Predictors of Anal High-Risk HPV Infection Across Time in a Cohort of Young Adult Sexual Minority Men and Transgender Women in New York City, 2015–2020

Caleb LoSchiavo, MPH1,2, Paul A. D’Avanzo, PhD, MS1,3, Connor Emmert, MPH1, Kristen D. Krause, PhD, MPH1,4, Danielle C. Ompad, PhD5,6, Farzana Kapadia, PhD5, and Perry N. Halkitis, PhD, MS, MPH1,4,7

Abstract
Cisgender sexual minority men (SMM) and transgender women are disproportionately vulnerable to HPV-related anal cancer, but little is known about longitudinal predictors of high-risk human papillomavirus (hrHPV) infection in this population. As such, this analysis aims to identify factors associated with incident anal hrHPV infection in a diverse cohort of young SMM and transgender women. This study of HPV infection, nested within a larger cohort study, took place between October 2015 and January 2020. Participants completed a brief computer survey assessing HPV symptomatology, risk, and prevention alongside multi-site testing, in addition to biannual cohort study assessments. In the analytic sample of 137 participants, 31.6% tested positive for an anal hrHPV infection, with 27.0% and 29.9% testing positive for incident anal hrHPV infections at Visits 2 and 3, respectively. When adjusting for time between study visits, participants had significantly greater odds of incident anal hrHPV at Visit 2 if they had a concurrent HSV infection (AOR = 5.08 [1.43, 18.00]). At Visit 3, participants had significantly greater odds of incident anal hrHPV infection if they reported a greater number of sex partners in the previous month (AOR = 1.25 [1.03, 1.51]). Prevalence of cancer-causing HPV at baseline was high and many participants tested positive for additional types of anal hrHPV at subsequent visits. Risk for newly detected anal hrHPV infection was significantly associated with biological and behavioral factors. Our findings strongly indicate a need for programs to increase uptake of HPV vaccination and provide HPV-related health education for sexual and gender minorities.

Keywords
LGBTQ health, human papillomavirus, HPV, anal cancer, men who have sex with men

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Introduction
Human papillomavirus (HPV) is the most prevalent sexually transmitted infection (STI) among adults in the United States (McQuillan et al., 2017), with high-risk HPV (hrHPV) strains causing 88%–94% of anal cancer cases (Muñoz et al., 2006). Although low-risk HPV strains are not directly associated with cancer risk, they may contribute to the transmission and acquisition of hrHPV or other infections and are most frequently associated with anogenital warts (Leszczyńska et al., 2014). Although most anal HPV infections resolve spontaneously within a relatively short amount of time, some high-risk infections may persist for several years or longer (Nyström, Carvalho da Silva, Baggio, Smith, et al., 2011). Persistent, long-term hrHPV infection increases the likelihood of developing pre-cancerous conditions and cancers (Dalstein et al., 2003). This is of particular
concern for younger cohorts who, if unvaccinated against hrHPV strains, may be at greater risk of persistent infection over a longer duration as a product of their age (Nyitray, Carvalho da Silva, Baggio, Lu, et al., 2011). Younger sexual minority men (SMM) and transgender women (TW) carry a disproportionate burden of HPV infections compared with the general population (Blondeel et al., 2016; Halkitis et al., 2019). Socio-behavioral and structural factors function to increase risk of HPV acquisition and transmission in populations of young SMM and TW.

Because the overall incidence and prevalence of HPV is greater in populations of younger SMM and TW, sexual transmission rates are also higher for these populations (Blondeel et al., 2016). Younger SMM and TW are more likely than cisgender and heterosexual peers to engage in sexual behaviors that transmit HPV, including condomless sex, higher numbers of sexual partners, and early age of sexual debut (Blondeel et al., 2016; Halkitis et al., 2021; Poynten et al., 2016). Barriers to accessing adequate and culturally competent health care (e.g., HIV and STI testing, treatment, and prevention; Griffin-Tomas et al., 2019; Jaiswal et al., 2018) contribute to higher prevalence of HIV and other STIs, including herpes simplex virus types 1 and 2 (HSV-1/2), which are in turn associated with acquisition and persistence of HPV infection (Alberts et al., 2013; Finan et al., 2006; Romanelli & Hudson, 2017). HIV infection, which is disproportionately prevalent and incident among young SMM and TW, is associated with greater risk of acquiring hrHPV, and coinfection of HPV and HIV has been shown to lead to even greater risk of developing anal cancer (Chin-Hong et al., 2009; Halkitis et al., 2019; Konopnick et al., 2013; Thompson et al., 2018). Evidence also suggests that current cigarette smoking, which is more common among SMM and trans populations (Hoffman et al., 2018), is associated with both incidence and persistence of hrHPV, possibly due to the immunosuppressant effects of smoking (Schabath et al., 2012). The risk of HPV-associated anal cancer among SMM and TW is exacerbated by low rates of HPV vaccination (Agénor et al., 2022; Amiling et al., 2021; Halkitis et al., 2019; Kaniuka et al., 2022), along with limited guidelines and inconsistent evidence regarding anal cancer screening (Albuquerque et al., 2019; Apaydin et al., 2018; Ghebre et al., 2021; Pernot et al., 2018).

