Prevalence of anal high-risk human papillomavirus infections among HIV-positive and HIV-negative men who have sex with men (MSM) in Nigeria

Rebecca G. Nowak, PhD[1,2], **Patti E. Gravitt, PhD**[3], **Xin He, PhD**[4], **Sosthenes Ketende, MSc**[5], **Wuese Anom, MBBS**[6], **Helen Omuh, MBBS, MS**[6], **William A. Blattner, MD**[1,2], and **Manhattan E. Charurat, PhD**[1,2] on behalf of the TRUST Study Group

[1]Institute of Human Virology, University of Maryland School of Medicine, Baltimore, MD

[2]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD

[3]University of New Mexico Health Sciences Center, Albuquerque, NM

[4]University of Maryland School of Public Health, College Park, MD

[5]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

[6]Institute of Human Virology Nigeria, Federal Capital Territory, Nigeria

Abstract

Background—Prevalence estimates of anal high-risk human papillomavirus (HR-HPV) are needed in sub-Saharan Africa where HIV is endemic. This study evaluated anal HR-HPV in Nigeria among HIV-positive and HIV-negative men who have sex with men (MSM) for future immunization recommendations.

Methods—We conducted a cross-sectional study to compare the prevalence of anal HR-HPV infections between 64 HIV-negative and 90 HIV-positive MSM. Multivariate Poisson regression analyses were used to examine demographic and behavioral risk factors associated with any HR-HPV infections.

Corresponding author: Rebecca Nowak, PhD, 725 W. Lombard Street, Baltimore, MD 21201, Tel: 410-706-4642, Fax: 410-706-1944, rnowak@ihv.umaryland.edu.

Results—The median age of the 154 participants was 25 years (interquartile range [IQR]: 22-28, range: 16-38) and the median age at initiation of anal sex with another man was 16 years (IQR: 13-18, range: 7-29). The prevalence of anal HR-HPV was higher among HIV-positive than HIV-negative MSM (91.1% vs. 40.6%, p<0.001). In the multivariate analysis, HIV infection (adjusted prevalence ratio [aPR]: 2.02, 95% CI: 1.49-2.72), ten years or more since anal sexual debut (aPR: 1.26, 95% CI: 1.07-1.49), and concurrent relationships with men (aPR: 1.32, 95% CI: 1.04-1.67) were associated with increased anal HR-HPV prevalence.

Conclusions—Anal HR-HPV infection is high for young Nigerian MSM and rates are amplified in those co-infected with HIV. Providing universal coverage as well as catchup immunization for young MSM may be an effective anal cancer prevention strategy in Nigeria.

Keywords

HIV; anal human papillomavirus; men who have sex with men; Africa

Introduction

The rising incidence of anal cancer in the US is linked to the syndemic of HIV and coincident high risk human papillomavirus (HR-HPV) infection among men who have sex with men (MSM). Anal cancer risk is 80 times higher among HIV-infected MSM as compared to HIV-uninfected individuals, with the most oncogenic genotypes being HPV16 followed by HPV18 and HPV33 [1-3]. Antiretroviral therapy (ART) has restored systemic immunity, but has done little to regress anal precancerous lesions [4, 5] or prevent an increase in anal cancer incidence in HIV-positive men [1, 6-7]. These unexpected trends in the era of ART highlight the complexity of HPV transformation and the need to prevent initial infection with effective HPV vaccines.

Most prevalence studies of anal HR-HPV in HIV-infected MSM have occurred in North America, Europe, Australia and Asia [8-14]. A meta-analysis of cross-sectional studies primarily from the United States estimated the pooled prevalence of any HPV was higher in HIV-positive as compared to HIV-negative MSM (93% vs. 64%) [15]. A similar pattern existed for HR-HPV (74% vs. 37%) [15]. More data are needed to describe the burden of anal HR-HPV in HIV-endemic regions such as sub-Saharan Africa for adequate anal cancer control program development. This is especially important since with longer survival times expected for HIV-infected populations in sub-Saharan Africa, anal cancer trends are likely to parallel and possibly surpass the current trends seen in the United States where the incidence rates among men increased between 2000 to 2009 [6]. The 9-valent HPV vaccine which includes protection against five additional HR-HPV types (31, 33, 45, 52, and 58) was recently approved in December 2014 by the U.S. Food and Drug Administration for males between the ages of 9 to 15 years [16]. The anticipated impact of the 9-valent HPV vaccine on anal HPV burden is difficult to estimate in an HIV endemic area such as Nigeria where the diversity of HR-HPV has not been characterized.

The objective of this study is thus to evaluate the prevalence of anal HR-HPV and associated demographic and behavioral risk factors in a cohort of young HIV-positive and HIV-negative Nigerian MSM to better inform future vaccination recommendations.

