

## Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

---

Leah Beth Loerinc

---

Date

**Factors Associated with High Grade Anal Dysplasia Among Young MSM and TW with HIV in  
Atlanta**

By

Leah Loerinc  
Master of Public Health

Epidemiology

---

Kristin M. Wall, PhD  
Committee Chair

**Factors Associated with High Grade Anal Dysplasia Among Young MSM and TW with HIV in Atlanta**

By

Leah Loerinc

B.A. Biology  
Brown University  
2015

Thesis Committee Chair: Kristin M. Wall, PhD

An abstract of  
A thesis submitted to the Faculty of the  
Rollins School of Public Health of Emory University  
in partial fulfillment of the requirements for the degree of  
Master of Public Health  
in Epidemiology  
2022

## Abstract

### Factors Associated with High Grade Anal Dysplasia Among Young MSM and TW with HIV in Atlanta

By Leah Loerinc

Men who have sex with men (MSM) and transgender women (TW) with HIV are disproportionately affected by anogenital human papillomavirus (HPV) infection with high rates of anal intraepithelial neoplasia (AIN) and subsequent anal cancer. However, there are no national guidelines for anal cancer screening and vaccination rates among men and TW remain low. There is a need to understand risk factors for high-grade anal dysplasia to better inform screening guidelines and preventative measures in these groups. In this study, we evaluated factors associated with high-grade anal dysplasia on anal biopsy among young MSM and TW with HIV in Atlanta, GA. Cross-sectional retrospective chart review was conducted for all cisgender MSM and TW with HIV aged 13-25 at the Grady Ponce and Family Youth Clinic in Atlanta, GA from 2009-2020. Participants who underwent anal biopsy over the study period were included. Data were collected on patient characteristics, sexual history, and anal histology results, with high-grade anal dysplasia defined as AIN 2, 3, or anal carcinoma. Associations between clinical and demographic factors with high-grade anal dysplasia were estimated using logistic regression. Adjusted odds ratios (aORs) and 90% confidence intervals (CIs) are reported. Statistical significance was assessed at the 0.10 alpha-level. 103 MSM and TW with HIV were included. The mean age was 19.7 (SD:  $\pm 1.9$ ) years. 91% were Black and 98% were horizontally infected with HIV. 63% of participants had high-grade anal dysplasia on anal biopsy. Being incompletely or unvaccinated against HPV (0-2 doses) relative to being fully vaccinated (3 doses) (aOR 5.34, 90%CI 1.30-21.93,  $p=0.05$ ) and having ever received surgical treatment for anogenital HPV (aOR 2.59, 90%CI 1.18-5.66,  $p=0.05$ ) were associated with high-grade anal dysplasia, controlling for age and CD4 T-cell count at time of biopsy. Our study found a high prevalence of high-grade anal dysplasia on anal biopsy among young MSM and TW with HIV. Those who had ever received surgical treatment for anogenital HPV and those who were incompletely or unvaccinated against HPV were more likely to have high-grade disease. To our knowledge, this is the first study to show an association between vaccination status and high-grade anal dysplasia in this population. Our data emphasize the urgent need to improve HPV vaccination efforts and to pursue larger surveillance studies of high-grade anal disease among young MSM and TW with HIV.

**Factors Associated with High Grade Anal Dysplasia Among Young MSM and TW with HIV in Atlanta**

By

Leah Loerinc

B.A. Biology  
Brown University  
2015

Thesis Committee Chair: Kristin M. Wall, PhD

A thesis submitted to the Faculty of the  
Rollins School of Public Health of Emory University  
in partial fulfillment of the requirements for the degree of  
Master of Public Health  
in Epidemiology  
2022

### **Acknowledgements**

I would like to express my deepest appreciation to my committee chair, Kristin Wall, for her incredible guidance and support throughout the data analysis and thesis writing phases of this process. I would also like to thank Amy Scheel, Amelia Thompson, Scott Gillespie, Molly McCallum, Lisa Flowers, and Andres Camacho-Gonzalez for their help with project conceptualization and data collection.

**Table of Contents**

<b>Chapter I: Literature Review</b> .....	8
<b>Chapter II: Manuscript</b>	
Abstract .....	10
Introduction .....	11
Methods .....	12
Results .....	15
Discussion .....	16
<b>References</b> .....	20
<b>Tables and Figures</b> .....	23

## Literature Review

Adolescents and young adults (AYAs) are disproportionately affected by sexually transmitted infections (STIs) in the United States (US), with half of all new STIs diagnosed each year occurring in individuals aged 15-24.<sup>1</sup> AYAs with HIV are at further risk of additional STIs<sup>2-5</sup> yet continue to engage in high-risk sexual activity.<sup>3, 6, 7</sup> HIV and STI co-infection has been associated with high HIV viral loads and lower CD4 T-cell counts,<sup>8, 9</sup> in addition to an increased risk of HIV and STI transmission.<sup>10-13</sup>