There are very few longitudinal cohort studies examining the association between incident and prevalent HPV and the risk of anal hrHPV infection over time, particularly in sexual and gender minority populations. Among the identified literature on anal HPV infection among SMM, most studies focus exclusively on HIV-positive SMM (Donà et al., 2022; Fuchs et al., 2016; González et al., 2013), few report on risk factors beyond HIV (Donà et al., 2022; González et al., 2013; Yunihastuti et al., 2020), and all are conducted outside the United States (Brown et al., 2018; Donà et al., 2022; Fuchs et al., 2016; González et al., 2013; Mooij et al., 2016; van Aar et al., 2013; Yunihastuti et al., 2020; Zou et al., 2015). Only one study included SMM residing in the United States, though they comprised less than 3% of the sample of heterosexual and sexual minority men across North and South America (Nyitray, Carvalho da Silva, Baggio, Smith, et al., 2011).

This analysis sought to address these gaps in the extant literature by assessing factors associated with incident anal hrHPV infection across three time points, in a cohort of young adult SMM and TW in New York City. This study provides one of the first assessments of the varying impact of anal hrHPV risk factors over time in a young, racially diverse, sexual and gender minority sample in the United States.

Methods

Study Design

The P18 Cohort Study was a prospective cohort study exploring syndemics of HIV, sexual health and behavior, mental health, and substance use among young adult SMM and TW in New York City. Further details about recruitment, enrollment, and findings of the P18 Cohort Study are available in previous publications (Halkitis et al., 2013, 2015). Only individuals enrolled in the P18 Cohort Study were eligible to participate in this sub-study of HPV and HSV. Participants provided written informed

1Center for Health, Identity, Behavior & Prevention Studies (CHIBPS), Rutgers School of Public Health, Piscataway, NJ, USA
2Department of Health Behavior, Society & Policy, Rutgers School of Public Health, Piscataway, NJ, USA
3The HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute, Columbia University, New York, NY, USA
4Department of Urban-Global Public Health, Rutgers School of Public Health, Piscataway, NJ, USA
5Department of Epidemiology, School of Global Public Health, New York University, New York City, USA
6Center for Drug Use and HIV/HCV Research (CDUHR), School of Global Public Health, New York University, New York City, USA
7Department of Biostatistics and Epidemiology, Rutgers School of Public Health, Piscataway, NJ, USA

Corresponding Author:
Dr. Perry N. Halkitis, PhD, MS, MPH, Department of Biostatistics and Epidemiology, Rutgers School of Public Health, 683 Hoes Ln W, Piscataway, NJ 08854, USA.
Email: perry.halkitis@rutgers.edu
consent to participate in the P18 Viral sub-study. All study activities were approved by the Rutgers University Biomedical and Health Sciences (RBHS) Institutional Review Board (Pro20170000863).

This sub-study of the P18 Cohort Study, known locally as the P18 Viral Study, explored factors related to HPV and HSV infection among P18 participants. At each study visit, participants completed a brief computer-based survey assessing HPV and HSV symptomatology, risk and protective factors, and testing, and underwent serologic HSV testing and multisite HPV testing. Further details about the study methodology and biological testing measures are available in previous publications (Halkitis, Valera, LoSchiavo, Goldstone, Kanztanou, Maiolatesi, Ompad, Greene and Kapadia, 2019; Jaiswal, LoSchiavo, Maiolatesi, Kapadia and Halkitis, 2020). The analytic sample for this study is limited to participants who completed the baseline visit and two follow-up visits (n = 137), and does not differ significantly from the overall study population based on key sociodemographic and health variables.

The baseline P18 Viral study visit took place between October 2015 and February 2017, with the subsequent follow-up visits taking place between April 2016 and October 2018 and March 2018 and January 2020, after which the study was indefinitely paused due to the COVID-19 pandemic. The average length of time between Baseline and Visit 2 was 13.15 months (SD = 7.14, range = 1.84–25.27 months) and between Visit 2 and Visit 3 was 23.43 months (SD = 14.39, range = 4.01–44.85 months).

The data in this analysis that are drawn from the P18 Cohort Study visits (i.e., sociodemographics, sexual behaviors, and smoking status) are concurrent with the P18 Viral Study baseline visit, but are not available longitudinally because a number of participants were retained in the P18 Viral Study following the completion of their final P18 Cohort Study visit. Data collected as part of the P18 Viral Study (i.e., HPV vaccination status, HPV status, HSV serostatus, HIV status) are available longitudinally, concurrent with each respective P18 Viral Study visit.

