = 1863	16.2 (2.9)
	Median (IQR), N = 1863	16 (15 – 18)
	<16 years	665 (35.7%)

Characteristic		No. (%)[†] (N = 1876) [¤]
	>= 16 years	1198 (64.3%)
Lifetime number of sex partners of any sex missing = 62	Mean (SD), N = 1814	41.9 (63.3)
	Median (IQR), N = 1814	21 (10 – 50)
	<=5	190 (10.5%)
	6 – 10	273 (15.0%)
	11 – 20	404 (22.3%)
	>20	947 (52.2%)
Number of male sex partners in the last 12 months missing = 124	Mean (SD), N = 1752	10.5 (17.4)
	Median (IQR), N = 1752	5 (2 – 12)
	None	62 (3.5%)
	1	198 (11.3%)
	2 – 4	482 (27.5%)
	5 – 9	438 (25.0%)
	>=10	572 (32.6%)
Number of male sex partners in the last 2 months missing = 118	Mean (SD), N = 1758	3.7 (4.6)
	Median (IQR), N = 1758	2 (1-5)
	None	168 (9.6%)
	1	443 (25.2%)
	2 – 4	701 (39.9%)
	5 – 9	283 (16.1%)
	>=10	163 (9.3%)
Any new male sex partners in the last 2 months; missing = 278	Yes	1155 (72.3%)
	No	443 (27.7%)
Recently gave oral sex in the last 2 months; missing = 119	Yes	1457 (82.9%)
	No	300 (17.1%)
Recently got oral sex in the last 2 months[^]; missing = 266	Yes	1365 (84.8%)
	No	245 (15.2%)
In the last 12 months was a bottom in anal sex; missing = 128	Yes	1369 (78.3%)
	No	379 (21.7%)
In the last 12 months engaged in condomless bottom anal sex missing = 152	Always	324 (18.8%)
	Not always	1017 (59.0%)
	Not a bottom in the last 12 months	383 (22.2%)
In the last 12 months was a top in anal sex; missing = 127	Yes	1343 (76.8%)
	No	406 (23.2%)
In the last 12 months engaged in condomless top anal sex missing = 149	Always	342 (19.8%)
	Not always	975 (56.5%)
	Not a top in the last 12 months	410 (23.7%)

Characteristic		No. (%)† (N = 1876) ▫
Ever had anogenital warts^ missing = 430	Yes	90 (6.2%)
	No	1356 (93.8%)
Ever had genital herpes^ missing = 425	Yes	60 (4.1%)
	No	1391 (95.9%)
History of chlamydia or gonorrhea in the last 12 months missing = 117	Yes	538 (30.6%)
	No	1221 (69.4%)
History of syphilis in the last 12 months missing = 129	Yes	150 (8.6%)
	No	1597 (91.4%)

† Presented as number (%) unless otherwise specified

▫ N includes 1876 participants, unless otherwise specified

▫ Unknown includes whenever a participant responded to a question with “Don’t know/Not sure”

* Other includes those who reported their race as American Indian, Alaskan Native, more than one race or other

^ These data were not available for participants from one of the clinic sites in Seattle

SD = Standard deviation, IQR = Inter-quartile range, PrEP = HIV Pre-exposure prophylaxis

Table 2 –

Prevalence of HPV-type categories at various anatomic sites and concordance across anatomic sites among MSM and transgender women enrolled in the VIM study, 3 U.S. cities, 2016-2018[*]