Anogenital human papillomavirus (HPV) infection is common among individuals with HIV in the US,<sup>14</sup> especially among AYAs younger than age 25.<sup>15-17</sup> Men who have sex with men (MSM) and transwomen (TW) with HIV are disproportionately affected by anogenital HPV,<sup>18-20</sup> even when compared to their HIV-negative counterparts.<sup>21</sup> Furthermore, it is well documented that MSM and TW with HIV have high rates of high-risk HPV (HR-HPV) infection,<sup>22, 23</sup> which is known to persist in these groups.<sup>17, 24</sup> Persistent anogenital infection with HR-HPV types increases the risk of anal intraepithelial lesions (ASIL)<sup>25</sup>, particularly high-grade intraepithelial lesions (HSIL),<sup>18</sup> and subsequent anal cancer.<sup>26, 27</sup> MSM and TW with HIV have the highest burden of anal cancer in the US, with documented rates as much as 30-100 times higher than the general population.<sup>23, 27-29</sup> However, there are no national guidelines for anal cancer screening in this group.<sup>29, 30</sup>

Elucidating factors that may be associated with high-grade anogenital disease in young MSM and TW with HIV, such as HPV vaccination status, CD4 T-cell count at time of biopsy, smoking status, or number of co-STIs would have a profound impact on the care of these patients by



informing screening guidelines and preventative measures in this population. We aimed to describe the distribution of anal cytology and histology results among young MSM and TW with HIV in Atlanta, GA, in addition to evaluating factors associated with high-grade anal dysplasia in these groups.

## Abstract

### Background

Men who have sex with men (MSM) and transgender women (TW) with HIV are disproportionately affected by anogenital human papillomavirus (HPV) infection with high rates of anal intraepithelial neoplasia (AIN) and subsequent anal cancer. However, there are no national guidelines for anal cancer screening and vaccination rates among men and TW remain low. There is a need to understand risk factors for high-grade anal dysplasia to better inform screening guidelines and preventative measures in these groups. In this study, we evaluated factors associated with high-grade anal dysplasia on anal biopsy among young MSM and TW with HIV in Atlanta, GA.

### Methods

Cross-sectional retrospective chart review was conducted for all cisgender MSM and TW with HIV aged 13-25 at the Grady Ponce and Family Youth Clinic in Atlanta, GA from 2009-2020. Participants who underwent anal biopsy over the study period were included. Data were collected on patient characteristics, sexual history, and anal histology results, with high-grade anal dysplasia defined as AIN 2, 3, or anal carcinoma. Associations between clinical and demographic factors with high-grade anal dysplasia were estimated using logistic regression. Adjusted odds ratios (aORs) and 90% confidence intervals (CIs) are reported. Statistical significance was assessed at the 0.10 alpha-level.

### Results

103 MSM and TW with HIV were included. The mean age was 19.7 (SD:  $\pm 1.9$ ) years. 91% were Black and 98% were horizontally infected with HIV. 63% of participants had high-grade anal dysplasia on anal biopsy. Being incompletely or unvaccinated against HPV (0-2 doses) relative to being fully vaccinated (3 doses) (aOR 5.34, 90%CI 1.30-21.93,  $p=0.05$ ) and having ever received surgical treatment for anogenital HPV (aOR 2.59, 90%CI 1.18-5.66,  $p=0.05$ ) were associated with high-grade anal dysplasia, controlling for age and CD4 T-cell count at time of biopsy.

### Conclusion

Our study found a high prevalence of high-grade anal dysplasia on anal biopsy among young MSM and TW with HIV. Those who had ever received surgical treatment for anogenital HPV and those who were incompletely or unvaccinated against HPV were more likely to have high-grade disease. To our knowledge, this is the first study to show an association between vaccination status and high-grade anal dysplasia in this population. Our data emphasize the urgent need to improve HPV vaccination efforts and to pursue larger surveillance studies of high-grade anal disease among young MSM and TW with HIV.

## Introduction

Adolescents and young adults with HIV are disproportionately affected by sexually transmitted infections (STIs) in the United States (US).<sup>1</sup> Anogenital human papillomavirus (HPV) infection is particularly common, demonstrated by consistently high rates of abnormal cytology in this group.<sup>4, 15-17, 31</sup> Men who have sex with men (MSM) and transgender women (TW) with HIV are particularly impacted by anogenital HPV infection,<sup>18-20</sup> even when compared to MSM and TW who are HIV-negative.<sup>21</sup>

It is well documented that MSM and TW with HIV have high rates of high-risk HPV (HR-HPV) infection,<sup>22, 23</sup> which is known to persist in these groups.<sup>17, 24</sup> Persistent anogenital infection with HR-HPV types increases the risk of anal intraepithelial lesions (ASIL)<sup>25</sup>, particularly high-grade intraepithelial lesions (HSIL)<sup>18</sup> and anal intraepithelial neoplasia (AIN).<sup>4, 24</sup> Furthermore, MSM and TW with HIV remain the highest risk group for developing anal cancer in the US,<sup>26, 27</sup> with documented rates as much as 30-100 times higher than the general population.<sup>23, 27-29</sup> Silverberg et al. found that the incidence of anal cancer among MSM with HIV was nearly three times higher than that in other men with HIV, and more than 65 times higher than men who were HIV-negative.<sup>32</sup>