Measures

Sociodemographics. As part of the P18 Cohort Study, participants self-reported data on race/ethnicity, gender, sexual identity, total annual income, and highest level of education via audio computer-assisted self-interview (ACASI). Sexual identity was measured using the 6-point Kinsey scale (Kinsey et al., 1948) and dichotomized as exclusively or not exclusively homosexual.

Health Behaviors Associated With HPV Risk. As part of the P18 Cohort Study, participants self-reported data on health behaviors associated with HPV risk, via ACASI and interviewer-administered timeline follow-back (TLFB; Ristuccia et al., 2018). The ACASI included an item asking participants whether they had smoked at least part or all of a cigarette in the past 6 months. The TLFB collected data for the 30 days prior to assessment, with data on the total number of sex partners and the total number of days participants had receptive anal sex. At each P18 Viral study visit, participants completed a brief ACASI, which included two items asking whether they had ever received an HPV vaccine and how many doses they received. This was recoded to a single variable categorizing participants as unvaccinated, partially vaccinated (one or two doses), and fully vaccinated (three doses).

HIV Status. At each P18 Viral study visit, participants received rapid HIV testing using the Alere Determine HIV-1/2 Ag/Ab Combo HIV-1/2 ABS (Alere Scarborough, Inc., Scarborough, ME, USA), with confirmatory polymerase chain reaction (PCR) testing for preliminary positive results.

HSV Serostatus. Participants had blood drawn by a trained phlebotomist at each P18 Viral study visit, with testing for HSV-1/2 via the LIAISON® HSV-1 and HSV-2 Type-Specific IgG, an indirect chemiluminescence immunoassay (DiaSorin, Inc., Stillwater, MN, USA; Maters et al., 2012). For analysis, a single variable was constructed for participants who tested positive for either or both types of HSV.

HPV Status. As described in previous study publications (Halkitis, Valera, LoSchiavo, Goldstone, Kanztanou, Maiolatesi, Ompad, Greene and Kapadia, 2019), multisite HPV status was assessed at each P18 Viral study visit using self-administered Dacron anal swabs and oral mouthwash samples. The primary outcome variable for our study was detection of any anal hrHPV (16, 18, 26, 31, 33, 34, 35, 39, 45, 52, 53, 56, 58, 59, 64, 66, 67, 68, 70, 73, and 82). A variable assessing concurrent infection with any other HPV was calculated, to assess presence of any oral HPV strains (6, 16, 18, 22, 31, 32, 33, 35, 45, 49, 51, 53, 58, 60, 61, 62, 66, 68, 69, 70, 71, 72, 73, 81, 82, 83, 84, 89) or anal non-hrHPV strains (6, 11, 22, 32, 40, 41, 44, 49, 54, 55, 57, 60, 61, 62, 71, 72, 74, 76, 77, 80, 81, 83, 84, 89).

Analytic Plan

All analyses were conducted using IBM SPSS version 27. Univariate analyses were used to report frequencies of sociodemographic characteristics and HPV-related risk factors. Bivariate associations between anal hrHPV
status and sociodemographic and risk factors were assessed through chi-square tests of independence and \( t \)-tests at each visit. Utilizing variables significantly associated \( (p < .05) \) with anal hrHPV status in bivariate associations, we constructed three binary logistic regression models to identify factors associated with baseline anal hrHPV status and predictors of anal hrHPV status at Visits 2 and 3.

**Results**

**Baseline Sample Characteristics**

At baseline, participants in the sample had a mean age of 24.11 years \( (SD = 0.66) \). The sample was predominately comprised of people of color, cisgender men, and lower income participants, and was balanced in terms of sexual identity and educational attainment (Table 1).

In terms of baseline HPV-related risk factors, the majority of the sample tested HIV-negative, did not test positive for another type of HPV, tested seropositive for HSV-1/2, did not report being fully vaccinated against HPV, and reported not smoking cigarettes in the past 6 months (Table 2). Participants had an average number of 2.45 sex partners in the previous 30 days \( (SD = 2.05) \) and reported having receptive anal sex on an average of 2.57 days of the previous 30 days \( (SD = 2.04) \).

The baseline prevalence of HPV, including all types and all sites, was 55.6% \( (n = 74) \), including 53.4% \( (n = 71) \) who tested positive for at least one type of anal HPV infection and 9.5% \( (n = 13) \) who tested positive for at least one type of oral HPV infection. Regarding anal hrHPV infection, 31.6% of the sample \( (n = 42) \) tested positive for at least one hrHPV strain that was tested for at all three visits.