	Any HPV type		Any high-risk HPV type[d]		Any 4-valent HPV type[e]		Any 9-valent HPV type[f]	
	no.	**%**	**no.**	**%**	**no.**	**%**	**no.**	**%**
Any site [*](n = 1876)	1336	71.2%	985	52.5%	520	27.7%	728	38.8%
Oral Site (n = 1868)	138	7.4%	58	3.1%	34	1.8%	41	2.2%
Anal Site (n = 1787)	1250	69.9%	916	51.3%	470	26.3%	667	37.3%
Genital Site (n = 701)	341	48.6%	207	29.5%	96	13.7%	136	19.4%
Both Oral & Anal sites[^](n = 1779)	116	6.5%	45	2.5%	23	1.3%	29	1.6%
No concordance[a]	74	63.8%	24	53.3%	5	21.7%	9	31.0%
Complete concordance[b]	6	5.2%	7	15.6%	8	34.8%	6	20.7%
Partial concordance[c]	36	31.0%	14	31.1%	10	43.5%	14	48.3%
Both Oral & Genital sites[^](n = 700)	24	3.4%	9	1.3%	3	0.4%	3	0.4%
No concordance[a]	16	66.7%	6	66.7%	0	0.0%	0	0.0%
Complete concordance[b]	2	8.3%	1	11.1%	1	33.3%	1	33.3%
Partial concordance[c]	6	25.0%	2	22.2%	2	66.7%	2	66.7%
Both Anal & Genital sites[^](n = 668)	273	40.9%	150	22.5%	56	8.4%	87	13.0%
No concordance[a]	77	28.2%	39	26.0%	6	10.7%	19	21.8%
Complete concordance[b]	29	10.6%	45	30.0%	39	69.6%	36	41.4%
Partial concordance[c]	167	61.2%	66	44.0%	11	19.6%	32	36.8%
All 3 sites[^](n = 667)	20	3.0%	8	1.2%	2	0.3%	3	0.4%
No concordance[a]	15	75.0%	5	62.5%	0	0.0%	1	33.3%
Complete concordance[b]	1	5.0%	1	12.5%	1	50.0%	0	0.0%
Partial concordance[c]	4	20.0%	2	25.0%	1	50.0%	2	66.7%

[*]These analyses are restricted to having an adequate sample at the site specified

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[*] HPV detected at either one of the three sites (oral, anal or genital)

[^] HPV genotype(s) detected at both all or three of the sites specified

[a] Among those with HPV detected at both or all three sites, no similar HPV genotype(s) were detected at these sites

[b] Among those with HPV detected at both or all three sites, the same HPV genotypes were detected at these sites

[c] Among those with HPV detected at both or all three sites, only some (not all) of the HPV genotypes detected were the same at these sites

[d] High risk HPV types = 16/18/31/33/35/39/45/51/52/56/58/59/66/68

[e] 4-valent HPV vaccine-types = 6/11/16/18

[f] 9-valent HPV vaccine-types = 6/11/16/18/31/33/45/52/58

Table 3.

HPV-type specific concordance in paired oral, anal and genital specimens among MSM and transgender women enrolled in the VIM study, 3 U.S. cities, 2016-2018

	No. of pairs*				PPA (%)	Kappa + ¤	(95% CI)
	+/+	+/−	−/+	−/−			
Any HPV type							
Oral/Anal	50	123	3851	61799	1.2%	0.01	0.01 - 0.01
Oral/Genital	10	31	682	25177	1.4%	0.01	0.00 - 0.02
Anal/Genital	299	1125	362	22930	16.7%	0.15	0.13 - 0.17
Any HR-HPV type							
Oral/Anal	24	39	1762	23081	1.3%	0.01	0.01 - 0.02
Oral/Genital	4	12	299	9485	1.3%	0.01	0.00 - 0.03
Anal/Genital	145	488	151	8568	18.5%	0.17	0.14 - 0.20
Any 4-valent HPV vaccine type							
Oral/Anal	18	15	561	6522	3.0%	0.03	0.01 - 0.04
Oral/Genital	3	5	104	2688	2.7%	0.02	0.00 - 0.06
Anal/Genital	53	164	51	2404	19.8%	0.18	0.13 - 0.23
HPV type 6 and/or 11							
Oral/Anal	10	9	309	3230	3.0%	0.03	0.01 −0.04
Oral/Genital	2	1	54	1343	3.5%	0.03	0.00 - 0.09
Anal/Genital	32	86	22	1196	22.9%	0.21	0.14 - 0.28
HPV type 16 and/or 18							
Oral/Anal	8	6	252	3292	3.0%	0.03	0.01 - 0.05
Oral/Genital	1	4	50	1345	1.8%	0.01	0.00 - 0.05
Anal/Genital	21	78	29	1208	16.4%	0.14	0.08 - 0.21