Materials and Methods

Study design and Population

We conducted a cross-sectional study at the Abuja site of the TRUST study that has been previously described [17]. In brief, the TRUST study has recruited Nigerian MSM through respondent-driven sampling (RDS) since March 2013. Eligibility criteria included: 1) a valid RDS coupon; 2) born male; 3) history of anal intercourse, insertive or receptive, with another man in the past 12 months; 3) age 16 years or older, with 16-17 year olds considered emancipated minors and exempt from parental consent; and 4) ability and willingness to provide written informed consent. At enrollment (visit 0), participants provided demographic, sexual behavior and clinical data through in person interviews by the trained staff using a standardized questionnaire. Two weeks after enrollment (visit 1), participants underwent HIV counseling and testing and received physical exams where anal swabs, urine and blood were collected for sexually transmitted infection (STI) diagnostics. Two anal swabs from the APTIMA swab kit were inserted by a doctor about 2cm into the anorectum, rotated, and placed in transport medium. Specimens were aliquoted and stored at minus 80°C prior to testing. At the time of this analysis, participants who had completed HIV testing, had an anal swab sample at visit 1, and were among those recruited early in the TRUST study by their peers (wave 1-10 of network chains) were included in this study (n=165).

This study was conducted in collaboration with the Institute of Human Virology at the University of Maryland, the Institute of Human Virology Nigeria, Johns Hopkins University, the International Center for Advocacy on the Right to Health, and the U.S. Military HIV Research Program. The study was approved by the Federal Capital Territory Health Research Ethics Committee in Nigeria, the University of Maryland Baltimore Institutional Review Board (IRB), and the Walter Reed Army Institute of Research IRB.

Laboratory Procedures

Whole blood was tested for HIV using rapid test kits (Abbott Determine HIV-1/2, Chembio HIV-1/2 Stat Pak, and Trinity biotech Uni-Gold HIV test for discordant results) as outlined by the parallel testing algorithm for high-risk individuals in Nigeria [18]. If a participant was HIV-positive, HIV RNA viral loads were quantified using the COBAS TaqMan HIV-1 Test (Roche Molecular Diagnostics, CA) and CD4 counts were estimated using the Partec CyFlow Counter. Anal swabs were tested for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* using the Aptima Combo 2 CT/NG Assay (Hologic, CA). Participants testing positive for HIV and/or STIs were offered ART regardless of CD4 counts and antibiotic therapies. A physical examination of the anorectum was conducted for detection of warts. Depending on the size of the warts, the participants were either treated with liquid nitrogen immediately or referred to the Nigerian Defense Headquarters Medical Center for surgical excision.

For HPV analyses, DNA was extracted from 250 μl of Aptima Specimen Transport medium using the QIAamp MinElute Media Kit (Qiagen, CA). DNA was resuspended in 100μl of Buffer AVE. A 10μl aliquot of the purified DNA was amplified using the PGMY 09/11 L1

consensus primer system [19] which co-ampifes 37 HPV genotypes and a human beta-globin internal control target. Both high and low-risk HPV genotypes were detected using the Linear Array HPV Genotyping Test (Roche Molecular Diagnostics, CA)[20]. HR-HPV included 13 type specific infections: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 [21]. HPV52 was considered positive if there was no cross reaction with HPV33, HPV35 or HPV58. HPV52 status in men with HPV33, HPV35, or HPV58 is therefore unknown. The remaining 24 genotypes detected were considered low-risk. Quality control samples were included during DNA extraction, PCR amplification and genotype detection steps. Among the 165 samples tested, 8 were excluded from the analysis because they did not have sufficient cellular material to detect HPV genotypes. The final analytic sample size was 157.

Statistical Analyses

The primary outcome variable for all analyses was a binary categorization of having any anal HR-HPV type specific infections. A person was considered positive if one or more of the 13 HR-HPVs was detected. Prevalence of any HPV, vaccine preventable-types in the 9-valent vaccine (HPV6, 11, 16, 18, 31, 33, 45, 52, 58), HR-HPV not in the 9-valent vaccine (HPV35, 39, 51, 56, 59, 68), and individual high-risk type specific infections between HIV-positive and HIV-negative were also assessed. The main independent variable was HIV infection status. Demographic characteristics (i.e., age, education, marital status, religion, and sexual orientation), behavioral factors [i.e., age at anal sexual debut, years since anal sexual debut, number of men had receptive sex in past year, sexual positioning (insertive only or any receptive), condom use with receptive sex, and any female sexual partners], and concurrent sexually transmitted infections (i.e., rectal gonorrhea, rectal chlamydia, and anal warts) were also evaluated as independent risk factors for HR-HPV. Variables related to immunodeficiency (CD4 counts, viral loads, WHO stage and ART status) were summarized for the HIV-positive MSM. The baseline demographics of HIV-positive and HIV-negative MSM were compared using Pearson's chi-square tests for categorical variables and Wilcoxon rank sum tests for continuous variables. Univariate and multivariate Poisson regression models with robust error variance were used to estimate prevalence ratios (PR) and 95% confidence intervals (CI) for the association between independent risk factors and anal HR-HPV infection. Size of personal network, as a form of weighting, was included in all multivariate models to account for the respondent driven sampling design. A directed acyclic graph (DAG) was generated using DAGitty [22] to identify the minimal set of *a priori* confounders (sexual behavior, size of personal network and age) needed to adjust for the association between HIV infection and HR-HPV without introducing selection bias from over adjustment [23] (see Figure, Supplemental Digital Content 2, for DAG illustration). The final multivariate model adjusted for years since anal sexual debut, sexual positioning, concurrency, and size of personal network. Female partners was not included in the final model because it did not confound the main association (<10% change in estimated effect) and was significantly associated with concurrency. Age was not included in the model because it was positively correlated with years since sexual debut. Analyses were performed using Stata Statistical Software: Release 13 (College Station, TX: StataCorp LP).