**Bivariate Associations With Baseline HPV Prevalence**

Few differences emerged between demographic variables and baseline anal hrHPV status (Table 1). Only education was significantly associated with HPV status; those with a high school diploma or GED or less were more likely to have anal hrHPV infection compared with those with a college or graduate degree, 41.2% versus 23.4%, \( \chi^2(1) = 4.022, p = .045 \). There was higher hrHPV prevalence among those who tested positive for either type of HSV compared with those with no HSV detected, 37.5% versus 20.5%, \( \chi^2(1) = 3.929, p = .047 \); for those who smoked cigarettes in the previous 6 months compared with those who did not, 42.9% versus 23.4%, \( \chi^2(1) = 5.694, p = .017 \); and for those with more sex partners in the previous 30 days, \( M = 3.21, SD = 2.59 \) versus \( M = 2.17, SD = 1.70, t(73) = -2.058, p = .043 \).

**Bivariate Associations With Baseline HPV and Incident Infection**

No differences in incident anal hrHPV at Visit 2 or Visit 3 were observed in association with sociodemographic variables (Table 2). At both timepoints, concurrent detection of HSV-1 and/or HSV-2 was significantly associated with incident anal hrHPV infection, Visit 2: 34.3% versus 8.3%, \( \chi^2(1) = 8.977, p = .003 \); visit 3: 35.6% versus 12.9%, \( \chi^2(1) = 5.806, p = .016 \). At Visit 2, the only other factor significantly associated with incident hrHPV infection was testing positive for any other type of HPV at the previous visit, 39.1% vs. 21.3%, \( \chi^2(1) = 4.820, p = .028 \). Anal hrHPV infection at Visit 3 was more likely among those who were HIV seropositive compared with those who were seronegative, 52.9% versus 27.1%, \( \chi^2(1) = 4.685, p = .030 \); those who tested positive for another anal hrHPV infection at the previous visit compared with those who did not, 39.6% versus 22.8%, \( \chi^2(1) = 4.081, p = .043 \); and those who reported a greater number of sex partners in the previous 30 days, \( M = 3.89, SD = 4.10 \) versus \( M = 2.18, SD = 1.84, t(112) = -3.078, p = .003 \).

**Multivariable Regression Models Predicting Anal hrHPV Status**

Binary logistic models were constructed to predict incident anal hrHPV infection at Visits 2 and 3 (Table 3). As variable selection was based on significance at the \( p < .05 \) level in bivariate analysis, all unadjusted regressions were significant. In the final adjusted model for Visit 2, when controlling for time between baseline and Visit 1, only current HSV status remained a significant predictor of incident hrHPV (adjusted odds ratio [AOR] = 5.08, 95% confidence interval [CI] = 1.43–18.00, \( p = .012 \)). In the final adjusted model for Visit 3, when controlling for time between Visits 2 and 3, the only factor that significantly predicted hrHPV incidence was the total number of unique sex partners reported at the previous visit; with each additional partner, odds of incident hrHPV infection increased by about 25% \( (AOR = 1.25, 95\% CI = 1.03–1.51, p = .025) \).

**Discussion**

The findings of our investigation corroborate previous studies regarding the high prevalence of HPV infection broadly, and oncogenic HPV infection (i.e., hrHPV) specifically, in sexual minority men (SMM) and transgender women (Baldwin et al., 2003; Cranston et al., 2019; Glick et al., 2014; Mooij et al., 2013; Nyitray, Carvalho da Silva, Baggio, Smith, et al., 2011; Singh et al., 2019; van Aar et al., 2013; Wei et al., 2021). The relatively young age of our sample—cisgender SMM and transgender women (TW) who came of age after the FDA-approved
HPV vaccination for adolescents assigned male at birth in 2009—is a call to action for more strategic development and implementation of gender-inclusive interventions to increase HPV vaccination uptake among young SMM and TW. Such messaging must also educate these communities about susceptibility to HPV infection, as studies have demonstrated low knowledge about HPV infection and prevention, including misconceptions that people assigned male at birth are not at risk for or do not need to be concerned about HPV (Jaiswal et al., 2020; Nadarzynski et al., 2014, 2017; Singh et al., 2019). This misunderstanding, alongside the results of our study, must be viewed in a historical context, whereby initial messaging from government organizations (e.g., CDC, FDA) and pharmaceutical companies (e.g., Merck) about HPV and HPV vaccination excluded people assigned

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**Table 1.** Sociodemographic and Behavioral Sample Characteristics and Associations With Baseline anal hrHPV Prevalence (n = 137).

