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Prevalence and Risk Factors for HPV in HIV-Positive Young Women Receiving Their First HPV Vaccination

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Abstract

Background—The objectives of this study were to describe the prevalence and risk factors for HPV infection among HIV-infected young women receiving their first quadrivalent HPV (HPV-6, -11, -16, -18) vaccine dose.

Methods—We recruited 16-23 year-old women from 14 sites for an HPV vaccine trial. At the first visit they completed a questionnaire and were tested for cervicovaginal HPV DNA (41 types) and HPV serology (4 vaccine types). Factors associated with any HPV, type-specific HPV, and high-risk (cancer-associated) HPV infection were identified using univariate and multivariable logistic regression.

Results—The mean age of participants (N=99) was 21.4 years, 30.3% were on antiretroviral therapy, 74.7% were positive for > 1 HPV DNA type, 53.5% for > 1 high-risk type, 12.1% for HPV-16, and 5.1% for HPV-18. Most were HPV DNA negative and seronegative for HPV-16 (55.6%) and HPV-18 (73.7%); 45.5% were HPV DNA and seronegative for both HPV-16 and -18. Three variables were associated with high-risk HPV DNA in multivariable analysis: non-Hispanic Black vs. Hispanic ethnicity (AOR 7.06, 95% CI 1.63-30.5), HIV viral load > 400 vs. < 400

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copies/mL (AOR 3.47, 95% CI 1.28-9.43), and frequency of vaginal sex in the past 90 days (AOR 5.82, 95% CI 1.30-26.11 for > 6 vs. 0 times).

Conclusions—The prevalence of > 1 HPV type was high in these young women, demonstrating the importance of vaccinating prior to sexual initiation. However, most were HPV DNA negative and seronegative for high-risk, vaccine-type HPV infection, supporting vaccination of sexually experienced HIV-positive young women.

Keywords

human papillomavirus; vaccine; epidemiology; women; HIV

Introduction

Human papillomavirus (HPV) is the most prevalent sexually transmitted infection (STI) globally, and infection with high-risk (cancer-associated) types is causally associated with the development of cervical and other anogenital cancers.¹ HIV-infected (HIV+) women have relatively high rates of HPV infection,²⁻⁴ and compared to HIV-negative (HIV-) women, are more likely to have multiple HPV types and persistent infections.⁴ Recent studies document a rapid rise in HPV-positivity after HIV seroconversion.⁵ HIV+ women are also at higher risk than HIV-women for cervical cancer precursors such as cervical intraepithelial neoplasia (CIN)⁶ and for invasive cervical cancer (ICC).^{7,8} Furthermore, CIN and ICC may be more aggressive and less responsive to treatment in HIV+ compared to HIV-women.^{9,10} Treatment of CIN in HIV+ women often fails, and even after initially successful treatment of CIN in HIV+ women, the lesions frequently recur.¹¹⁻¹³ Finally, oral and anogenital condylomata are more common and often more severe in HIV+ compared to HIV-individuals.^{14,15}

Two prophylactic HPV vaccines have been licensed that have the potential to substantially decrease CIN and ICC among HIV+ individuals: a bivalent (HPV-16, -18) vaccine that prevents infection with the types that cause approximately 70% of cervical cancers,¹⁶ and a quadrivalent (HPV-6, -11, -16, -18) vaccine that also targets the HPV types that cause condylomata. In HIV-individuals, HPV vaccines are highly effective in preventing vaccine-type HPV infection.^{17,18} Early adolescents are targeted for HPV vaccination,¹⁹ as they are less likely to have initiated sexual intercourse than older women and clinical trials have demonstrated that HPV vaccines are most effective in preventing type-specific HPV infection if given to women who have not been exposed to those HPV types at the time of vaccination; i.e. those who are HPV DNA and seronegative for vaccine-type HPV.²⁰

Although HPV vaccines are recommended for adolescents in many countries,¹⁹ the clinical benefit of vaccinating HIV+ adolescents is uncertain. First, the immunologic response to vaccination may not be as high in HIV+ vs. HIV-adolescents.²¹ Second, HIV+ adolescents may be at higher risk for pre-existing HPV infection at the time of vaccination, which could limit the health benefits of vaccination. Adolescents who were infected with HIV behaviorally may be at higher risk for HPV infection because of sexual behaviors, and both behaviorally and perinatally infected adolescents may be at higher risk for HPV infection and persistence because of immunologic compromise. Finally, there might be important differences in HPV prevalence and viral characteristics, as well as vaccine immunogenicity and tolerability, among those with HIV infection who are untreated compared to those who have demonstrated immune reconstitution with antiretroviral therapy (ART).