Despite exceedingly high rates of HSIL, AIN, and anal cancer among MSM and TW with HIV, there are no national guidelines for anal cancer screening in these groups.<sup>29, 30</sup> The timing and frequency of anal cytology remains controversial,<sup>27, 33</sup> and follow-up of abnormal anal cytology or positive HR-HPV testing with high-resolution anoscopy (HRA) and biopsy is recommended yet

underutilized.<sup>18, 29, 34-36</sup> Furthermore, preventative measures of anogenital HPV infection in this population are suboptimal. While the HPV vaccine has been routinely recommended for boys since 2011,<sup>37</sup> only half of boys aged 13-17 were fully vaccinated in 2019.<sup>38</sup> However, the HPV vaccine has been shown to be effective in reducing high-grade AIN and anal cancer in young MSM.<sup>39</sup> It is imperative to understand risk factors for high-grade anal dysplasia to better inform screening guidelines and preventative measures in these groups.

In this cross-sectional study, we aimed to 1) determine the prevalence and distribution of abnormal anal cytology and histology among young MSM and TW with HIV in Atlanta, GA and 2) to evaluate factors associated with high-grade anal dysplasia on anal biopsy in this population.

## **Materials and Methods**

### Study participants

Retrospective chart review was conducted on all cisgender men and TW at the Grady Ponce and Family Youth Clinic (GPFYC), an exclusive HIV care clinic and the primary referral site for youth with HIV in Atlanta, GA, from January 1, 2009 to March 31, 2020. All cisgender men and TW with HIV aged 13-25 who self-identified as having sex with men, had at least once visit to GPFYC over the study period, and underwent anal biopsy were included. Anal biopsies were completed in HRA clinic or in the operating room during follow-up evaluation for an abnormal anal pap smear. Indication for biopsy was determined by the individual provider based on the extent of abnormality visualized at the time of follow-up. Patients who self-identified as not yet having

their sexual debut, in addition to those who did not self-report sex with men, were excluded.

This study received approval from the Institutional Review Boards of both Emory University and Grady Health System prior to initiation.

### Data collection

All data were collected using the electronic medical record (Epic) and entered directly into REDCap, a standardized online research database hosted at Emory University.<sup>40</sup> Data were collected on patient demographics and clinical characteristics, HIV infection, sexual history, HPV vaccination status, treatment history of anogenital HPV infection, and anal cytology and histology samples received. Additional STIs for each participant occurring within 3-months before or after their anal biopsy date were recorded, including infections with *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, syphilis, herpes simplex virus, trichomonas, hepatitis C, lymphogranuloma venereum, bacterial vaginosis, and chancroid. CD4 T-cell count at time of biopsy was also collected.

### Outcome and exposures of interest

High-grade anal dysplasia, defined as AIN 2, 3, or anal carcinoma on anal biopsy (staged by trained attending pathologists at GPFYC), was our outcome of interest. Those with AIN 1 or no intraepithelial lesions noted on anal biopsy were considered to have low-grade anal dysplasia. Categorical exposures of interest included race (black vs. other), gender (cisgender man vs. transgender woman), sexuality (gay vs. other), mode of HIV transmission (horizontal vs. vertical), history of tobacco use (yes vs. no), HPV vaccination status (incomplete (0, 1, or 2

doses) vs. complete (3 doses)), history of anogenital condyloma (yes vs. no), condom use (always or inconsistent vs. never), number of sexual partners at baseline (0-20 vs. >20), history of transactional sex (yes vs. no), history of sexual abuse (yes vs. no), history of receptive anal sex (yes vs. no), ever receiving medical treatment for anogenital HPV (yes vs. no) and ever receiving surgical treatment for anogenital HPV (yes vs. no). Of note, HPV vaccination status was originally looked at in three groups (3-doses, 1-2-doses, and 0-doses); however, due to relatively small sample sizes in each category, 0-, 1-, and 2-doses were combined into one group. Continuous exposures of interest included age at first observation, CD4 T-cell count at time of biopsy, and number of co-STIs diagnosed within 3-months before or after participants' biopsy.

#### Statistical analysis

All demographic and clinical criteria were summarized using means and standard deviations (SD) for normally distributed continuous variables (age at first observation and CD4 T-cell count at time of biopsy), medians and interquartile ranges for non-normally distributed continuous variables (co-STIs within 3-months before or after biopsy), and frequencies and percentages for discrete characteristics, both for the entire study population in addition to by outcome designation. Chi-squared or Fisher's exact tests for categorical variables, Student's t-tests for normally distributed continuous variables, and Wilcoxon Mann-Whiney U-tests for non-normally distributed continuous variables were used for each covariate in relation to the outcome of interest with 2-tail *p*-values reported. Association of clinical and demographic factors with high-grade anal dysplasia were analyzed using univariate and multivariate logistic

regression. Univariate analysis was performed on all covariates, while the multivariate logistic regression model, based on *a priori* criteria and results of the univariate analysis, included age (per year increase), CD4 T-cell count at time of biopsy (per cell/ $\mu$ L increase), vaccination status (incomplete vs. complete), and having ever received surgical treatment for anogenital HPV infection (yes vs. no). Crude odds ratios (cORs) and adjusted odds ratios (aORs) with associated 90% confidence intervals (CI) are reported. All statistical analyses were conducted in SAS v.9.4. (Cary, NC) and statistical significance was assessed at the 0.10 alpha level.