| Characteristics                        | Total % (n) | No hrHPV % (n) | ≥1 hrHPV % (n) | p-value |
|----------------------------------------|-------------|----------------|----------------|---------|
| Total                                   | —           | 68.4 (91)      | 31.6 (42)      | —       |
| Age*                                   | 24.11 (.66) | 24.17 (.68)    | 24.04 (.62)    | .268    |
| Race/ethnicity                          |             |                |                | .192    |
| Hispanic/Latine                        | 33.3 (46)   | 57.8 (26)      | 42.2 (19)      |         |
| Black non-Hispanic                     | 26.3 (36)   | 80.0 (28)      | 20.0 (7)       |         |
| Other non-Hispanic                     | 15.3 (21)   | 66.7 (14)      | 33.3 (7)       |         |
| White non-Hispanic                     | 24.8 (34)   | 71.9 (23)      | 28.1 (9)       |         |
| Gender                                 |             |                |                | .400    |
| Cisgender man                          | 92.0 (126)  | 69.1 (85)      | 30.9 (38)      |         |
| Trans/nonbinary                        | 7.3 (10)    | 55.6 (5)       | 44.4 (4)       |         |
| Kinsey sexual identity                 |             |                |                | .878    |
| Exclusively homosexual                  | 46.0 (63)   | 68.9 (42)      | 31.1 (19)      |         |
| Not exclusively homosexual             | 53.3 (73)   | 67.6 (48)      | 32.4 (23)      |         |
| Total annual income                    |             |                |                | .933    |
| <$5,000                                | 27.0 (37)   | 63.9 (24)      | 36.1 (12)      |         |
| $5,000–24,999                          | 38.0 (52)   | 68.0 (34)      | 32.0 (16)      |         |
| $>25,000                               | 32.8 (45)   | 70.5 (31)      | 29.5 (13)      |         |
| Educational attainment                 |             |                |                | .045    |
| High school/GED or less                | 49.6 (68)   | 58.8 (41)      | 41.2 (27)      |         |
| College/graduate degree                | 49.6 (68)   | 76.6 (49)      | 23.4 (15)      |         |
| HIV status                             |             |                |                | .574    |
| Negative                               | 90.5 (124)  | 69.2 (83)      | 30.3 (37)      |         |
| Positive                               | 9.5 (13)    | 61.5 (8)       | 38.5 (5)       |         |
| Co-infection with HSV                  |             |                |                | .047    |
| No HSV detected                        | 33.8 (46)   | 79.5 (35)      | 20.5 (9)       |         |
| HSV-1 and/or HSV-2                     | 66.2 (90)   | 62.5 (55)      | 37.5 (33)      |         |
| Sexual behavior, past 30 days*         |             |                |                | .043    |
| Total number of sex partners           | 2.45 (2.05) | 2.17 (1.70)    | 3.21 (2.59)    |         |
| Total days anal sex, receptive         | 2.57 (2.04) | 2.33 (2.08)    | 2.95 (2.01)    | .333    |
| HPV vaccination status                 |             |                |                | .672    |
| Unvaccinated (0 shots)                 | 39.4 (54)   | 71.2 (37)      | 28.8 (15)      |         |
| Incomplete (1 or 2 shots)              | 29.9 (41)   | 65.9 (27)      | 34.1 (14)      |         |
| Complete (3 shots)                     | 19.0 (26)   | 76.0 (19)      | 24.0 (6)       |         |
| Missing—Unsure if vaccinated           | 11.7 (16)   | —              | —              |         |
| Smoked cigarettes, past 6 months       |             |                |                | .017    |
| No                                     | 58.4 (80)   | 76.6 (59)      | 23.4 (18)      |         |
| Yes                                    | 41.6 (57)   | 57.1 (32)      | 42.9 (24)      |         |

Note. HPV = human papillomavirus; hrHPV = high-risk human papillomavirus.

*Reported as M (SD).
Table 2. Sociodemographic and Behavioral Correlates of Incident Anal hrHPV at Visits 2 and 3 (n = 137).