Information about the epidemiology of and risk factors for HPV in HIV+ adolescents at the time of vaccination is important for 1) understanding the potential impact of vaccination on HPV acquisition and HPV-related disease, and 2) informing vaccination guidelines in this

population. The epidemiology of HPV infection in HIV+ adult women has been well-described,^{2,4,22} but little is known about rates of type-specific HPV DNA and HPV seropositivity or factors associated with infection in HIV+ adolescent and young adult women.²³ Thus, we conducted a study with the following aims: 1) to describe rates of type-specific HPV infection (for 41 anogenital HPV types) and HPV seropositivity (for the four vaccine-type HPVs) among HIV+ adolescent and young adult women receiving their first quadrivalent HPV vaccination, and 2) to determine which demographic, virologic, immunologic and behavioral factors were associated with HPV infection among these young women.

Methods

Data for this study were collected at the baseline visit of a phase II, open-label, multi-center trial, conducted from 07/2008-02/2011, to evaluate the immunogenicity and safety of an HPV-6, -11, -16, -18 vaccine (Gardasil®) in 16- to 23-year-old HIV-infected young women (N=99). All young women had acquired HIV through sexual behaviors except one, who acquired HIV through a blood transfusion in Africa. Two groups of young women were recruited. Participants in group A were either naïve to ART or had not received ART for at least the six months prior to study entry. Participants in group B had received ART for at least six months at the time of study entry. The trial was conducted by the Adolescent Medicine Trials Network (ATN) for HIV/AIDS Interventions, and young women were recruited from 14 sites across the U.S. and Puerto Rico. The Institutional Review Board for each participating site approved the study, and written informed consent was obtained from all participants > 18 years of age or from the parents or guardians of participants < 18 years of age.

The protocol specified that three doses of the vaccine be administered at day 0, week 8, and week 24. At baseline, participants completed a confidential, paper-and-pencil questionnaire assessing sociodemographic characteristics, knowledge, risk perceptions and sexual behaviors. Participants then underwent testing for *Trichomonas vaginalis*, gonorrhea, and Chlamydia per site protocol, and for peripheral blood CD4+ T cell count (CD4), plasma HIV-1 RNA viral load (HIV VL), and serology for HPV-6, -11, -16, and -18. Serology was measured using a competitive Luminex-based immunoassay (cLIA; developed by Merck Research Laboratories)²⁴ A clinician used a sterile Dacron swab to collect cervicovaginal samples for HPV DNA testing using a standardized method, during a speculum exam or using a blind vaginal swab. Swabs were placed in a vial prefilled with PreservCyt solution (Cytoc) and frozen for shipment. They were tested for HPV DNA using an MY09/11 assay and dot blot method to detect 41 HPV types.²⁵ Samples were tested for beta-globin to assess adequacy of DNA amplification; six negative controls were also included.

The main outcome variables were infection with at least one HPV type, HPV 16 and/or 18, HPV 6, 11, 16, and/or 18, and at least one high-risk HPV type (positive for HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and/or 68)²⁶. Other outcome measures of interest included type-specific HPV infection, multiple HPV types (positive for two or more HPV DNA types), number of HPV types, HPV viral load (measured on a scale of 1 to 5 as previously described^{25,27}), and HPV-6, -11, -16, and -18 serology.

Independent variables included demographic and baseline characteristics, knowledge about HPV and HPV vaccines (assessed using a 12-item true/false knowledge scale;²⁸⁻³⁰ results described previously³¹), sexual behaviors, and STI diagnosis at the first vaccine visit. Univariate regression analyses were used to examine whether independent variables (demographic characteristics, CD4, HIV VL, HPV knowledge, sexual behaviors, and STI diagnosis) were associated with HPV positivity, defined as infection with one or more of the

following: 1) > 1 HPV type, 2) HPV types 16 and/or 18, 3) HPV types 6, 11, 16, and/or 18, and 4) > 1 high-risk HPV type. For multivariable analyses, data from groups A and B were combined because the two groups were similar in terms of almost all baseline variables and group status was not associated with any of the four outcome variables. Variables associated with outcomes at a p value of < 0.20 were eligible for multivariable models; CD4 T-cell count and lifetime number of sexual partners were also forced into the models given their clinical significance. Stepwise and backward model selection procedures were used, and variables with a p value of < 0.05 were retained in the final models.

Results

The mean age of participants was 21.4 years, 79 (79.8%) were Non-Hispanic Black, 4 (4.0%) were Non-Hispanic White, and 16 (16.2%) were Hispanic. Thirty (30.3%) participants were on an ART regimen, 98 (99%) had CD4+ counts > 200, 40 (40.4%) had an HIV VL < 400 copies/mL, and mean length of HIV infection was 2.8 years. Thirty-six participants (37.5%) reported > 10 lifetime male sexual partners, 16 (16.3%) reported two or more male sexual partners in the previous 90 days, 72 (72.7%) had used a condom at last sexual intercourse, and 13 (13.1%) were positive for an STI (*Trichomonas vaginalis*, gonorrhea, or Chlamydia) at baseline. Subjects in group B were significantly more likely than those in group A to have an HIV VL < 400 copies/mL ($p < 0.0001$); otherwise, the groups did not differ significantly in terms of demographic characteristics, immunologic factors, or behaviors. All cervicovaginal samples that were HPV-negative were positive for beta-globin, indicating adequacy of DNA amplification.