## Results

A total of 103 MSM and TW with HIV who received anal biopsies during the study period were included in analysis. Patient demographics and baseline characteristics, both for the entire group and by outcome designation, are demonstrated in **Table 1**. The mean age at first observation was 19.7 (SD:  $\pm$  1.9) years. The majority were cisgender men (n=100, 97%), Black (n=94, 91%), and horizontally infected with HIV (n=101, 98%). Twelve participants (12%) were completely vaccinated against HPV (3-dose series) and 67 (65%) had ever received surgical treatment for anogenital HPV infection.

Of the 103 MSM and TW included, 97 (94%) received a valid anal pap smear over the study period. Of these, the most common results on initial pap smear were low-grade anal intraepithelial lesion (LSIL, n=43, 42%) and atypical squamous cells of undetermined significance (ASCUS, n=33, 32%) (**Table 2**). **Figure 1** demonstrates the distribution of anal biopsy

results for all 103 participants. The majority (n=65, 63%) had high-grade anal dysplasia, including AIN 2, AIN 3, carcinoma in-situ, and squamous cell carcinoma.

Univariate logistic regression of all covariates is highlighted in **Table 3**. Age (cOR: 1.33, CI: 1.09–1.63, *p*-value 0.017), CD4 T-cell count at time of biopsy (cOR: 0.99, CI: 0.99–1.00, *p*-value 0.098), having ever received surgical treatment for anogenital HPV infection (cOR: 3.40, CI: 1.67–6.95, *p*-value 0.005), and being incompletely or unvaccinated against HPV (cOR: 11.25, CI: 2.98–42.44, *p*-value 0.003) were all significantly associated with high-grade anal dysplasia on anal biopsy.

A multivariate logistic regression model was built including age (per year increase), CD4 T-cell count at time of biopsy (per cell/ $\mu$ L increase), vaccination status (incomplete vs. complete), and surgical treatment for anogenital HPV infection (yes vs. no). Results are highlighted in **Table 4**. When controlling for age and CD4-T cell count at time of biopsy, having ever received surgical treatment for anogenital HPV infection (aOR: 2.59, CI: 1.18–5.66, *p*-value 0.046) and being incompletely or unvaccinated against HPV relative to being fully vaccinated (aOR: 5.34, CI: 1.30–21.93, *p*-value 0.051) were strongly associated with high-grade anal dysplasia on anal biopsy.

## Discussion

To our knowledge, this is the first study to evaluate risk factors for high-grade anal dysplasia on anal biopsy among young MSM and TW living with HIV. Our study population was



predominantly Black, cisgender MSM who were horizontally infected with HIV, reflecting the current HIV epidemic in the US.<sup>41</sup> HPV infection and anogenital dysplasia remain highly prevalent among MSM and TW with HIV, with many individuals having persistent and progressive disease.<sup>21</sup> Furthermore, MSM and TW with HIV continue to be the highest risk group for developing anal cancer,<sup>23,32</sup> yet no national screening guidelines exist.<sup>29</sup> It is imperative to further characterize risk factors for high-grade anal dysplasia to better inform screening practices and preventative measures in these groups.

Data published earlier this year on all sexually active youth with HIV in Atlanta demonstrated that HPV was the most common incident STI, with an overall incidence rate of 19.38 cases per 100 person years.<sup>31</sup> The overwhelming majority of our cohort had an abnormal pap smear at baseline, with LSIL and ASCUS being the most common diagnoses (42% and 32%, respectively). This is consistent with previously reported data on this group of young MSM and TW with HIV in Atlanta,<sup>4</sup> in addition to other reports in the literature.<sup>16,20</sup> Furthermore, 63% had high-grade disease on anal biopsy, indicating clinically advanced anogenital disease in the majority of our cohort. Previous studies of MSM and TW in the literature reveal a similar burden of high-grade disease.<sup>14,19,24</sup> However, risk factors for developing high-grade dysplasia in these groups remain poorly understood.

Multivariate logistic regression analysis on our cohort revealed having ever received surgical treatment for anogenital HPV and being incompletely or unvaccinated against HPV were associated with high-grade anal dysplasia on anal biopsy when controlling for age and CD4 T-

cell count at time of the procedure (aOR: 2.59, CI: 1.18–5.66 and aOR: 5.34, CI: 1.30–21.93, respectively). Participants in our study received surgical treatment predominantly for treatment or removal of extensive anal condyloma. Extensive anal condyloma, when present, may be useful in identifying who is at highest risk for developing high-grade anal dysplasia and prompt earlier referral for biopsy.