| Characteristics                              | Visit 2          | Visit 3          |
|----------------------------------------------|------------------|------------------|
|                                              | % (n)            | % (n)            | p-value | % (n)            | % (n)            | p-value |
| Total                                        | 72.6 (98)        | 27.4 (37)        | —       | 69.6 (94)        | 30.4 (41)        | —       |
| Age*                                         | 24.07 (0.65)     | 24.24 (0.69)     | .198    | 25.19 (0.81)     | 25.22 (0.71)     | .846    |
| Race/ethnicity                               |                  |                  |         |                  |                  |         |
| Hispanic/Latine                              | 77.8 (35)        | 22.2 (10)        |         | 64.4 (29)        | 35.6 (16)        |         |
| Black non-Hispanic                           | 62.9 (22)        | 37.1 (13)        |         | 57.1 (20)        | 42.9 (15)        |         |
| Other non-Hispanic                           | 71.4 (15)        | 28.6 (6)         |         | 85.7 (18)        | 14.3 (3)         |         |
| White non-Hispanic                           | 76.5 (26)        | 23.5 (8)         |         | 79.4 (27)        | 20.6 (7)         |         |
| Gender                                       |                  |                  | .708    |                  |                  | .349    |
| Cisgender man                                | 72.0 (90)        | 28.0 (35)        |         | 71.3 (87)        | 28.7 (35)        |         |
| Trans/nonbinary                              | 77.8 (7)         | 22.2 (2)         |         | 58.3 (7)         | 41.7 (5)         |         |
| Kinsey sexual identity                       |                  |                  | .466    |                  |                  | .941    |
| Exclusively homosexual                       | 69.4 (43)        | 30.6 (19)        |         | 70.4 (50)        | 29.6 (21)        |         |
| Not exclusively homosexual                   | 75. (54)         | 25.0 (18)        |         | 69.8 (44)        | 30.2 (19)        |         |
| Total annual income                          |                  |                  | .382    |                  |                  | .271    |
| <$5,000                                      | 81.1 (30)        | 18.9 (7)         |         | 64.0 (16)        | 36.0 (9)         |         |
| $5,000–$24,999                               | 68.0 (34)        | 32.0 (16)        |         | 64.2 (34)        | 35.8 (19)        |         |
| ≥$25,000                                     | 71.1 (32)        | 28.9 (13)        |         | 77.4 (41)        | 22.6 (12)        |         |
| Educational attainment                       |                  |                  | .492    |                  |                  | .852    |
| High school/GED or less                      | 69.7 (46)        | 30.3 (20)        |         | 69.4 (43)        | 30.6 (19)        |         |
| College/graduate degree                      | 75.0 (51)        | 25.0 (17)        |         | 70.8 (51)        | 29.2 (21)        |         |
| Current HIV status                           |                  |                  | .436    |                  |                  | .030    |
| Negative                                     | 73.7 (87)        | 26.3 (31)        |         | 72.9 (86)        | 27.1 (32)        |         |
| Positive                                     | 64.7 (11)        | 35.3 (6)         |         | 47.1 (8)         | 52.9 (9)         |         |
| Current HSV status                           |                  |                  | .003    |                  |                  | .016    |
| No HSV detected                              | 91.7 (33)        | 8.3 (3)          |         | 87.1 (27)        | 12.9 (4)         |         |
| HSV-1 and/or HSV-2                           | 65.7 (65)        | 34.3 (34)        |         | 64.4 (67)        | 35.6 (37)        |         |
| Anal hrHPV at previous visit                 |                  |                  | .656    |                  |                  | .043    |
| No                                          | 74.4 (67)        | 25.6 (23)        |         | 77.2 (61)        | 22.8 (18)        |         |
| Yes                                         | 70.7 (29)        | 29.3 (12)        |         | 60.4 (29)        | 39.6 (19)        |         |
| Any other HPV at previous visit              |                  |                  | .028    |                  |                  | .162    |
| No                                          | 78.7 (70)        | 21.3 (19)        |         | 74.4 (58)        | 25.6 (20)        |         |
| Yes                                         | 60.9 (28)        | 39.1 (18)        |         | 63.2 (36)        | 36.8 (21)        |         |
| Sexual behavior, past 30 days*              |                  |                  |         |                  |                  |         |
| Total number of sex partners                 | 2.36 (1.91)      | 2.68 (2.40)      | .532    | 2.18 (1.84)      | 3.89 (4.10)      | .003    |
| Total days anal sex, receptive               | 2.57 (2.01)      | 2.69 (2.21)      | .856    | 3.62 (3.12)      | 3.81 (3.17)      | .854    |
| HPV vaccination status                       |                  |                  | .549    |                  |                  | .620    |
| Unvaccinated (0 shots)                       | 71.7 (38)        | 28.3 (15)        |         | 63.6 (28)        | 36.4 (16)        |         |
| Incomplete (1 or 2 shots)                    | 80.0 (32)        | 20.0 (8)         |         | 67.4 (31)        | 32.6 (15)        |         |
| Complete (3 shots)                           | 69.2 (18)        | 30.8 (8)         |         | 73.7 (28)        | 26.3 (10)        |         |
| Smoked cigarettes, past 6 months             |                  |                  | .892    |                  |                  | .382    |
| No                                          | 72.2 (57)        | 27.8 (22)        |         | 73.1 (57)        | 26.9 (21)        |         |
| Yes                                         | 73.2 (41)        | 26.8 (15)        |         | 66.1 (37)        | 33.9 (19)        |         |

Note. HPV = human papillomavirus; hrHPV = high-risk human papillomavirus.