Results

A total of 154 participants (64 HIV-negative and 90 HIV-positive) were included in the analytic sample size, after removing 3 subjects with any missing data on *a priori* confounders (years since sexual debut, sexual positioning or female partners). Participants missing data on descriptive covariates were retained in the analysis.

Overall, participants were young (median age=25 years; interquartile range [IQR]: 22-28, range: 16-38) and initiated anal sex at a young age (median age=16 years; IQR: 13-18, range: 7-29). Participants engaged in sexual activities both with men (median number of receptive sexual partners=3; IQR: 1-5) and women (median number of vaginal sexual partners=1; IQR:0-2).

Compared to HIV-negative men, HIV-positive men were older, had larger personal networks of MSM, engaged in more unprotected receptive sex, and were diagnosed with concurrent anal warts (Table 1). For HIV-positive MSM, less than half were receiving antiretroviral therapy (ART; n=39, 43%) at study entry, the median CD4+ cell count was 320 cells/μl (IQR: 221-425), a third (n=29, 32%) had a viral load 100,000 copies/ml, and 24% (n=22) had a WHO stage of 2 at enrollment.

The prevalence of any HPV, any HR-HPV, any of the 9 vaccine-preventable HPV strains (6/11/16/18/31/33/45/52/58), and any non-vaccine HR-HPV strain ((35/39/51/56/59/68) was higher in the HIV-positive MSM as compared to the HIV-negative MSM (Figure 1). Approximately 59% (53/90) of HIV-positive and 83% (53/64) of HIV-negative MSM did not have a prevalent HPV16 or HPV18 infection. HPV35 had the highest point prevalence (34.4%) among HIV-positive MSM, followed by HPV58 (27.8%), HPV51 (26.7%), HPV18 (25.6%), HPV45 (25.6%) and HPV16 (23.3%) (see Figure, Supplemental Digital Content 1, for type-specific prevalence by HIV status). HPV16 had the highest point prevalence (12.5%) among HIV-negative MSM, followed by HPV51 (9.4%), HPV35 (7.8%), HPV58 (7.8%), HPV52 (6.3%) and HPV31 (6.3%) (see Figure, Supplemental Digital Content 1, for type-specific prevalence by HIV status).

As shown in the unadjusted analysis in Table 2, risk factors for HR-HPV included HIV infection, longer duration since anal sexual debut, and larger personal networks of MSM. Younger age and having female sex partners were associated with a lower prevalence of HR-HPV. Initiation of anal sex before age 13, any receptive sex in the past year, and increasing numbers of anal receptive sex partners in the past year were positively associated with HR-HPV. For HIV-positive MSM, there was no difference in HR-HPV by category of CD4 counts (<200, 200-349, 350+, p=0.90), viral load (<100, 100-99,999, 100,000+, p=0.81), WHO stage (1 vs. 2, p=0.34), or self-report of ART at study entry (p=0.94).

As shown in the multivariate analysis in Table 3, HIV infection was significantly associated with a 2-fold increased prevalence of HR-HPV infection (Table 3). The proportion of MSM with anal HR-HPV was approximately 26% higher if they had ten or more years since sexual debut. Similarly, MSM in concurrent relationships strictly with men had an approximately 32% higher prevalence of anal HR-HPV, as compared to MSM with no

concurrent relationships. Practicing any receptive sex was no longer significantly associated with anal HR-HPV.

Discussion

Our study of young Nigerian MSM demonstrated a high prevalence of anal HR-HPV during HIV infection. The most prevalent HR-HPV type specific infections that occurred in both the HIV-positive and HIV-negative MSM were HPV35, HPV58, HPV51 and HPV16, with HPV16 not being the dominant HR-HPV infection among the HIV-positive. Given the diversity of HR-HPV infection, most of the HR-HPV types would be prevented with the 9-valent vaccine except HPV35 and HPV51. Interestingly, a large proportion of our participants were not currently HPV16 or 18 DNA positive, highlighting an opportunity to provide catch up immunization to prevent infection with the most oncogenic genotypes. In terms of risk factors, HIV infection was the strongest predictor for anal HR-HPV infection. In addition, more than ten years since anal sexual debut and concurrent relationships with men were independently associated with an increased prevalence of anal HR-HPV infections.