The distribution of HPV types is shown in Table 1: 74.7% of participants were positive for > 1 HPV type, 16.2% for HPV 16 and/or 18, 18.2% for HPV 6, 11, 16, and/or 18, 53.5% for > 1 high-risk type, 12.1% for HPV-16, 5.1% for HPV-18, 2.0% for HPV-6, and 1.0% for HPV-11. The mean number of types among subjects who were HPV positive was 3.1 (standard deviation 2.1, median 3.0, range 1-9). HPV-related outcome measures did not differ significantly for group A compared to group B (data not shown) except for two of the individual HPV types for which prevalence was lower in group A than group B: HPV-32 ($P = 0.03$) and HPV-42 ($P = 0.03$).

HPV DNA and serology results are shown in Table 2. Only 1.0% of subjects were both HPV DNA and HPV seropositive for one of the following: HPV-6, -11, or -18; 9.1% were DNA and seropositive for HPV-16. Between 42.4% and 73.7% were both HPV DNA negative and HPV seronegative for HPV-6, -11, -16, and -18, 45.5% were DNA and seronegative for HPV-16 and -18, and 23.2% were DNA and seronegative for all four vaccine types.

The results of univariate analyses examining associations between baseline characteristics and HPV infection are shown in Table 3. Frequency of vaginal sexual intercourse with a male partner in the past 90 days and HIV VL were associated at $p < .20$ with any HPV infection and therefore eligible for inclusion in the multivariable model. Race/ethnicity, knowledge about HPV and condom use at last sexual intercourse were associated with HPV-16 and/or -18 infection, and race/ethnicity and knowledge about HPV were associated with HPV-6, -11, -16, and/or -18 infection. Variables associated with high-risk HPV were race/ethnicity, CD4, HIV VL, number of male partners in the past 90 days, frequency of vaginal sexual intercourse with a male partner in the past 90 days, and number of male partners with whom the participant had unprotected sex within the past 90 days.

In the three multivariable models evaluating factors associated with any HPV infection, HPV-16 and/or -18 infection, and HPV-6, -11, -16, and/or -18 infection, no independent predictors were identified. In the model evaluating factors associated with high-risk HPV

infection, three variables were retained: race/ethnicity, HIV VL, and frequency of vaginal sexual intercourse in the past 90 days (Table 4). Non-Hispanic Black participants had approximately 7 times the odds of high-risk HPV infection compared to Hispanic participants, participants who had an HIV VL > 400 copies/mL had approximately 3.5 times the odds of infection compared to those with a lower HIV VL, and participants who reported 6 or more (vs. 0) episodes of vaginal sexual intercourse over the prior 90 days had almost 6 times the odds of high-risk HPV.

Discussion

In this study, we determined rates of type-specific HPV infection for 41 HPV types, HPV serology for the four vaccine types, and factors associated with HPV infection in HIV+ adolescent and young adult women receiving the first quadrivalent HPV vaccine dose. The effectiveness of vaccinating HIV+ young women is uncertain in the absence of information about HPV exposure at the time of vaccination, as young women who have been infected with vaccine-type HPV at the time of vaccination are not expected to derive as much clinical benefit from vaccination as those who were not infected. HIV+ young women may be at relatively high risk for previous or current HPV infection because of their sexual behaviors, and may be at a higher risk for persistent HPV infection and progression to CIN because of their compromised immune status.

We found that the prevalence of overall and type-specific HPV, including HPV-16 and -18, were high in this sample. Almost 75% of participants were positive for at least one HPV type, 12% were positive for HPV-16, and 5% were positive for HPV-18. In comparison, the overall prevalence of HPV in a representative sample of U.S. women 14 to 59 years of age was 24.5% among 14- to 19-year-olds and 44.8% among 20- to 24-year-olds.³² HPV-16 was detected in only 1.5% of all women and HPV-18 in 0.8% of all women. Interestingly, however, the rates of HPV found in our study are comparable to those found in several other studies that enrolled HIV-negative adolescent and young adult women who were similar to the young women in our study in terms of demographic characteristics.^{30,33,34} For example, in a previous study of predominantly low-income, African-American, HIV-negative but at-risk young women 13-26 years of age receiving primary care in an urban, hospital-based teen health center, 68% were HPV-positive, 17% HPV-16 positive, and 12% HPV-18 positive.³⁰ The similarities in rates of HPV likely reflect similar demographic characteristics (e.g., high poverty rates) and sexual behaviors that are established risk factors for HPV.^{32,35-37} In contrast, several studies involving adult women and one involving adolescent women have demonstrated substantially higher rates of HPV in HIV+ compared to HIV-women.^{2-4,22} These higher HPV rates could reflect riskier sexual behaviors, higher incident detection of HPV infection, higher rates of HPV persistence, or more common reactivation of previously acquired latent HPV.⁴ The relatively high HPV rates in HIV+ women could also reflect alterations in viral-host interactions that increase the risk of HPV acquisition or persistence in HIV-infected individuals.^{3,38,39}