*Reported as M (SD).
Table 3. Unadjusted and Adjusted Binary Logistic Regressions Predicting Incident Anal hrHPV at Visits 2 and 3 (n = 137).

| Characteristics                      | OR   | 95% CI       | p-value | AOR   | 95% CI       | p-value |
|--------------------------------------|------|--------------|---------|-------|--------------|---------|
| **Visit 2**                           |      |              |         |       |              |         |
| Current HSV status                   |      |              |         |       |              |         |
| Negative                             | 1.00 | [1.00, 1.00] |         | 1.00  | [1.00, 1.00] |         |
| Positive                             | 5.75 | [1.64, 20.13]| **.006**| 5.08  | [1.43, 18.00]| **.012**|
| Any other HPV at previous visit      |      |              |         |       |              |         |
| No                                   | 1.00 | [1.00, 1.00] |         | 1.00  | [1.00, 1.00] |         |
| Yes                                  | 2.37 | [1.09, 5.16] | **.030**| 1.91  | [0.82, 4.42] | .133    |
| **Visit 3**                           |      |              |         |       |              |         |
| Current HIV status                   |      |              |         |       |              |         |
| Negative                             | 1.00 | [1.00, 1.00] |         | 1.00  | [1.00, 1.00] |         |
| Positive                             | 3.02 | [1.07, 8.51] | **.036**| 1.63  | [0.43, 6.07] | .469    |
| Current HSV status                   |      |              |         |       |              |         |
| Negative                             | 1.00 | [1.00, 1.00] |         | 1.00  | [1.00, 1.00] |         |
| Positive                             | 3.73 | [1.21, 11.47]| **.022**| 2.78  | [0.71, 10.97]| .144    |
| Anal hrHPV at previous visit         |      |              |         |       |              |         |
| No                                   | 1.00 | [1.00, 1.00] |         | 1.00  | [1.00, 1.00] |         |
| Yes                                  | 2.22 | [1.02, 4.85] | **.046**| 1.63  | [0.65, 4.10] | .301    |
| Sexual behavior, past 30 days        |      |              |         |       |              |         |
| Total no. of sex partners            | 1.22 | [1.04, 1.42] | **.013**| 1.25  | [1.03, 1.51] | **.025**|

Note. Adjusted regressions are adjusted for time since previous visit. OR = odds ratio; AOR = adjusted odds ratio; HPV = human papillomavirus; hrHPV = high-risk human papillomavirus.

We detected ongoing hrHPV infection in our sample across three time points, spanning an average of 2 years. The consistent presence of the pathogen in the anal canal, manifesting through both persistent and incident infections, may suggest a need for screening and potential treatments of SMM and TW engaging in anal sexual behavior. Although there are no recommendations for routine screening for anal HPV, as there are for cervical HPV infection, the Infectious Diseases Society of America (IDSA) suggests there is moderate quality evidence supporting anal HPV testing for men who have sex with men, women with a history of receptive anal sex or abnormal cervical Pap test results, and anyone living with HIV who presents with HPV symptoms such as anogenital warts (Aberg et al., 2014). We detected that prior HPV infection, including anal hrHPV and other types or sites, predicted future HPV infection. The presence of multiple strains of HPV, and particularly of hrHPV, supports the need for more research on effective screening methods and guidelines for early detection of HPV-associated anal cancers.

Several other factors were associated with hrHPV infection in our sample. Specifically, concurrent HSV-1/2 seropositivity was associated with baseline HPV prevalence and incident HPV infection at Visits 2 and 3, consistent with existing literature on the relationship between HSV and HPV (Guidry & Scott, 2017). Other studies have also noted the high prevalence of bacterial and viral STIs among SMM and TW (Chuerduangphui et al., 2018; Hernandez et al., 2017; Quinn et al., 2012; Van Gerwen et al., 2020), which is consistently demonstrated to have a strong association with HPV infection (Dempsey, 2008; Mboumba Bouassa et al., 2018; Müller et al., 2016; Soares et al., 2014), including in previous studies from the P18 cohort (Halkitis, Valera, LoSchiavo, Goldstone, Kanzianenou, Maiolatesi, Ompad, Greene and Kapadia, 2019). Second, we detected that reporting higher numbers of sexual partners was associated with hrHPV at our final time point of assessment. This finding illuminates the heightened risk for acquiring infections, including but not limited to HPV, as more frequent engagement in sexual behavior provides more opportunities for STI exposure, as substantiated by a robust literature (Castillo et al., 2015; Guimarães et al., 2011, 2018; Marcus et al., 2015; Nyitray, Carvalho da Silva, Baggio, Lu, et al., 2011; Slurink et al., 2020; Yu et al., 2013).