Our baseline prevalence of anal HR-HPV infection in those co-infected with HIV, was similar to the prevalence observed in Australia (94%) [12] and higher than those reported from North America (ranging from 56% to 80%) [7-9], Europe (ranging from 65% to 79%) [10-11], Asia (ranging from 58% to 61%) [13-14], and the summary prevalence of 74% (95% CI, 64-83) from a meta-analysis [15]. Although the Australian study had a similar prevalence, its study population significantly differed in their age composition and sexual risk behavior. The Australian study was comprised of much older men in their mid-forties with an initiation of sex over 20 years prior and more than a third reporting over 500 lifetime number of sex partners. In contrast, our study was comprised of much younger HIV-positive MSM (79% less than 30 years of age) with lower risk behavior. Sexual debut occurred 10 years prior and their personal networks included a median of 35 men. Geographic distributions of HPV prevalence may explain the higher detectability of HR-HPV in our study as compared to the other studies. In a meta-analysis comparing the prevalence of cervical human papillomavirus among women with normal cytological findings, the prevalence of HPV was higher in Western Africa which includes Nigeria (19.6%) as compared to North America (4.7%) [24]. The higher prevalence may also be the result of underreporting of sexual risk behavior because our observed prevalence among the HIV-negative MSM was the same as the prevalence reported from a geographically distinct region (Seattle, Washington). The Seattle study population had a similar age composition and exposure time since sexual debut with another man [25]. Other studies of HIV-negative MSM with differing age compositions and exposure times have estimated anal HR-HPV in the range of 27% to 73% [7, 9, 11-15, 26]. Additional studies of anal HPV are needed from young MSM in sub-Saharan Africa to confirm the breadth of diversity observed in our study.

Among HIV-positive MSM, HPV35 and 51 were among the most common and HPV16 ranked 6th in prevalence. Other studies among Nigerian women documented HPV35 as one of the more prevalent high-risk type specific infections [27, 28]. One Nigerian study found

invasive cervical cancers were predominantly associated with HPV16 (68%) and 18 (10%) as compared to HPV35 (6%) [28], therefore HPV35 and possibly HPV51, even though highly prevalent, may not be as persistent or oncogenic as HPV16 and HPV18. Longitudinal studies are needed to better understand persistence of and progression of non-HPV16 or 18 HR-HPVs in Nigeria to better understand their contribution to anal cancer risk.

Similar to other studies, HIV infection and markers of sexual behavior (ie. longer duration since sexual debut) were independent predictors of anal HR-HPV [7-8, 11-12, 25-26]. The prevalence of anal HR-HPV was higher among MSM who had concurrent relationships with men. Having female partners was initially protective in the univariate analysis. This finding is consistent with a study from China, where female partnerships were not associated with anal HR-HPV [29]. Female partners are potentially a surrogate marker of lower exposure to HPV from receptive sex. However, this risk is not mitigated for their female partners given the high prevalence of HIV and HR-HPV among the MSM. Additional studies are needed to to find effective interventions that increase uptake of cervical cancer screening among female partners of MSM, who may not be aware of their exposure risk. Other markers of sexual behavior, such as number of receptive partners and unprotected receptive sex, were positively associated with anal HR-HPV.

Our study had a few limitations. Data on lifetime number of sexual partners, one of the strongest sexual risk factors, was not collected in this cohort, but estimates of personal networks of MSM was available and potentially accounted for this risk factor in the analysis. Another strong risk factor for HPV is smoking, which was not collected in our cohort. If smoking behavior is differential by HIV status, then the independent estimates of HIV would move towards the null. Next, participants were asked to report their sexual behavior over the past 12 months potentially introducing recall bias in terms of their behavior with men, women and condom use. However, most of these variables were in the expected direction and the precision of these associations would have been strengthened with a larger sample size. Lastly, this was a cross sectional study that was not able to assess directionality between HIV and anal HR-HPV infections. Despite these limitations, estimates of anal HR-HPV prevalence in Nigeria are not based on a convenient sample and may be generalizable to other young MSM with similar risk behaviors given that this sample achieved greater than 8 waves of recruitment. There was no significant difference in the prevalence of anal HR-HPV between waves 1-5 vs. waves 6-10 (data not shown), suggesting that equilibrium was reached [30]. Because the sampling design was accounted for in the analysis by adjusting for personal network size, inferences about the study population are generalizable to other comparable MSM populations in sub-Saharan Africa. Overall, these baseline estimates of anal HR-HPV are needed to inform follow-up analyses on incident and persistent infections.