*Represents the number of participants multiplied by the number of HPV types evaluated per participant multiplied by the number of valid samples evaluated per participant

¤Kappa + is calculated based on the percent positive agreement

PPA = percent positive agreement

Sex Transm Dis. Author manuscript; available in PMC 2025 April 01.

Table 4.

Correlates of HPV type-specific concordance in paired oral-anal specimens among MSM and transgender women enrolled in the VIM study, 3 U.S. cities, 2016-2018

Characteristic		Crude (N= 4024)				Adjusted† (N = 3869)			
		N	n	OR	95% CI	N	n	aOR	95% CI
Age (years)	18 – 21	1091	14	Ref	0.48 - 1.89				
	22 – 26	2933	36	0.96					
Sexual orientation	Straight, bisexual or other	939	11	Ref	0.52-2.26				
	Gay/Homosexual	3085	39	1.08					
Race	Non-Hispanic White	1037	15	Ref	Ref				
	Non-Hispanic Black	771	9	0.8	0.32 - 2.02				
	Hispanic	1277	19	1.03	0.46 - 2.30				
	Other/Unknown *	939	7	0.51	0.18-1.43				
Smoking status ≠	Never smoked or unknown	2173	17	Ref	1.19-4.47	2085	17	Ref	0.96 - 3.77
	Ever smoked	1851	33	2.30		1784	32	1.91	
Most recent HIV test result	Negative or unknown	3343	38	Ref	0.70-3.46				
	Positive	681	12	1.56					
History of PrEP for HIV prevention	No or unknown	2853	36	Ref	0.45-1.99				
	Yes	1171	14	0.95					
Ever received any HPV vaccine	No or other/unknown	2402	31	Ref	0.47-1.75				
	Yes, any	1622	19	0.91					
Age at first HPV vaccination	<19	497	3	Ref	Ref				
	>=19	1011	14	2.31	0.64 - 8.33				
	Unvaccinated or unknown	2516	33	2.19	0.67-7.20				
Age at first sex with any partner ≠	<16 years	1615	29	Ref	0.26 - 0.91	1545	29	Ref	0.27 - 0.93
	≥16 years	2398	21	0.48		2324	20	0.50	
Lifetime number of sex partners of any sex ≠	≤10	662	2	0.22	0.05 - 0.93	662	2	0.30	0.07 - 1.33
	11 - 20	701	13	1.37	0.62 - 3.07	700	13	1.57	0.71 - 3.49
	≥21	2508	34	Ref	-	2507	34	Ref	Ref

