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Prevalence of anal squamous intraepithelial lesions in HIV-1 infected young men who have sex with men and transwomen

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Précis:

High-grade anal squamous intraepithelial lesions are more prevalent in HIV-1 infected young persons with high numbers of sexual partners

Introduction

The incidence of genital human papillomavirus (HPV) infection is high, up to 7,440 per 100,000 person-years, in HIV-infected youth in the United States [1]. While HPV infections often self-resolve, up to 69% of anal HPV persists after two years in men who have sex with men (MSM) [2]. Persistent anal infection with high-risk HPV types increases the risk of anal squamous intraepithelial lesions (ASIL) in HIV-infected MSM [3]. While HPV vaccination

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Contributors

ABT conceptualized and designed the study, collected and analyzed the data, and drafted the initial manuscript. MM performed the pathology analysis. SEG analyzed the data. AFCG and LF conceptualized and designed the study and helped edit the manuscript. ABT, SEG, MM, SH, LF, and AFCG reviewed and revised the manuscript, and approved the final manuscript as submitted.

Declaration of interests

IRB Status: Ethical approval for this study was obtained from the Emory University Institutional Review Board and the Grady Memorial Hospital research oversight committee.

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can reduce this risk [4], and has been recommended for boys since 2011 [5], vaccination completion rates remain poor [6]. Therefore, many HIV healthcare providers rely on secondary prevention of anal cancer with early detection and management of ASIL [7].

The epidemiology of cancer in HIV-infected persons has changed over time, with increased anal cancer incidence in the last 20 years [8]. HIV-infected MSM have the highest rates of invasive anal cancer (131 per 100,000 person-years), up to three times higher than other HIV-infected men (46 per 100,000 person-years), and 60–100 times higher than the general population (0–2 per 100,000 person-years) [8, 9]. Although the data are limited, one study suggests that the rate of histologic ASIL is at least as high in HIV-infected male-to-female transgender women (transwomen) as it is in HIV-infected MSM at 91% and 84% respectively [10]. There are no national guidelines for anal cancer screening, although experts recommend screening high-risk populations [7]. As a result, screening practices vary in age at initiation, type and frequency [7]. One commonly adopted screening method includes detecting abnormalities via anal cytology and confirming the diagnosis with high-resolution anoscopy (HRA)-guided or intra-operative biopsy [11]. This process rarely begins before age 25 years in HIV-infected men [12].

In the southern United States, the rates of HIV and other sexually transmitted infections (STIs) are disproportionately high in young black MSM and transwomen [13, 14]. Our study aims to characterize the prevalence and severity of abnormal anal cytology and histology in HIV-infected young MSM and transwomen in Atlanta, GA. We also aim to determine the demographic, behavioral and clinical factors associated with ASIL.

Methods

Setting

This single-center, retrospective study was conducted at a publicly-funded HIV clinic affiliated with a teaching hospital. The clinic is the primary referral center for HIV-infected youth in Atlanta, GA, and serves a diverse socioeconomic patient population. Informed consent was waived in accordance with institutional guidelines. Ethical approval for this study was obtained from the Emory University Institutional Review Board (IRB000–57152, 03/21/2019) and the Grady Memorial Hospital research oversight committee.

Subjects

We reviewed the medical records of young MSM and transwomen with HIV-1 infection and a history of sexual intercourse with a male. Subjects were included if they were 13 to 24 years of age at the time anal cytology was first obtained and attended the clinic between January 2009 and December 2016. A transwoman was defined as a male-to-female transgender woman who was receiving hormonal therapy.

Procedures

Sexually active young MSM and transwomen had previously undergone screening per the process outlined in Figure 1. Anal cytology samples were obtained by their regular HIV healthcare providers (medical doctors, physician assistants) according to the clinic's

standard operating procedures and as previously described in the literature [10]. For those with abnormal cytology, the decision to repeat anal cytology or refer for diagnostic anal tissue biopsy by a surgeon or a specialist in high-resolution anoscopy was made at the discretion of each provider. Samples for cytology and histology were evaluated by licensed clinical pathologists according to their standard operating procedures.