In summary, our study documents a high burden of anal HR-HPV infection among young MSM from Nigeria, particularly those infected with HIV. HPV35, 58 and 51 were more common than 18, 45, and 16 among the HIV-positive MSM. The high proportion of MSM naïve to HPV16 and 18 offers an opportunity to provide catch up immunization to prevent anal cancer. Future studies are needed to assess anal HR-HPV persistence and progression to neoplasia given the breadth of types detected in this study to better understand the potential effectiveness of the 9-valent vaccine to reduce the burden of HPV-associated malignancies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

References

1. Silverberg MJ, Lau B, Justice AC, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. Clinical Infectious Diseases. 2012; 54:1026–1034. [PubMed: 22291097]

2. Chaturvedi AK. Beyond cervical cancer: burden of other HPV-related cancers among men and women. J Adolesc Health. 2010; 46:S20–6. [PubMed: 20307840]

3. International Agency for Research on Cancer. Monographs on the Evaluation of Carcinogenic Risks to Humans. 2007. p. 90

4. Palefsky JM, Holly EA, Efirdc JT, et al. Anal intraepithelial neoplasia in the highly active antiretroviral therapy era among HIV-positive men who have sex with men. AIDS. 2005; 19:1407–1414. [PubMed: 16103772]

5. Simard EP, Watson M, Saraiya M, et al. Trends in the occurrence of high-grade anal intraepithelial neoplasia in San Francisco: 2000-2009. Cancer. 2013; 119:3539–3545. [PubMed: 23861091]

6. Piketty C, Selinger-Leneman H, Grabar S, et al. Marked increase in the incidence of invasive anal cancer among HIV-infected patients despite treatment with combination antiretroviral therapy. AIDS. 2008; 22:1203–1211. [PubMed: 18525266]

7. Jemal A, Simard EP, Dorell C, et al. Annual Report to the Nation on the Status of Cancer, 1975-2009, featuring the burden and trends in human papillomavirus(HPV)-associated cancers and HPV vaccination coverage levels. J Natl Cancer Inst. 2013; 105:175–201. [PubMed: 23297039]

8. Hernandez AL, Efird JT, Holly EA, et al. Risk factors for anal human papillomavirus infection type 16 among HIV-positive men who have sex with men in San Francisco. J Acquir Immune Defic Syndr. 2013; 63:532–539. [PubMed: 23614994]

9. Wiley DJ, Li X, Hsu H, et al. Factors affecting the prevalence of strongly and weakly carcinogenic and lower-risk human papillomaviruses in anal specimens in a cohort of men who have sex with men (MSM). PLoS One. 2013; 8:e79492. [PubMed: 24278140]

10. Videla S, Darwich L, Canadas MP, et al. Natural history of human papillomavirus infections involving anal, penile, and oral sites among HIV-positive men. Sex Transm Dis. 2013; 40:3–10. [PubMed: 23250297]

11. van Aar F, Mooij SH, van der Sande MA, et al. Anal and penile high-risk human papillomavirus prevalence in HIV-negative and HIV-infected MSM. AIDS. 2013; 27:2921–2931. [PubMed: 23921617]

12. Vajdic CM, van Leeuwen MT, Jin F, et al. Anal human papillomavirus genotype diversity and co-infection in a community-based sample of homosexual men. Sex Transm Infect. 2009; 85:330–335. [PubMed: 19342375]

13. Phanuphak N, Teeratakulpisarn N, Pankam T, et al. Anal human papillomavirus infection among Thai men who have sex with men with and without HIV infection: prevalence, incidence, and persistence. J Acquir Immune Defic Syndr. 2013; 63:472–479. [PubMed: 23514956]

14. Hu Y, Qian HZ, Sun J, et al. Anal human papillomavirus infection among HIV-infected and uninfected men who have sex with men in Beijing, China. J Acquir Immune Defic Syndr. 2013; 64:103–114. [PubMed: 23732908]

15. Machalek DA, Poynten M, Jin F, et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. Lancet Oncol. 2012; 13:487–500. [PubMed: 22445259]

16.
Available at: www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm426485.html.

17. Charurat ME, Emmanuel B, Akolo C, et al. Uptake of treatment as prevention for HIV and continuum of care among HIV-positive men who have sex with men in Nigeria. J Acquir Immune Defic Syndr. 2015; 68(Suppl 2):S114–23. [PubMed: 25723975]

18. FMOH. Laboratory-Based HIV Rapid Test Validation in Nigeria. Abuja, Nigeria: Federal Ministry of Health; 2007.

19. Coutlee F, Gravitt P, Kornegay J, et al. Use of PGMY primers in L1 consensus PCR improves detection of human papillomavirus DNA in genital samples. J Clin Microbiol. 2002; 40:902–907. [PubMed: 11880413]