Furthermore, our study demonstrated that individuals who were incompletely or unvaccinated against HPV were more likely to have high-grade disease on anal biopsy. This is both intuitive and congruent with the literature. A large, randomized, double-blind clinical trial assessing the safety and effectiveness of the quadrivalent HPV vaccine in MSM showed the vaccine successfully reduced both persistent anal infection with HR-HPV types and rates of high-grade AIN in study participants.<sup>39</sup> Additionally, Nyitray et al. found that 93% of MSM with HIV in their cohort were infected with at least one HR-HPV type, and 92% had at least one type found in the 9-valent vaccine.<sup>22</sup> Our data, combined with other reports in the literature, suggest an urgent need to prioritize and increase HPV vaccination efforts among young MSM and TW living with HIV. Additionally, those who remain incompletely or unvaccinated should be monitored closely for anal dysplasia through early referral for anal biopsy.

There are several limitations in our study. First, because this study was retrospective in nature, we were limited to information already documented in the medical chart. Therefore, several exposures had occasional missing values. Second, this study was conducted at a single HIV care center and included predominantly young Black MSM living with HIV, which may limit

generalizability to other populations. Lastly, and importantly, this study was done on a small sample size. Many exposures of interest had few observations, including vaccination status. There is a need for further studies with larger sample sizes to validate the association between vaccination status and high-grade anal dysplasia in young MSM and TW with HIV.

In conclusion, young MSM and TW with HIV in Atlanta have a high prevalence of high-grade anal dysplasia on anal biopsy. Furthermore, those who had ever received surgical treatment for anogenital HPV infection and those who were incompletely or unvaccinated against HPV were more likely to have high-grade disease. Our data emphasize the urgent need to improve HPV vaccination efforts and pursue larger surveillance studies of high-grade anal dysplasia among young MSM and TW with HIV.

## References

1. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2019. Atlanta: U.S. Department of Health and Human Services; 2021.
2. Brownstein PS, Gillespie SE, Leong T, Chahroudi A, Chakraborty R, Camacho-Gonzalez AF. The association of uncontrolled HIV infection and other sexually transmitted infections in metropolitan Atlanta youth. *Pediatr Infect Dis J*. 2015;34:e119-124.
3. Rieg G, Lewis RJ, Miller LG, Witt MD, Guerrero M, Daar ES. Asymptomatic sexually transmitted infections in HIV-infected men who have sex with men: prevalence, incidence, predictors, and screening strategies. *AIDS Patient Care STDS*. 2008;22:947-954.
4. Thompson AB, Gillespie SE, Mosunjac MB, Hussen SA, Flowers LC, Camacho-Gonzalez AF. Prevalence of Anal Squamous Intraepithelial Lesions in HIV-1-Infected Young Men Who Have Sex With Men and Transwomen. *J Low Genit Tract Dis*. 2018;22:340-347.
5. Kalichman SC, Pellowski J, Turner C. Prevalence of sexually transmitted co-infections in people living with HIV/AIDS: systematic review with implications for using HIV treatments for prevention. *Sex Transm Infect*. 2011;87:183-190.
6. Weiser J, Tie Y, Beer L, Pearson WS, Shouse RL. Receipt of Prevention Services and Testing for Sexually Transmitted Diseases Among HIV-Positive Men Who Have Sex With Men, United States. *Ann Intern Med*. 2020.
7. Koenig LJ, Pals SL, Chandwani S, et al. Sexual transmission risk behavior of adolescents With HIV acquired perinatally or through risky behaviors. *J Acquir Immune Defic Syndr*. 2010;55:380-390.
8. Mullins TLK, Li SX, Bethel J, Goodenow MM, Hudey S, Sleasman JW. Sexually transmitted infections and immune activation among HIV-infected but virally suppressed youth on antiretroviral therapy. *J Clin Virol*. 2018;102:7-11.
9. Buchacz K, Patel P, Taylor M, et al. Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. *Aids*. 2004;18:2075-2079.
10. Ward H, Rönn M. Contribution of sexually transmitted infections to the sexual transmission of HIV. *Curr Opin HIV AIDS*. 2010;5:305-310.
11. Cohen MS, Hoffman IF, Royce RA, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDS CAP Malawi Research Group. *Lancet*. 1997;349:1868-1873.
12. Johnson LF, Lewis DA. The effect of genital tract infections on HIV-1 shedding in the genital tract: a systematic review and meta-analysis. *Sex Transm Dis*. 2008;35:946-959.
13. McCoy SI, Eron JJ, Kuruc JD, et al. Sexually transmitted infections among patients with acute HIV in North Carolina. *Sex Transm Dis*. 2009;36:372-374.
14. Gaisa M, Sigel K, Hand J, Goldstone S. High rates of anal dysplasia in HIV-infected men who have sex with men, women, and heterosexual men. *Aids*. 2014;28:215-222.
15. Camacho-Gonzalez AF, Chernoff MC, Williams PL, et al. Sexually Transmitted Infections in Youth With Controlled and Uncontrolled Human Immunodeficiency Virus Infection. *J Pediatric Infect Dis Soc*. 2017;6:e22-e29.