If an anal tissue sample was previously diagnosed as anal intraepithelial neoplasia 2 (AIN 2) prior to the routine use of p16 staining, it was retrieved and re-examined using p16 for adjudication of the AIN2 diagnosis [15]. Per our local histopathology protocol, serial sections cut at 5 microns were taken from these formalin-fixed paraffin-embedded specimens and stained with hematoxylin and eosin. Adjacent samples were then stained with p16 (clone D25, MAB4133, Millipore Sigma, Billerica, Massachusetts) at a single laboratory (Winship Cancer Institute Pathology laboratory, Atlanta GA). A licensed pathologist and a senior pathology resident independently examined the specimens to determine the diagnosis according to the Lower Anogenital Squamous Terminology Standardization Project (LAST) guidelines [15].

Data Collection

Demographic, behavioral, and clinical exposure data were abstracted from medical records and analyzed. Demographics included age, race, education level, employment, housing, gender identity such as cisgender male or transwoman, and gender of sex partners such as men only or both men and women. Self-reported behavioral data included drug, alcohol and tobacco use patterns; history and types of sexually transmitted infections (STIs); history of sexual abuse; participation in transactional sex, defined as the exchange of sex for payment or gifts, including but not limited to prostitution; type of anal intercourse defined as receptive, insertive or both; age at coitarche and lifetime number of sex partners of any gender. Information that was documented closest to the time of anal cytology was used for analysis.

As standard of care, clinic healthcare providers offered the HPV vaccine to all subjects 18 years of age or younger through the Centers for Disease Control and Prevention Vaccines for Children (VFC) program. Subjects between the ages of 19 and 24 were ineligible to receive the HPV vaccine free of charge in the clinic, but could complete the series at their local health department. HPV vaccination status at or before the time anal cytology was obtained was abstracted from the medical and state immunization records. Other clinical data included the presence or absence of anal condylomata (warts) on physical examination, CD4+ T-cell counts (CD4) and HIV quantitative RNA PCR or viral load (VL) at the time of HIV diagnosis (baseline), the first valid anal cytology test result, i.e. quantity and quality of specimen obtained was sufficient for analysis, and anal histology result. An undetectable VL (viral suppression) was defined as < 40 copies/mL.

The primary outcome of interest was ASIL as identified on histology: negative, histologic Low-grade Squamous Intraepithelial Lesion (hLSIL), or High-grade Squamous Intraepithelial Lesion (hHSIL). The secondary outcome was cytology interpretation defined as negative, Atypical Squamous Cells of Undetermined Significance (ASCUS), cytologic Low-grade Squamous Intraepithelial Lesion (cLSIL), Atypical Squamous Cells-cannot

exclude High-grade (ASC-H), or cytologic High-grade Squamous Intraepithelial Lesions (cHSIL).

Statistical Analysis

Statistical analyses were performed using SAS v9.4 (Cary, NC). Significance was evaluated two-sided at the 0.05 level. Demographic, behavioral and clinical characteristics were summarized using means and standard deviations, medians and interquartile ranges (IQR), or frequencies and percentages. One-way analysis of variance (ANOVA) and Chi-square tests of independence were employed to evaluate bivariate associations and identify risk factors between categories of squamous intraepithelial lesion on anal histology and cytology. For data with non-normal distribution or low frequency counts, we used non-parametric equivalents (Kruskal-Wallis and Fisher's exact tests, respectively). For clinical CD4 and VL variables, differences between categories of squamous intraepithelial lesion on anal histology and cytology were considered continuously using one-way ANOVA after square-root transformation for CD4, and nominally for HIV suppression (VL <40 versus VL ≥40) using Chi-square tests of independence. Interaction between categories of squamous intraepithelial lesion on anal histology and cytology for CD4 was assessed using two-way ANOVA. Unadjusted, pairwise post-hoc tests were reported whenever omnibus tests were significant. Cohen's *d* effect sizes were interpreted as small (≥0.2), moderate (≥0.5), and large (≥0.8), hereafter referred to as *d*.