The high prevalence of overall and type-specific HPV identified in our participants has implications for vaccination recommendations in HIV+ young women. First, it points to the importance of vaccination prior to acquisition of HPV, when vaccination is most effective. Our findings provide compelling support for recommendations to target vaccination to girls 11-12 years of age or younger, when they are unlikely to have initiated sexual intercourse.^{40,41} Second, the findings support the importance of continued cervical cancer screening after vaccination, whether by Papanicolaou or HPV testing, to prevent cervical cancer in those young women who were already infected at the time of vaccination. HIV+ women, compared to HIV-women, may have a higher incidence, persistence, or recurrence

of HPV-related anogenital dysplasia and cancer,^{4,42-45} or develop dysplasias or cancers that are more aggressive and less responsive to treatment.^{9,13}

Although the prevalence of overall and type-specific HPV was relatively high compared to the general population, a significant proportion were negative for vaccine-type HPVs at the time of vaccination: 89% were negative for HPV-16 and 95% were negative for HPV-18. Furthermore, more than 50% of participants were both HPV DNA negative and seronegative for HPV-16, and almost 75% for HPV-18. These results indicate that a substantial proportion of these HIV+ young women had neither evidence of current HPV-16/-18 infection nor past exposure, and would therefore likely benefit from vaccination, if the HPV vaccine is demonstrated to be effective at preventing HPV infection and disease in HIV+ individuals.

Identification of factors associated with HPV in HIV+ young women may be helpful in guiding the design of HPV prevention strategies or vaccination guidelines in this population. Even in this relatively homogeneous population in terms of their high levels of exposure to genital HPV, three variables were significantly associated with high-risk HPV: non-Hispanic Black ethnicity, HIV VL, and frequency of vaginal intercourse in the past 90 days. The presence of HIV-1 viremia, but not CD4 cell count, was associated with high-risk HPV detection: associations between HIV VL, CD4 and HPV infection have been inconsistent in previous studies. In a study of 1778 HIV+ adult women in the Women's Interagency HIV Study (WIHS), CD4 was inversely associated with HPV and HIV VL positively associated with HPV ($p < 0001$).² Overall, women with highest prevalence of HPV were those with a $CD4 < 200/mm^3$, regardless of HIV VL. Among women with $CD4 > 200/mm^3$, a higher prevalence of HPV was found among those women with a higher HIV VL ($> 20,000$ copies/mL) compared to a lower HIV VL ($< 20,000$ copies/mL). The lowest prevalence of HPV was found in women with a $CD4 > 500/mm^3$ and HIV VL $< 4,000$ copies/mL. This interaction was also evident in a subsequent prospective analysis of WIHS data, in which investigators found that the interaction between CD4 and HIV VL was significantly associated with both prevalent and incident HPV infection. A high HIV VL was strongly associated with prevalent and incident HPV in women with a high (> 500 cells/ mm^3) or moderate (200-500 cells/ mm^3) CD4, but not a low CD4 ($< 50/mm^3$ for prevalent HPV, < 200 cells/ mm^3 for incident HPV).⁴ The investigators also found that CD4/HIV VL strata were more strongly associated with incident HPV than persistent HPV in more immune compromised HIV+ women. In contrast to the WIHS analyses, several studies of HIV+ adults demonstrated no association between CD4 and HPV detection.^{46,47} It is possible that the relatively small numbers of HIV+ women and high proportion of women who were HPV-positive in these studies limited the power to detect associations between CD4+ count and HPV. Similarly, in a study of HIV+ adolescent girls neither CD4 nor HIV VL were associated with HPV infection.³ The lack of an association between CD4 and HPV in that study, as in our study, may have been due to the relatively small number of participants and/or the lack of variation in CD4+ count: in our study, only 1% of participants had a $CD4 < 200/mm^3$ and 13% had a $CD4 < 350/mm^3$. The positive association between HIV VL and HPV in the WIHS and our study raises the question as to whether improved control of HIV replication either through treatment with antiretroviral medications or from immune-mediated mechanisms of the host could prevent HPV infection and subsequent adverse outcomes. It is also possible that the fact that HPV was associated with HIV VL but not CD4 could be related to immune dysregulation; i.e. the higher levels of immune activation that are noted among untreated HIV+ individuals.