20. Gravitt PE, Peyton CL, Apple RJ, et al. Genotyping of 27 human papillomavirus types by using L1 consensus PCR products by a single-hybridization, reverse line blot detection method. J Clin Microbiol. 1998; 36:3020–3027. [PubMed: 9738060]

21. Munoz N, Bosch FX, de Sanjose S, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. N Engl J Med. 2003; 348:518–527. [PubMed: 12571259]

22.
Available at: www.dagitty.net/dags.html.

23. Textor J, Hardt J, Knuppel S. DAGitty: a graphical tool for analyzing causal diagrams. Epidemiology. 2011; 22:745. [PubMed: 21811114]

24. Bruni L, Diaz M, Castellsague X, et al. Cervical human papillomavirus prevalence in 5 continents: Meta-analysis of 1 million women with normal cytological findings. J Infect Dis. 2010; 202:1789–1799. [PubMed: 21067372]

25. Glick SN, Feng Q, Popov V, et al. High rates of incident and prevalent anal human papillomavirus infection among young men who have sex with men. J Infect Dis. 2014; 209:369–376. [PubMed: 23956439]

26. Nyitray AG, Carvalho da Silva RJ, Baggio ML, et al. Age-specific prevalence of and risk factors for anal human papillomavirus (HPV) among men who have sex with women and men who have sex with men: the HPV in men (HIM) study. J Infect Dis. 2011; 203:49–57. [PubMed: 21148496]

27. Akarolo-Anthony SN, Famooto AO, Dareng EO, et al. Age-specific prevalence of human papilloma virus infection among Nigerian women. BMC Public Health. 2014; 14 656-2458-14-656.

28. Okolo C, Franceschi S, Adewole I, et al. Human papillomavirus infection in women with and without cervical cancer in Ibadan, Nigeria. Infect Agent Cancer. 2010; 5 24-9378-5-24.

29. Li Z, Zhang H, Li X, et al. Anal Human Papillomavirus Genotyping among HIV-Positive Men Who Have Sex with Men in Xi'an, China. PLoS One. 2015; 10:e0125120. [PubMed: 25923768]

30. McCreesh N, Frost SD, Seeley J, et al. Evaluation of respondent-driven sampling. Epidemiology. 2012; 23(1):138–147. [PubMed: 22157309]
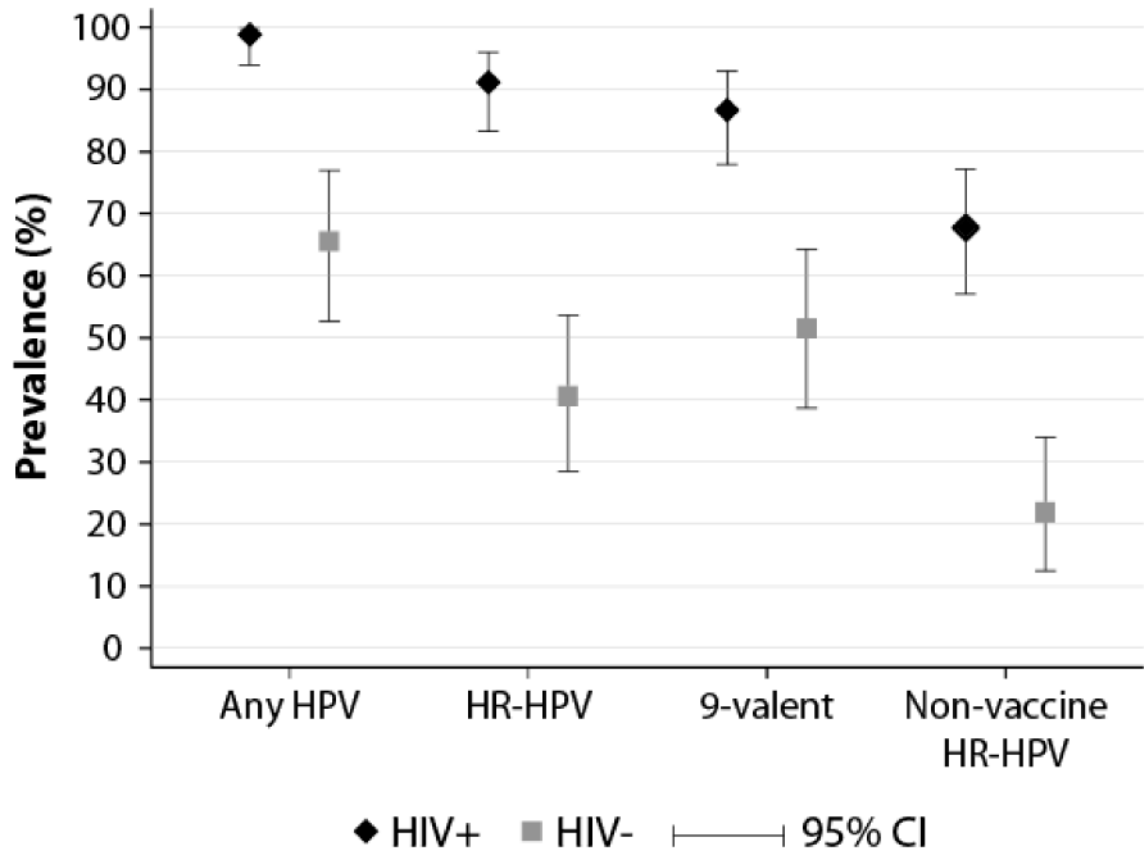
Figure 1. Prevalence of any HPV, high-risk HPV, nonavalent vaccine types, and non-vaccine HR-HPV types in HIV+ and HIV- MSM (n=154 men)