Our sample included a majority of participants who, despite their year of birth and the availability of the first generation quadrivalent HPV vaccine for adolescents
assigned male at birth in 2009, were either unvaccinated or incompletely vaccinated for HPV, consistent with the findings of other studies in this population (Bednarczyk et al., 2017; Gorbach et al., 2017; Halkitis et al., 2019; Loreta et al., 2019; McClung et al., 2020; Meites et al., 2022; Reiter et al., 2015; Singh et al., 2019). These data however are limited by the self-reported nature of this variable; though other studies have demonstrated the accuracy of self-reported HPV vaccination status (Oliveira et al., 2020; Thomas et al., 2018), we noted that many participants reported their vaccination status inconsistently across the three study visits. Although we did not detect an association between vaccination and hrHPV infection, the lack of vaccine initiation and completion continues to create a risk state for SMM and TW across their sexual lifespans. Low rates of vaccination among SMM and TW may be attributed to population-specific factors such as limited knowledge within the community; limited communication from health care providers about sexual behaviors, sexual orientation, and HPV vaccination; and low perceived threat of HPV, including gendered misconceptions about HPV risk (Gerend et al., 2019; Jaiswal et al., 2020; Meites et al., 2022; Nadarzynski et al., 2014; Wheldon et al., 2018), alongside overall lagging rates of vaccination among people assigned male at birth (Chen et al., 2021; Preston & Darrow, 2019). Efforts to vaccinate members of this population must be ongoing, especially in light of the upper age range being expanded to 45 (with shared clinical decision-making) and findings that a two-dose series of the nonavalent HPV vaccine can confer sufficient protection if initiated at an early age, prior to 15 (Meites et al., 2019).

**Limitations**

The findings of our study are robust in that they point to hrHPV infection in SMM and TW across time. First, our data may present an undercount of incident infections—while our measure of incident infections accounted for those who tested positive for a strain of HPV that was not detected at their previous visit (e.g., HPV-16 was detected at visit 2 but not at visit 1), it is possible that infections designated as prevalence (e.g., HPV-16 was detected at baseline and visit 2) may have been an incident infection of a strain that had previously cleared. As clearance of HPV infection typically takes place within 6 months to a year (Giuliano et al., 2008), the length of time between visits allows for this possibility. However, the high incidence of infection across timepoints and its association with both biological and behavioral determinants remains noteworthy. Future studies should consider using more frequent and more consistently-timed visits, which will also allow for more accurate categorization of incident infections.

Second, we recognize that the self-selected nature of our sample drawn from an ongoing cohort study in a large, urban center may inhibit generalizability. However, the sample was diverse in terms of numerous characteristics and representative of young SMM and TW in this region. Regarding generalization to the United States more broadly, the high prevalence of hrHPV and low rates of vaccination in this sample from New York City, where access to LGBTQ-competent care is more widely available than in other areas, suggests that rates of infection and prevention uptake may be worse in other regions with more limited access to culturally competent care. This underscores the importance of ensuring nationwide access to providers who are knowledgeable in attending to the unique sexual health needs of SMM and TW.

Third, while our investigation also gathered information on non-oncogenic strains of HPV, we chose to focus on high-risk anal HPV given its association with anal cancer, and as such the risk factors and predictors of infection may differ for other types or sites of infection. Future studies should explore factors associated with a broader range of infection sites, including oncogenic and non-oncogenic oral and genital HPV infections, and should seek to identify whether there are differences in risk factors based on site and type of HPV infection.

Finally, our study included both cisgender and transgender participants who were assigned male at birth, but does not contain a sufficient number of trans participants to provide robust data about HPV within this population. Although it is important to, whenever possible, treat SMM and TW as discrete populations, acknowledging the distinct social and structural contexts that influence their health and health behaviors (Poteat et al., 2021), we felt it was important to respect their ongoing participation in our cohort study by retaining them in our analysis.

**Conclusions**

In summary, hrHPV infection in young SMM and TW represents a significant issue of concern, with high incidence indicating greater risk for HPV-associated anal cancer. These findings must be contextualized within the ongoing HIV epidemic and the biological and behavioral drivers of HPV infection that increase risk for acquisition of other STIs and, more broadly, undermine the health and well-being of young SMM and TW. Primary and secondary methods of HPV-related cancer prevention were initially focused on cervical cancer, which has led to significant gaps in knowledge among both health care providers and the general population, low uptake of vaccination for people who were assigned male at birth, and limited understanding of appropriate screening methods for anal cancer (Amiling et al., 2021; Apaydin et al., 2018; Daley et al., 2017; Ghebre et al., 2021; Jaiswal et al., 2020; Meites et al., 2017; Gorbach et al., 2017; Halkitis et al., 2019; Loreta et al., 2019; McClung et al., 2020; Meites et al., 2022; Reiter et al., 2015; Singh et al., 2019).
et al., 2020). Efforts to develop evidence-based screening guidelines and increase vaccine uptake among SMM and TW, alongside education for health care providers to deliver this care in affirming and culturally-competent ways, must be scaled up substantially to address the burden that HPV infection can create in the lives of these individuals.

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ORCID iD

Caleb LoSchiavo https://orcid.org/0000-0001-7631-6405

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