16. Coromilas A, Brozovich A, Nelson J, Neu N. Epidemiology and Prevalence of Abnormal Results for Anal Cytology Screening in HIV-Infected Young Men Who Have Sex with Men. *LGBT Health*. 2014;1:58-61.
17. Glick SN, Feng Q, Popov V, Koutsky LA, Golden MR. 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.
18. Sambursky JA, Terlizzi JP, Goldstone SE. Testing for Human Papillomavirus Strains 16 and 18 Helps Predict the Presence of Anal High-Grade Squamous Intraepithelial Lesions. *Dis Colon Rectum*. 2018;61:1364-1371.
19. Kobayashi T, Sigel K, Gaisa M. Prevalence of Anal Dysplasia in Human Immunodeficiency Virus-Infected Transgender Women. *Sex Transm Dis*. 2017;44:714-716.
20. Sendagorta E, Herranz P, Guadalajara H, et al. Prevalence of abnormal anal cytology and high-grade squamous intraepithelial lesions among a cohort of HIV-infected men who have sex with men. *Dis Colon Rectum*. 2014;57:475-481.
21. D'Souza G, Wentz A, Wiley D, et al. Anal Cancer Screening in Men Who Have Sex With Men in the Multicenter AIDS Cohort Study. *J Acquir Immune Defic Syndr*. 2016;71:570-576.
22. Nyitray AG, Fujimoto K, Zhao J, Giuliano AR, Schneider JA, Hwang LY. Prevalence of and Risk Factors for Anal Human Papillomavirus Infection in a Sample of Young, Predominantly Black Men Who Have Sex With Men, Houston, Texas. *J Infect Dis*. 2018;217:777-784.
23. Patel P, Bush T, Kojic EM, et al. Prevalence, Incidence, and Clearance of Anal High-Risk Human Papillomavirus Infection Among HIV-Infected Men in the SUN Study. *J Infect Dis*. 2018;217:953-963.
24. 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.
25. Darwich L, Cañadas MP, Videla S, et al. Prevalence, clearance, and incidence of human papillomavirus type-specific infection at the anal and penile site of HIV-infected men. *Sex Transm Dis*. 2013;40:611-618.
26. Hoots BE, Palefsky JM, Pimenta JM, Smith JS. Human papillomavirus type distribution in anal cancer and anal intraepithelial lesions. *Int J Cancer*. 2009;124:2375-2383.
27. Krzowska-Firych J, Lucas G, Lucas C, Lucas N, Pietrzyk Ł. An overview of Human Papillomavirus (HPV) as an etiological factor of the anal cancer. *J Infect Public Health*. 2019;12:1-6.
28. Patel P, Hanson DL, Sullivan PS, et al. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992-2003. *Ann Intern Med*. 2008;148:728-736.
29. Wells JS, Holstad MM, Thomas T, Bruner DW. An integrative review of guidelines for anal cancer screening in HIV-infected persons. *AIDS Patient Care STDS*. 2014;28:350-357.
30. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1-137.

31. Loerinc L, Scheel A, Jordan-Thompson S, Gillespie S, Camacho-Gonzalez A. Incidence, Reinfection, and Discrepancy Between Sexual Practice and Anatomic Site Positivity of Sexually Transmitted Infections in Youth With HIV. *Pediatr Infect Dis J*. 2021.
32. Silverberg MJ, Lau B, Justice AC, et al. Risk of anal cancer in HIV-infected and HIV-uninfected individuals in North America. *Clin Infect Dis*. 2012;54:1026-1034.
33. Chin-Hong PV, Palefsky JM. Natural history and clinical management of anal human papillomavirus disease in men and women infected with human immunodeficiency virus. *Clin Infect Dis*. 2002;35:1127-1134.
34. Thompson MA, Horberg MA, Agwu AL, et al. Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2020.
35. Palefsky JM. Practising high-resolution anoscopy. *Sex Health*. 2012;9:580-586.
36. Palefsky JM. Screening to prevent anal cancer: Current thinking and future directions. *Cancer Cytopathol*. 2015;123:509-510.
37. Recommendations on the use of quadrivalent human papillomavirus vaccine in males--Advisory Committee on Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep*. 2011;60:1705-1708.
38. Elam-Evans LD, Yankey D, Singleton JA, et al. National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years - United States, 2019. *MMWR Morb Mortal Wkly Rep*. 2020;69:1109-1116.
39. Palefsky JM, Giuliano AR, Goldstone S, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. *N Engl J Med*. 2011;365:1576-1585.
40. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377-381.
41. Centers for Disease Control and Prevention. HIV Surveillance Report, 2019. Vol 32 May 2021.