Characteristic		Crude (N= 4024)				Adjusted† (N = 3869)			
		N	n	OR	95% CI	N	n	aOR	95% CI
Number of male sex partners in the last 12 months missing = 285 ▫	≤1	400	9	1.73	0.67 - 4.50				
	2-4	868	10	0.88	0.36 - 2.11				
	5-9	868	8	0.70	0.28 - 1.75				
	≥10	1603	21	Ref	Ref				
Number of male sex partners in the last 2 months; missing = 278 ▫	≤1	1089	16	Ref	Ref				
	2-4	1480	16	0.73	0.33 - 1.63				
	5-9	710	12	1.15	0.49 - 2.72				
	≥10	467	4	0.58	0.11 - 3.03				
Any new male sex partners in the last 2 months; missing = 566 ▫	No	786	15	Ref	0.30 - 1.36				
	Yes	2672	33	0.64					
Recently gave oral sex in the last 2 months; missing = 277 ▫	No	473	4	Ref	0.46 - 5.58				
	Yes	3274	44	1.60					
Recently got oral sex in the last 2 months^; missing = 553 ▫	No	516	7	Ref	0.38 - 2.76				
	Yes	2955	41	1.02					
In the last 12 months was a bottom in anal sex; missing = 302 ▫	No	420	7	Ref	0.30 - 1.83				
	Yes	3302	41	0.74					
In the last 12 months engaged in condomless bottom anal sex missing = 343 ▫	Always	541	7	Ref	Ref				
	Not always	2714	33	0.94	0.37 −2.39				
	Not a bottom	426	7	1.27	0.39 - 4.14				
In the last 12 months was a top in anal sex ≠	No	929	6	Ref	Ref	906	6	Ref	Ref
	Yes	2800	42	2.34	0.87 - 6.28	2679	41	1.97	0.72 - 5.39
	Missing**	295	2	1.05	0.20 - 5.56	284	2	0.98	0.18 - 5.31
In the last 12 months engaged in condomless top anal sex missing = 346 ▫	Always	581	8	Ref	Ref				
	Not always	2153	30	1.01	0.42 - 2.42				
	Not a top	944	6	0.46	0.14 - 1.52				
Ever had anogenital warts^ missing = 949 ▫	No	2779	32	Ref	0.25 - 5.52				
	Yes	296	4	1.18					

Characteristic		Crude (N= 4024)				Adjusted† (N = 3869)			
		N	n	OR	95% CI	N	n	aOR	95% CI
Ever had genital herpes^ missing = 937 ▫	No	2890	36	Ref	0 - 1.60				
	Yes	197	0	0					
History of chlamydia or gonorrhea in the last 12 months; missing = 274 ▫	No	2124	27	Ref	0.49 – 1.92				
	Yes	1626	20	0.97					
History of syphilis in the last 12 months missing = 321 ▫	No	3184	38	Ref	0.52 - 4.12				
	Yes	519	9	1.46					

† Adjusted for smoking status, age at first sex, lifetime number of sex partners, and being a top in anal sex in the last 12 months

▫ Missing data is presented for variables where there was more than 5% missing data

* Other includes those who reported their race as either Asian, Pacific Islander, American Indian, Alaskan Native, more than one race or other

^ Data were not available for participants from one of the clinics in Seattle

ǂ $p < 0.1$

** Missing has been included as a category for a variable that had substantial missing data (i.e., >= 5%) and was found to be significant in the univariate analysis

OR = odds ratio, aOR = adjusted odds ratio

Table 5.

Correlates of HPV type-specific concordance in paired anal-genital specimens among MSM and transgender women enrolled in the VIM study, 3 U.S. cities, 2016-2018

Characteristic		Crude (N= 1786)				Adjusted† (N = 1778)			
		N	n	OR	95% CI	N	n	aOR	95% CI
Age (years) ‡	18 – 21	423	91	Ref	0.47 - 0.93	421	91	Ref	0.44 - 0.87
	22 – 26	1363	208	0.66		1357	208	0.62	
Sexual orientation	Straight, bisexual or other	514	80	Ref	0.80-1.59				
	Gay/Homosexual	1272	219	1.13					
Race	Non-Hispanic White	854	142	Ref	-				
	Non-Hispanic Black	139	24	1.05	0.48 - 2.29				
	Hispanic	423	62	0.86	0.58 - 1.28				
	Other/Unknown *	370	71	1.19	0.84 – 1.70				
Smoking status	Never smoked or unknown	1273	215	Ref	0.68-1.36				
	Ever smoked	513	84	0.96					
Most recent HIV test result ‡	Negative or unknown	1715	279	Ref	Ref	1707	279	Ref	Ref
	Positive	71	20	2.02	0.92-4.44	71	20	2.21	0.99-4.89
History of PrEP for HIV prevention	No or unknown	1234	200	Ref	0.82-1.55				
	Yes	552	99	1.13					
Ever received any HPV vaccine	No or other/unknown	900	153	Ref	0.71-1.30				
	Yes, any	886	146	0.96					
Age at first HPV vaccination	≤ 18 years	163	20	Ref	Ref				
	> 18 years	609	104	1.47	0.74 - 2.93				
	Unvaccinated or unknown	1014	175	1.49	0.77-2.91				
Age at first sex with any partner ‡	<16 years	575	78	Ref	1.02 - 2.01	575	78	Ref	1.06-2.08
	≥16 years	1203	221	1.43		1203	221	1.48	
Lifetime number of sex partners of any sex missing = 136 ¤	≤10	203	36	1.04	0.66 - 1.66				
	11 - 20	307	43	0.79	0.53 - 1.18				
	>20	1140	195	Ref	Ref				