Results

Baseline Characteristics

Table 1 delineates the baseline characteristics of our study population. Ninety-five percent identified as African-American. Among 314 subjects, the majority (99%) acquired HIV through sexual transmission. Most (98%) identified as cisgender male. We did not conduct a separate analysis to evaluate for unique risk factors in transwomen due to the low number of subjects, 7 (2%), in that group. Gender of sex partner was categorized as men only (76%) or men and women (24%). Drug use was frequently documented in our study population with marijuana use reported in 60% and tobacco use in 56%. Other illicit drug use was reported in 14% of subjects, and included cocaine, methamphetamines (meth, ecstasy or molly), benzodiazepines, and lysergic acid diethylamide (LSD or acid).

Behavioral data were incomplete due to the retrospective nature of the study design. However, sexual abuse or transactional sex histories were documented in 33% (75/229) and 20% (35/179) respectively of those with data. Of the 266 subjects who had a documented number of lifetime sexual partners, 41% had more than 20 partners. For those with reported data, the mean age at coitarche was 14.5 years (standard deviation (SD) 3.3 years), and 9% (23/246) reported coitarche before age 9 years. Most subjects (87%) had a history of any sexually transmitted infection (STI), while 51% (153/303) had a history of rectal STIs, including herpes simplex virus, gonorrhea, chlamydia, lymphogranuloma venereum and/or trichomonas. Examiners identified external anal warts in 45% (130/288) of subjects with data.

Almost 90% (272/314) of subjects had no documentation of HPV vaccine receipt, while 5% were identified as having completed the three-dose vaccine series. As documented by their healthcare providers, subjects identified the following barriers to HPV vaccine completion: HIV diagnosis and entry into care after age 18 years with ineligibility for the VFC program, long wait times at the health department and high cost of the HPV vaccine for persons without health insurance.

Prevalence and risk factors for abnormal anal cytology

Figure 1 outlines the process for anal cancer screening in our clinic. Of note, 314 subjects met inclusion criteria, and 267 of those had been screened with anal cytology. Providers obtained anal cytology more frequently from subjects who practiced any receptive anal intercourse (86%), than from those who reported exclusive insertive intercourse (58%). Two hundred and forty nine (93%) specimens with a valid result were obtained from screened subjects. The mean age at anal cytology testing was 20.7 years (SD 2 years, range 15–24 years).

Very few subjects had negative cytology tests (5%). Most had cLSIL (43%) or ASCUS (41%) (Table 2). Our analysis of the association between demographic, behavioral and clinical factors and cytology results is displayed in Table 3. The significant behavioral factors included number of lifetime sex partners (χ^2 = 17.3, p=0.044, d=0.51) and history of transactional sex (Fisher Table Probability (TP) <0.001, p=0.038, d=0.57), though, for the latter, pairwise comparisons only showed a difference between ASCUS versus negative groups. A history of sexual abuse was not associated with abnormal cytology (Fisher TP=0.001, p=0.276), nor were tobacco, marijuana, alcohol use or a history of rectal STIs.

The few significant clinical associations with degree of ASIL included low CD4 counts ($F_{3,34.7}$=3.2, p=0.034, d=0.35) and the presence of anal warts at the time of cytology (χ^2= 8.28, p=0.041, d=0.25). Specifically, there were significant pairwise differences in CD4s between ASC-H/HSIL and negative group samples, and in the LSIL group relative to those with ASCUS and negative cytology. A large proportion of subjects who were screened with cytology, 48% (116/240), had documented anal warts. Those with cLSIL were more likely to have anal warts than subjects with ASC-H/cHSIL and ASCUS cytology. The proportion of subjects with an undetectable VL at the time of anal cytology was not associated with the degree of cytologic ASIL (χ^2=3.64, p=0.303).