## Tables and Figures

**Table 1: Demographic and Clinical Characteristics of Young MSM and TW with HIV by Anal Biopsy Result**

Characteristic	Total N=103		High-grade dysplasia <sup>1</sup> N=65		Low-grade dysplasia <sup>2</sup> N=38		p-value (2-tail)
	No.	%	No.	%	No.	%	
<b>Age at first observation (years), mean ± SD</b>	19.71 ± 1.89		20.06 ± 1.85		19.12 ± 1.83		0.014
<b>Race</b>							
Black	94	91	58	89	36	95	0.479
Other	9	9	7	11	2	5	
<b>Gender</b>							
Cisgender male	100	97	64	98	36	95	0.553
Transgender female	3	3	1	2	2	5	
<b>Sexuality, N=101</b>							
Gay	80	79	51	81	29	76	0.578
Other	21	21	12	19	9	24	
<b>Mode of HIV transmission</b>							
Horizontal	101	98	63	97	38	100	0.530
Vertical	2	2	2	3	0	0	
<b>History of tobacco use</b>							
Yes	38	37	24	37	14	37	0.993
No	65	63	41	63	24	63	
<b>Vaccination status</b>							
Complete (3-doses)	12	12	2	3	10	26	0.001
Not complete (0, 1, 2 doses)	91	88	63	97	28	74	
<b>History of anogenital condyloma</b>							
Yes	85	83	56	86	29	76	0.205
No	18	17	9	14	9	24	
<b>Condom use, N=93</b>							
Always	23	25	15	25	8	25	0.997
Inconsistent	61	66	40	66	21	66	
Never	9	10	6	10	3	9	
<b>Number of sexual partners at baseline, N=90</b>							
0-20	53	59	30	54	23	68	0.188
>20	37	41	26	46	11	32	
<b>History of transactional sex, N=50</b>							
Yes	15	30	11	33	4	24	0.474
No	35	70	22	67	13	76	
<b>History of sexual abuse, N=74</b>							

Yes	24	32	15	31	9	35	0.768
No	50	68	33	69	17	65	
<b>History of receptive anal sex, N=102</b>							
Yes	102	100	64	100	38	100	NA
No	0	0	0	0	0	0	
<b>CD4 count at time of biopsy (cells/<math>\mu</math>L), mean <math>\pm</math> SD, N=101</b>							
	441.93 $\pm$ 243.33		410.4 $\pm$ 241.7		494.1 $\pm$ 240.0		0.094
<b>Medical treatment for anogenital HPV ever</b>							
Yes	51	50	31	48	20	53	0.629
No	52	50	34	52	18	47	
<b>Surgical treatment for anogenital HPV ever</b>							
Yes	67	65	49	75	18	47	0.004
No	36	35	16	25	20	53	
<b>Number of co-STIs within 3-months of biopsy<sup>3</sup></b>							
Median (IQR)	0 (1.00)		1 (1.00)		0 (1.00)		0.159
By category							
0	54	52	30	46	24	63	0.084
1	34	33	25	38	9	24	
2	10	10	7	11	3	8	
3	3	3	3	5	0	0	
4	2	2	0	0	2	5	

Abbreviations: MSM, men who have sex with men; TW, transgender women; SD, standard deviation; HPV, human papillomavirus; co-STI, co-sexually transmitted infections; IQR, interquartile range

<sup>1</sup>High-grade anal dysplasia defined as anal intraepithelial lesion 2, 3, or anal carcinoma

<sup>2</sup>Low-grade anal dysplasia defined as anal intraepithelial lesion 1 or no intraepithelial lesion present

<sup>3</sup>Within 3-months before or after biopsy date



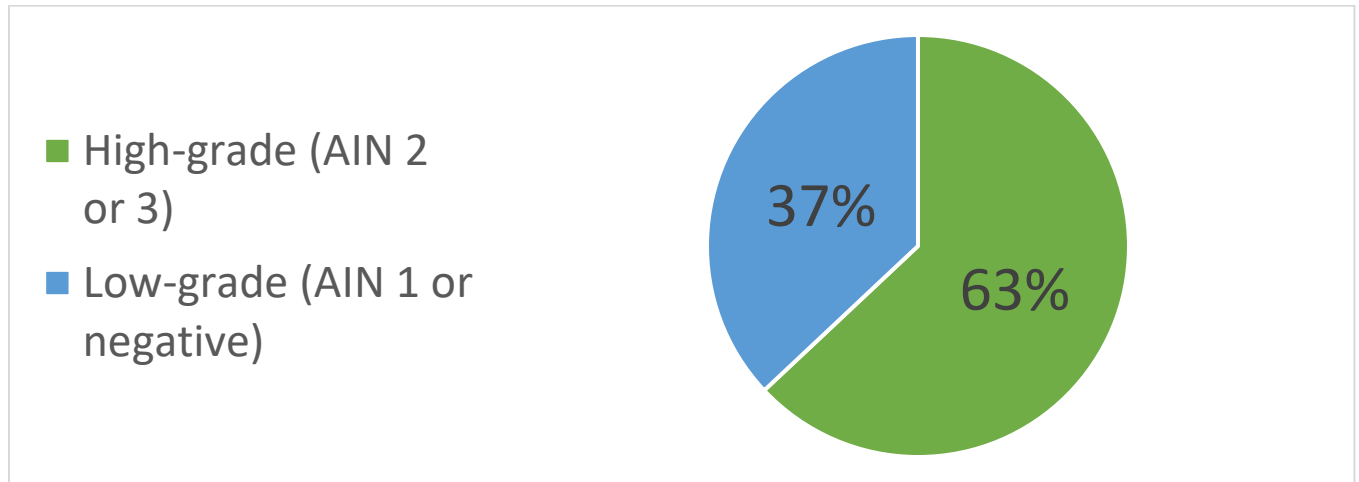
**Table 2: Anal Cytology Results on Initial Pap Smear Among Young MSM and TW with HIV**