Table 1

Baseline Demographics of HIV-positive and HIV-negative MSM

Baseline Characteristics	HIV+ n=90 No. (%)	HIV- n=64 No. (%)	P*
Age (years)			0.11
16-19	8 (8.9)	13 (20.3)	
20-29	63 (70.0)	41 (64.1)	
30-38	19 (21.1)	10 (15.6)	
Median [IQR]	26 [23-28]	24 [20-28]	**0.03**
Education			0.06
Primary	9 (10.5)	2 (3.1)	
Secondary	43 (50.0)	43 (67.2)	
Tertiary	34 (39.5)	19 (29.7)	
Marital status			0.18
Never married	73 (81.1)	57 (89.1)	
Ever married	17 (18.9)	7 (10.9)	
Religion			0.36
Christian/Protestant	71 (79.8)	47 (73.4)	
Muslim/Other	18 (20.2)	17 (26.6)	
Sexual Orientation			0.82
Bisexual	61 (68.5)	45 (70.3)	
Homosexual	28 (31.5)	19 (29.7)	
Age of anal sexual debut (years)			0.33
12	31 (34.4)	15 (23.4)	
13-18	48 (53.3)	39 (60.9)	
19-27	11 (12.2)	10 (15.6)	
Median [IQR]	15 [12-18]	16 [15-20]	**0.03**
Number of years since first anal sex			**0.01**
0-9	45 (50.0)	45 (70.3)	
10-26	45 (50.0)	19 (29.7)	
Median [IQR]	10 [6-15]	5 [3-11]	**<0.001**
Size of personal network (No. of men)			0.14
10	23 (25.6)	23 (35.9)	
11-50	40 (44.4)	30 (46.9)	
51	27 (30.0)	11 (17.2)	
Median [IQR]	35 [10-80]	16 [10-38]	**0.02**
No. of men had receptive sex in past year			0.10
None	14 (15.9)	19 (30.7)	
1-6	57 (64.8)	33 (53.2)	
7+	17 (19.3)	10 (16.1)	
Median [IQR]	3 [1-6]	3 [0-5]	0.21
Sexual positioning in past year			**0.04**

Baseline Characteristics	HIV+ n=90 No. (%)	HIV- n=64 No. (%)	P*
Insertive only	14 (15.6)	19 (29.7)	
Any receptive	76 (84.4)	45 (70.3)	
Receptive sex and condom use in past year			**0.02**
No receptive sex	12 (13.5)	19 (30.2)	
Always condoms	33 (37.1)	25 (39.7)	
Inconsistent condoms	44 (49.4)	19 (30.2)	
Any female sexual partners in past year			0.54
No	41 (45.6)	26 (40.6)	
Yes	49 (54.4)	37 (59.4)	
Concurrency in past year			0.41
None	22 (24.4)	14(21.9)	
Men only	42 (46.7)	25 (39.1)	
Both men and women	26 (28.9)	25 (39.1)	
Rectal gonorrhea			0.93
Neg	63 (74.1)	47 (73.4)	
Pos	22 (25.9)	17 (26.6)	
Rectal chlamydia			0.87
Neg	69 (86.3)	52 (85.3)	
Pos	11 (13.8)	9 (14.8)	
Anal warts			**<0.01**
No	73 (82.0)	62 (96.9)	
Yes	16 (18.0)	2 (3.1)	
Any HPV type			**<0.001**
No	1 (1.1)	22 (34.4)	
Yes	89 (98.9)	42 (65.6)	
Any HR-HPV types[†]			**<0.001**
No	8 (8.9)	38 (59.4)	
Yes, a 9-valent type	21 (23.3)	12 (18.8)	
Yes, a non-vaccine type	61 (67.8)	14(21.9)	

Note: No=number; IQR=interquartile range; Neg=negative; Pos=positive; HR-HPV=high-risk human papillomavirus; *P*=p-value

* Pearson's chi-square test for categorical variables and Wilcoxon rank sum test for continuous variables