Frequency of vaginal sexual intercourse with a male partner in the past 90 days was also positively associated with high-risk HPV in the multivariable model. The association between sexual behaviors and HPV is well-established in adolescents and

adults,^{4,32,35,37,48-50} and points to the importance of effective strategies to promote safer sexual behaviors among HIV+ young women to prevent STI acquisition and HIV transmission.⁵¹

Finally, non-Hispanic Black participants had substantially higher odds of high-risk HPV than Hispanic participants in the multivariable model. Racial and ethnic differences in HPV prevalence have been shown in previous studies, and are concerning in that they may account in part for disparities in cervical cancer incidence and mortality.⁵² In a nationally-representative sample of U.S. women, Black women had significantly higher rates of HPV (39.2%) compared to White (24.2%) and Hispanic (24.3%) women.³² In a study of college women, HPV prevalence rates were highest in Black women, lower in Hispanic women, and lowest in White women,^{53,54} while in a study of urban adolescents, Black race but not Hispanic ethnicity was associated with HPV infection.³⁷ The elevated risk in Black participants may be related to complex interactions between race, ethnicity and poverty.³⁶ In the study of U.S. women noted previously, poverty was strongly associated with high-risk HPV infection, and among participants living below the poverty line, Mexican-American ethnicity was inversely associated with high-risk HPV, whereas among participants living above the poverty line, Black race was positively associated with high-risk HPV.³⁶ These interactions between race/ethnicity, poverty, and HPV infection deserve further exploration because they have implications for the design of interventions to decrease existing disparities in HPV-related disease.⁵²

Limitations of this study include the relatively small sample size, which limited the power to detect associations between demographic, virologic, immunologic and behavioral factors and HPV infection. In addition, behavioral data were self-reported, which may affect their validity. Importantly, serology has limited sensitivity for detection of previous HPV infection and thus seropositivity rates may underestimate previous exposure to HPV. Seropositivity may indicate infection at sites other than the cervix; e.g. the anus. Furthermore, women with more advanced immune compromise may not generate as high an immune response to natural infection, which may affect baseline serology results. The cross-sectional design of this study limits the ability to detect persistent and incident HPV infection. Lastly, the population consisted of all high-risk young women with high levels of sexual exposure and those willing to enroll in a vaccination study; these factors may increase or decrease the risk of HPV, which limits the generalizability of the results. However, the clinical sites in the ATN are generally the largest of the clinics offering comprehensive services to HIV positive youth in the U.S., and thus likely to be representative of HIV+ youth in care. In conclusion, the high rates of HPV identified in this cohort of HIV-positive young women provide strong support for targeting HPV vaccination to girls 11-12 years of age or younger to maximize the health benefits of vaccination. The data also support vaccination of sexually experienced HIV+ young women, as the majority was HPV DNA negative and seronegative for high-risk, vaccine-type HPV infection at the time of vaccination.

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Table 1

Prevalence of human papillomavirus types and viral characteristics (N=99)

HPV ^a types	Definition	N (%)
All types	Positive for one or more types	74 (74.7)
High-risk types in the bivalent and quadrivalent vaccines	Positive for 16 and 18	1 (1.0)
	Positive for 16 or 18	15 (15.2)
Low-risk types in the quadrivalent vaccine	Positive for 6 and/or 11	3 (3.0)
High- and low-risk types in the quadrivalent vaccine	Positive for 6, 11, 16 and/or 18	18 (18.2)
High- and low-risk types in the nonavalent vaccine ^b	Positive for 6, 11, 16, 18, 31, 33, 45, 52, and/or 58	41 (41.4)
High-risk types	Positive for 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and/or 68	53 (53.5)
Multiple type infection (among those who are HPV positive)	2 HPV types	51 (68.9)
	1 HPV type	23 (31.1)
Number of types (among those who are HPV positive)	1	23 (31.1)
	2	12 (16.2)
	3	14 (18.9)
	4	6 (8.1)
	5	6 (8.1)
	6	4 (5.4)
	7	7 (9.5)
	8	1 (1.4)
	9	1 (1.4)
Global HPV Viral Load (among those who are HPV positive)	1-3	21 (28.4)
	4+	53 (71.6)
Viral load for HPV-16 (among those who are HPV-16 positive)	1-3	2 (16.7)
	4+	10 (83.3)
Viral load for HPV-18 (among those who are HPV-18 positive)	1-3	2 (40.0)
	4+	3 (60.0)
Individual HPV types	HPV-6	2 (2.0)
	HPV-11	1 (1.0)
	HPV-16	12 (12.1)
	HPV-18	5 (5.1)
	HPV-26	4 (4.0)
	HPV-30	3 (3.0)
	HPV-31	7 (7.1)
	HPV-32	3 (3.0)
	HPV-33	3 (3.0)
	HPV-35	11 (11.1)
	HPV-39	3 (3.0)
	HPV-42	3 (3.0)
	HPV-45	3 (3.0)