Characteristic		Crude (N= 1786)				Adjusted† (N = 1778)			
		N	n	OR	95% CI	N	n	aOR	95% CI
Number of male sex partners in the last 12 months missing = 323 ▫	≤1	36	1	0.14	0. 02 - 1.11				
	2-4	283	57	1.26	0.79 - 2.00				
	5-9	382	71	1.14	0.80 - 1.64				
	≥10	762	127	Ref	Ref				
Number of male sex partners in the last 2 months missing = 323 ▫	≤1	197	27	Ref	Ref				
	2-4	689	123	1.37	0.75 - 2.50				
	5-9	364	71	1.53	0.82 - 2.84				
	≥10	213	35	1.24	0.62 - 2.47				
Any new male sex partners in the last 2 months; missing = 606 ▫	No	193	24	Ref	0.82 - 3.43				
	Yes	987	190	1.68					
Recently gave oral sex in the last 2 months; missing = 323 ▫	No	99	13	Ref	0.77 - 2.67				
	Yes	1364	243	1.43					
Recently got oral sex in the last 2 months^; missing = 597 ▫	No	77	22	Ref	0.23 - 1.20				
	Yes	1112	193	0.53					
In the last 12 months was a bottom in anal sex; missing = 326 ▫	No	117	15	Ref	0.84 – 2.60				
	Yes	1343	240	1.48					
In the last 12 months engaged in condomless bottom anal sex missing = 384 ▫	Always	144	27	Ref	Ref				
	Not always	1141	196	0.90	0.56 – 1.45				
	Not a bottom	117	15	0.64	0.32 – 1.28				
In the last 12 months was a top in anal sex; missing = 334 ▫	No	282	50	Ref	0.65 - 1.49				
	Yes	1170	205	0.99					
In the last 12 months engaged in condomless top anal sex missing = 372 ▫	Always	156	20	Ref	Ref				
	Not always	976	175	1.49	0.90 - 2.44				
	Not a top	282	50	1.47	0.81 - 2.64				
Ever had anogenital warts^ missing = 534 ▫	No	1152	200	Ref	0.82 - 2.21				
	Yes	100	22	1.34					
Ever had genital herpes^ missing = 534 ▫	No	1166	209	Ref	0.37 - 1.81				
	Yes	86	13	0.82					

Characteristic		Crude (N= 1786)				Adjusted† (N = 1778)			
		N	n	OR	95% CI	N	n	aOR	95% CI
History of chlamydia or gonorrhea in the last 12 months; missing = 259 ▫	No	810	138	Ref	0.75 - 1.43				
	Yes	717	126	1.04					
History of syphilis in the last 12 months missing = 259 ▫	No	1326	226	Ref	0.67 - 1.93				
	Yes	201	38	1.13					

† Adjusted for age, most recent HIV test result, and age at first sex

▫ Missing data is presented for variables where there was more than 5% missing data

* Other includes those who reported their race as either Asian, Pacific Islander, American Indian, Alaskan Native, more than one race or other

^ Data were not available for participants from one of the clinics in Seattle

‡ $p < 0.1$

** Missing has been included as a category for a variable that had substantial missing data (i.e., >= 5%) and was found to be significant in the univariate analysis

OR = odds ratio, aOR = adjusted odds ratio

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