	<b>No. (%)</b>
<b>Pap smear result</b>	N=103
LSIL	43 (41.75)
ASCUS	33 (32.04)
Negative	11 (10.68)
ASC-H	8 (7.77)
HSIL	2 (1.94)
None <sup>1</sup>	6 (5.83)

Abbreviations: MSM, men who have sex with men; TW, transgender women; LSIL, low-grade squamous intraepithelial lesion; ASCUS, atypical squamous cells of undetermined significance; ASC-H, atypical squamous cells, cannot rule out high-grade; HSIL, high-grade squamous intraepithelial lesion

<sup>1</sup>No valid pap smear obtained during the study period

**Figure 1: Distribution of Anal Biopsy Results Among Young MSM and TW with HIV**



Abbreviations: MSM, men who have sex with men; TW, transgender women; AIN, anal intraepithelial neoplasia

**Table 3: Unadjusted Associations Between Clinical Characteristics and High-Grade Anal Dysplasia on Anal Biopsy Among Young MSM and TW with HIV**

<b>Characteristic, N=103</b>	<b>Crude Odds Ratio (Exact 90% CI)</b>	<b>p-value (2-tail)</b>
<b>Age at first observation (per year increase)</b>	1.33 (1.09, 1.63)	0.017
<b>Race</b>		
Black vs. other	0.46 (0.12, 1.80)	0.350
<b>Gender</b>		
Cisgender male vs. TW	3.55 (0.46, 27.42)	0.307
<b>Sexuality</b>		
Gay vs. other	1.32 (0.58, 3.00)	0.579
<b>Mode of HIV transmission</b>		
Horizontal vs. vertical	0.00 (0.00, 999.99)	0.981
<b>History of tobacco use</b>		
Yes vs. no	1.00 (0.50, 2.01)	0.993
<b>Vaccination status (complete vs. not complete)</b>		
Not complete (0, 1, 2 doses) vs. complete (3-doses)	11.25 (2.98, 42.44)	0.003
<b>History of anogenital condyloma</b>		
Yes vs. no	1.93 (0.82, 4.57)	0.209
<b>Condom use</b>		
Always vs. never	0.94 (0.24, 3.68)	0.945
Inconsistent vs. never	0.95 (0.27, 3.31)	0.974
<b>Number of sexual partners at baseline</b>		
0-20 vs. >20	0.55 (0.26, 1.17)	0.191
<b>History of transactional sex</b>		
Yes vs. no	1.63 (0.53, 4.98)	0.476
<b>History of sexual abuse</b>		
Yes vs. no	0.859 (0.37, 2.01)	0.768
<b>CD4 count at time of biopsy (per cell/<math>\mu</math>L increase), N=101</b>	0.99 (0.99, 1.00)	0.098
<b>Medical treatment for anogenital HPV ever</b>		
Yes vs. no	0.82 (0.42, 1.61)	0.629
<b>Surgical treatment for anogenital HPV ever</b>		
Yes vs. no	3.40 (1.67, 6.95)	0.005
<b>Number of co-STIs within 3-months of biopsy (per 1 co-STI increase)<sup>1</sup></b>	1.19 (0.80, 1.75)	0.472

Abbreviations: MSM, men who have sex with men; TW, transgender women; CI, confidence interval

<sup>1</sup>Within 3-months before or after biopsy date

**Table 4: Adjusted Associations Between Clinical Characteristics and High-Grade Anal Dysplasia on Anal Biopsy Among Young MSM and TW with HIV**

<b>Characteristic, N=103</b>	<b>Adjusted Odds Ratio (Exact 90% CI)</b>	<b>p-value (2-tail)</b>
Age (per year increase)	1.22 (0.98, 1.53)	0.135
CD4 count at time of biopsy (per cell/ $\mu$ L increase)	1.00 (0.99, 1.00)	0.734
Vaccination status (not complete (0, 1, 2 doses) vs. complete (3-doses))	5.34 (1.30, 21.93)	0.051
Surgical treatment for anogenital HPV ever (yes vs. no)	2.59 (1.18, 5.66)	0.046

Abbreviations: MSM, men who have sex with men; TW, transgender women; CI, confidence interval; HPV, human papillomavirus