HPV ^a types	Definition	N (%)
	HPV-51	2 (2.0)
	HPV-52	12 (12.1)
	HPV-53	8 (8.1)
	HPV-54	7 (7.1)
	HPV-56	4 (4.0)
	HPV-58	17 (17.2)
	HPV-59	3 (3.0)
	HPV-61	16 (16.2)
	HPV-62	14 (14.1)
	HPV-66	4 (4.0)
	HPV-67	1 (1.0)
	HPV-68	7 (7.1)
	HPV-69	4 (4.0)
	HPV-70	7 (7.1)
	HPV-71	7 (7.1)
	HPV-72	8 (8.1)
	HPV-81	8 (8.1)
	HPV-82	3 (3.0)
	HPV-83	8 (8.1)
	HPV-84	7 (7.1)
	HPV-85	1 (1.0)
	HPV-86	1 (1.0)
	HPV-87	1 (1.0)
	HPV-89	1 (1.0)
	HPV-90	7 (7.1)
	HPV-97	1 (1.0)
	HPV-102	1 (1.0)
	HPV-106	7 (7.1)
	HPV-a8	7 (7.1)

^aHPV = human papillomavirus

^bThe nonavalent HPV vaccine is in clinical trials.⁵⁵

Table 2

HPV DNA and HPV serology results

	N (%)
HPV DNA positive and seropositive	
HPV-6	1 (1.0)
HPV-11	1 (1.0)
HPV-16	9 (9.1)
HPV-18	1 (1.0)
HPV-16 and -18	0 (0.0)
HPV-6, -11, -16, and -18	0 (0.0)
HPV DNA negative and seronegative	
HPV-6	42 (42.4)
HPV-11	67 (67.7)
HPV-16	55 (55.6)
HPV-18	73 (73.7)
HPV-16 and -18	45 (45.5)
HPV-6, -11, -16, and -18	23 (23.2)
HPV DNA positive and seronegative	
HPV-6	1 (1.0)
HPV-11	0 (0.0)
HPV-16	3 (3.0)
HPV-18	4 (4.0)
HPV-16 and -18	1 (1.0)
HPV-6, -11, -16, and -18	0 (0.0)
HPV DNA negative and seropositive	
HPV-6	55 (55.6)
HPV-11	31 (31.3)
HPV-16	32 (32.3)
HPV-18	21 (21.2)
HPV-16 and -18	9 (9.1)
HPV-6, -11, -16, and -18	5 (5.1)

Table 3
Baseline participant characteristics and univariate associations between characteristics and human papillomavirus (HPV) infection

Demographic, physical and viral characteristics	Positive for any HPV		Positive for HPV 16 and/or 18		Positive for HPV 6, 11, 16, and/or 18		Positive for 1 high-risk HPV type ^a	
	# HPV+/n (%) ^b	OR (95% CI) ^c	# HPV+/n (%)	OR (95% CI)	# HPV+/n (%)	OR (95% CI)	# HPV+/n (%)	OR (95% CI)
Age, years		0.94 (0.74-1.19)		0.94 (0.72-1.22)		0.96 (0.74-1.24)		0.92 (0.75-1.12)
Race/ethnicity ^d								
Non-Hispanic black	58/79 (73.4)	0.92 (0.27-3.17)	13/79 (16.5)	2.95 (0.36-24.35)	15/79 (19.0)	3.52 (0.43-28.73)	45/79 (57.0)	2.91 (0.92-9.17) ^e
Hispanic	12/16 (75.0)	1.00	1/16 (6.3)	1.00	1/16 (6.3)	1.00	5/16 (31.3)	1.00
Length of HIV infection (years)		0.97 (0.78-1.20)		1.27 (0.36-4.44)		1.03 (0.81 - 1.32)		0.96 (0.80 - 1.17)
BMI								
Obese (≥ 30.0)	30/40 (75.0)	1.04 (0.37-2.94)	7/40 (17.5)	1.27 (0.36-4.44)	7/40 (17.5)	0.85 (0.27-2.71)	20/40 (50.0)	0.84 (0.34-2.09)
Overweight (25-29.9)	17/23 (73.9)	0.98 (0.30-3.26)	4/23 (17.4)	1.26 (0.30-5.30)	4/23 (17.4)	0.84 (0.22-3.28)	13/23 (56.5)	1.09 (0.38-3.16)
Normal (18.5-24.9)	26/35 (74.3)	1.00	5/35 (14.3)	1.00	7/35 (20.0)	1.00	19/35 (54.3)	1.00
Knowledge about HPV/HPV vaccine		1.01 (0.98-1.04)		0.98 (0.94-1.01)^e		0.97 (0.94-1.01)^e		0.99 (0.97-1.02)
CD4+ T cell count (cells/mm ³)								
<350	10/14 (71.4)	0.82 (0.23-2.89)	1/14 (7.1)	0.36 (0.04-2.96)	1/14 (7.1)	0.31 (0.04-2.52)	5/14 (35.7)	0.43 (0.13-1.39)^e
350	64/85 (75.3)	1.00	15/85 (17.6)	1.00	17/85 (20.0)	1.00	48/85 (56.5)	1.00
HIV viral load (copies/mL)								
400	47/59 (79.7)	1.89 (0.75-4.71)^e	10/59 (16.9)	1.16 (0.38-3.48)	12/59 (20.3)	1.45 (0.49-4.24)	37/59 (62.7)	2.52 (1.11-5.75)^f
<400	27/40 (67.5)	1.00	6/40 (15.0)	1.00	6/40 (15.0)	1.00	16/40 (40.0)	1.00
Behaviors								
Number of male sexual partners, lifetime								
11+	25/36 (69.4)	0.87 (0.29-2.55)	6/36 (16.7)	1.73 (0.39-7.63)	6/36 (16.7)	0.96 (0.26-3.53)	18/36 (50.0)	0.81 (0.30-2.17)
6-10	26/31 (83.9)	1.98 (0.56-6.96)	6/31 (19.4)	2.08 (0.47-9.24)	6/31 (19.4)	1.15 (0.31-4.28)	17/31 (54.8)	0.99 (0.36-2.73)
0-5	21/29 (72.4)	1.00	3/29 (10.3)	1.00	5/29 (17.2)	1.00	16/29 (55.2)	1.00
Number of male sexual								