[†]9-valent HPV vaccine types [16/18/31/33/45/52/58] and non-vaccine types [35,39,51,56,59,68]

Table 2

Characteristics and factors associated with high-risk HPV (HR-HPV) among Nigerian MSM

	Total	HR-HPV+	%	P*	Crude PR (95% CI) **
Total	154	110	70.0		
HIV				<0.001	
Neg	64	26	40.6		Ref.
Pos	90	82	91.1		**2.24 (1.65-3.04)**
Age (years)				0.01	
16-19	21	9	42.9		**0.57 (0.34-0.95)**
20-29	104	78	75.0		Ref.
30-38	29	21	72.4		0.97 (0.75-1.24)
Education				0.23	
Primary	11	9	81.8		1.28 (0.93-1.76)
Secondary	86	55	64.0		Ref.
Tertiary	53	40	75.5		1.18 (0.95-1.47)
Marital status				0.12	
Never	130	88	67.7		Ref.
Ever	24	20	83.3		1.23 (0.99-1.53)
Religion				0.83	
Christian/Protestant	118	82	69.5		Ref.
Muslim/Other	35	25	71.4		1.03 (0.81-1.31)
Sexual Orientation				0.67	
Bisexual	106	73	68.9		Ref.
Homosexual	47	34	72.3		1.05 (0.84-1.31)
Age at anal sexual debut (years)				0.31	
12	46	36	78.3		1.15 (0.93-1.42)
13-18	87	59	67.8		Ref.
19-27	21	13	61.9		0.91 (0.63-1.32)
Number of years since first anal sex				<0.01	
0-9	90	54	60.0		Ref.
10-26	64	54	84.4		**1.40 (1.15-1.72)**

	Total	HR-HPV+	%	P*	Crude PR (95% CI) **
Total	**154**	**110**	**70.0**		
Size of personal network (No. of men)				**0.02**	
10	46	26	56.5		Ref.
11-50	70	50	71.4		1.26 (0.94-1.70)
51	38	32	84.2		**1.49 (1.11-1.99)**
No. of men had receptive sex‡				0.08	
None	33	18	54.6		Ref.
1-6	90	66	73.3		1.34 (0.96-1.88)
7+	27	21	77.8		1.43 (0.98-2.07)
Sexual positioning‡				**0.03**	
Insertive only	33	18	54.6		Ref.
Any receptive	121	90	74.4		1.36 (0.98-1.90)
Receptive sex and condom use‡				0.09	
No receptive sex	31	17	54.8		Ref.
Always condoms	58	42	72.4		1.32 (0.92-1.89)
Inconsistent condoms	63	48	76.2		1.39 (0.98-1.97)
Any female sexual partners‡				**0.01**	
No	67	54	80.6		Ref.
Yes	87	54	62.1		**0.77 (0.63-0.94)**
Concurrency‡				**0.02**	
None	36	23	63.9		Ref.
Men only	67	55	82.1		1.28 (0.98-1.68)
Both men and women	51	30	58.8		0.92 (0.66-1.29)
Rectal gonorrhea				0.62	
Neg	110	78	70.9		Ref.
Pos	39	26	66.7		0.94 (0.73-1.21)
Rectal chlamydia				0.52	
Neg	121	82	67.8		Ref.
Pos	20	15	75.0		1.11 (0.83-1.47)
Anal warts†				0.19	

	Total	HR-HPV+	%	P^*	Crude PR (95% CI) **
Total	**154**	**110**	**70.0**		
No	135	92	68.2		Ref.
Yes	18	15	83.3		1.22 (0.96-1.55)

Note: HPV=human papillomavirus; MSM=men who have sex with men; Neg=negative; No.=number; IQR=interquartile range; PR=Prevalence Ratio; CI=Confidence Intervals; Ref.=reference category; *P*=p-value.

*
Pearson's chi-square test

**
Poisson regression model

‡
reported in past year

Table 3

Multivariate Poisson regression analysis of characteristics and factors associated with high-risk HPV (HR-HPV) among MSM in Nigeria

Variable	aPR (95% CI)
HIV	
Neg	Ref.
Pos	**2.02 (1.49-2.72)**
Years since first anal sex	
0-9	Ref.
10-26	**1.26 (1.07-1.49)**
Sexual positioning[†]	
Insertive only	Ref.
Any receptive	1.26 (0.91-1.73)
Concurrency[†]	
None	Ref.
Men only	**1.32 (1.04-1.67)**
Both men and women	1.00 (0.76-1.31)
Size of personal network (No. of MSM)[‡]	1.00 (1.00-1.00)

Note: HPV=human papillomavirus; MSM=men who have sex with men; aPR=adjusted prevalence ratio; CI=confidence intervals; Neg=negative; Pos=positive; No.=number; Ref.= reference category.

[†]reported in past year

[‡]continuous variable