	Positive for any HPV		Positive for HPV 16 and/or 18		Positive for HPV 6, 11, 16, and/or 18		Positive for 1 high-risk HPV type ^a	
	# HPV+/n (%) ^b	OR (95% CI) ^c	# HPV+/n (%)	OR (95% CI)	# HPV+/n (%)	OR (95% CI)	# HPV+/n (%)	OR (95% CI)
partners, past 90 days								
2	12/16 (75.0)	1.71 (0.41-7.14)	3/16 (18.8)	2.31 (0.34-15.8)	3/16 (18.8)	1.46 (0.25-8.40)	9/16 (56.3)	2.25 (0.60-8.38)
1	47/60 (78.3)	2.07 (0.71-5.99)	10/60 (16.7)	2.00 (0.40-9.95)	11/60 (18.3)	1.42 (0.36-5.66)	35/60 (58.3)	2.45 (0.89-6.72) ^e
0	14/22 (63.6)	1.00	2/22 (9.1)	1.00	3/22 (13.6)	1.00	8/22 (36.4)	1.00
Number of times had vaginal sex with a male partner, past 90 days								
6+	32/42 (76.2)	2.84 (0.87-9.33) ^e	8/42 (19.0)	3.76 (0.43-32.7)	8/42 (19.0)	1.10 (0.25-4.75)	24/42 (57.1)	4.33 (1.21-15.5) ^f
1-5	26/33 (78.8)	3.30 (0.93-11.7) ^e	5/33 (15.2)	2.86 (0.31-26.7)	5/33 (15.2)	0.83 (0.17-4.00)	19/33 (57.6)	4.41 (1.18-16.4) ^f
0	9/17 (52.9)	1.00	1/17 (5.9)	1.00	3/17 (17.6)	1.00	4/17 (23.5)	1.00
Number of times had vaginal sex with a male partner without a condom, past 90 days								
6+	14/16 (87.5)	3.20 (0.65-15.8)	1/16 (6.3)	0.42 (0.05-3.69)	1/16 (6.3)	0.31 (0.04-2.67)	8/16 (50.0)	1.04 (0.34-3.20)
1-5	23/30 (76.7)	1.50 (0.54-4.22)	7/30 (23.3)	1.91 (0.60-6.12)	7/30 (23.3)	1.42 (0.47-4.31)	18/30 (60.0)	1.56 (0.63-3.89)
0	35/51 (68.6)	1.00	7/51 (13.7)	1.00	9/51 (17.6)	1.00	25/51 (49.0)	1.00
Number of male partners with whom had sex without condom past 90 days								
1+	32/39 (82.1)	1.90 (0.70-5.12)	7/39 (17.9)	1.37 (0.45-4.14)	7/39 (17.9)	1.05 (0.36-3.04)	25/39 (64.1)	2.05 (0.89-4.72) ^e
0	41/58 (70.7)	1.00	8/58 (13.8)	1.00	10/58 (17.2)	1.00	27/58 (46.6)	1.00
Number of main sex partners, past 90 days								
2+	4/6 (66.7)	0.67 (0.11-3.88)	2/6 (33.3)	2.79 (0.47-16.7)	2/6 (33.3)	2.38 (0.40-14.1)	4/6 (66.7)	1.83 (0.32-10.5)
0-1	69/92 (75.0)	1.00	14/92 (15.2)	1.00	16/92 (17.4)	1.00	48/92 (52.2)	1.00
Number of casual sexual partners, past 90 days								
2+	6/7 (85.7)	2.15 (0.25-18.8)	2/7 (28.6)	2.20 (0.39-12.5)	2/7 (28.6)	1.88 (0.33-10.5)	4/7 (57.1)	1.19 (0.25-5.64)
0-1	67/91 (73.6)	1.00	14/91 (15.4)	1.00	16/91 (17.6)	1.00	48/91 (52.7)	1.00
Pregnancy prevention method at last sexual intercourse with main partner								
Others	20/27 (74.1)	0.95 (0.35-2.62)	2/27 (7.4)	0.33 (0.07-1.57) ^e	3/27 (11.1)	0.48 (0.13-1.79)	13/27 (48.1)	0.74 (0.31-1.80)

	Positive for any HPV		Positive for HPV 16 and/or 18		Positive for HPV 6, 11, 16, and/or 18		Positive for 1 high-risk HPV type ^a	
	# HPV +/n (%) ^b	OR (95% CI) ^c	# HPV+/n (%)	OR (95% CI)	# HPV+/n (%)	OR (95% CI)	# HPV+/n (%)	OR (95% CI)
Condom	54/72 (75.0)	1.00	14/72 (19.4)	1.00	15/72 (20.8)	1.00	40/72 (55.6)	1.00
STI^h diagnosed								
Trichomonas	7/9 (77.8)	1.17 (0.23-6.04)	2/9 (22.2)	1.65 (0.31-8.83)	2/9 (22.2)	1.39 (0.26-7.36)	5/9 (55.6)	1.09 (0.27-4.33)
Gonorrhea	N/A ^g	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Chlamydia	5/5 (100.0)	Inf (0.31-Inf) ^j	1/5 (20.0)	1.32 (0.14-12.6)	1/5 (20.0)	1.13 (0.12-10.8)	5/5 (100.0)	Inf (0.82-Inf) ^j
At least one STI	11/13 (84.6)	2.01 (0.41-9.75)	2/13 (15.4)	0.94 (0.19-4.69)	2/13 (15.4)	0.80 (0.16-3.95)	9/13 (69.2)	2.15 (0.61-7.50)

^aHigh-risk HPV was defined as HPV-16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, or 68

^b# HPV+ = number of HPV positive subjects; n = total number of subjects in a specific category; % = percentage of HPV positive subjects within the specific category

^cOR = odds ratio, CI = confidence interval

^dThe number of non-Hispanic White participants (N=4) was too small to generate a stable estimate; therefore, the non-Hispanic White participants were not included in this model and Hispanic was used as the reference group.

^e.05 p < .20. For variables with more than two categories, the overall (Type III) p-value was used to determine if the variable was eligible to be entered into the multivariable models.

^f.01 p < .05. For variables with more than two categories, the overall (Type III) p-value was used to determine if the variable was eligible to be entered into the multivariable models.

^gN/A = not applicable; unable to calculate as no participants were diagnosed with gonorrhea.

^hSTI = sexually transmitted infection present at the time of HPV testing. The reference group was defined as negative for diagnosis of an STI.

ⁱDue to zero cell frequencies in some cells, the odds ratios and 95% confidence intervals for these variables were calculated using exact logistic regression.

Table 4Independent risk factors for high-riska human papillomavirus prevalence^b

	OR (95% CI) ^c	P-value
Race/ethnicity ^d		
Non-Hispanic Black	7.06 (1.63-30.5)	0.0089
Hispanic (reference)	1.00	
Viral load (copies/mL)		
400	3.47 (1.28-9.43)	0.015
<400 (reference)	1.00	
Number of times had vaginal sex with a male partner, past 90 days		
6+	5.82 (1.30-26.11)	0.022
1-5	6.12 (1.38-27.16)	0.017
0 (reference)	1.00	

^aHigh-risk defined as positive for at least one of the following types: HPV-16, -18, -31, -33, -35, -39, -45, -51, , -52, -56, -58, -59, or -68.

^bCovariates with an overall p-value <0.20 from the univariate models were considered as candidates in the multivariable model (race/ethnicity, CD4 count, viral load, number of sex partners in the past 90 days, number of times had vaginal sex with a male partner in the past 90 days, and number of partners with whom the participant had unprotected sex in the past 90 days). CD4 T-cell count and lifetime number of sexual partners were forced into the model given their clinical significance.

^cOR = odds ratio, CI = confidence interval

^dThe number of non-Hispanic White participants (N=4) was too small to generate a stable estimate; therefore, the non-Hispanic White participants were not included in this model and Hispanic was used as the reference group.