Prevalence and risk factors for abnormal anal histology

Our analysis of the association between demographic, behavioral and clinical factors and anal histology is displayed in Table 4. The mean age at biopsy was 22 years (SD 2.11 years, range 17–26 years). While 92% of those referred for surgical examination under anesthesia presented for biopsies, only 28% of those referred for HRA presented for the procedure. Seventy-two subjects underwent confirmatory diagnostic testing with either intra-operative or HRA-guided anal tissue biopsy. The majority of those (58%) had hHSIL including carcinoma *in situ* (CIS), while the remainder had hLSIL-AIN1 (28%) or were negative (14%) (Table 2). Of note, the two subjects with hHSIL-CIS were diagnosed at ages 20 and 23 years. One subject with negative histology had been referred for surgical removal of anal

warts without preliminary cytologic screening. Subjects reporting more sexual partners (≥21) exhibited a significantly higher degree of ASIL (Fisher TP <0.001, p=0.017, d=1.3). The majority of subjects, 60 (83%) had anal warts at the time of biopsy. There was no association between presence of external anal warts and findings on histology (Fisher TP=0.074, p=0.737).

Discussion

To our knowledge, this study is the first to investigate the prevalence and associations of ASIL in this age-group using a combined cytologic and histologic approach. Previous studies in adolescents and/or young adult MSM have focused on cytologic abnormalities or HPV infection without confirmed histologic ASIL and, in all but one, have excluded persons with HIV-infection [16–19].

Our study population, young African-American MSM and transwomen, represent the demographic groups most affected by HIV in the Southeast United States at this time [13, 14]. In our study, the vast majority (95%) of those screened had detectable cytologic ASIL. This was significantly higher than the prevalence of abnormal anal cytology (53%) in another urban population of HIV-infected young adult MSM ages 17–25 years (mean age 21.2 years) [19], and in HIV-infected adult MSM (47–62%) [20, 21]. Furthermore, the type of abnormal cytology was more heavily skewed toward cLSIL and ASC-H in our population (43% and 9% respectively). These results were more consistent with those seen in HIV-infected adult MSM (cLSIL 54%, ASC-H 6%) [20] than in the other study population of young adults (cLSIL 28%, ASC-H 3%) despite the slightly younger mean age of our subjects [19]. There is less known about the prevalence of ASIL in HIV-infected transwomen, particularly in the younger age group. However, in one study of HIV-infected adult transwomen, abnormal anal cytology rates were similar to those seen in MSM (cLSIL 36%, cHSIL 14%, ASC-H 5%) [10].

Most of our subjects who underwent biopsy (58%) had hHSIL (Table 2). This is similar to rates seen in adult HIV-infected transwomen (59%) [10], but higher than published rates of hHSIL (31–52%) in adult HIV-infected MSM [22–24]. While hHSIL often takes years to progress to anal cancer [24], some have shown this progression in as few as 8 months [25] though these data may be limited due to diagnostic bias. At this time, it remains unclear what factors hasten progression to anal cancer. In our study, hHSIL was significantly associated with a high number (≥21) of lifetime sexual partners. Various behavioral factors such as participation in transactional sex, anonymous sex and history of incarceration may explain why some young MSM and transwomen have high numbers of sex partners [26]. This study did not reveal additional behavioral or clinical associations with cHSIL or hHSIL that might be used for risk-stratification, though current or prior tobacco use has been identified as a possible risk factor in older adults in some studies [27, 28].

Our study highlighted some of the challenges in relying solely on primary prevention with vaccination in these populations. The nonavalent HPV vaccine includes the most common high risk HPV types in adult HIV-infected MSM [29]. Only 5% of our study population had documentation of completing the HPV vaccine series, though we could not account for those

who may have received HPV vaccination without documentation in the state immunization record or medical chart. Of note, almost 10% of subjects with data had experienced coitarche prior to age 9 years when they would have become eligible to receive the vaccine. Therefore, these young MSM and transwomen are at risk for early HPV infection, and many do not receive HPV vaccination prior to exposure.

Although national HPV vaccination rates in boys are increasing, they remain suboptimal. According to the National Immunization Survey-Teen (NIS-Teen) estimates, only 36.2 ± 9% of boys age 13–17 were up to date with their HPV vaccine series in the state of Georgia in 2016 [30]. This indicates that although there have been some improvements over the years, a significant portion of young MSM and transwomen will remain at-risk for HPV infection and its potential complications until vaccination rates improve. Due to the large population of HIV-infected young MSM and transwomen that are at-risk for ASIL and cancer, there is a need for a standardized, evidence-based screening process. Therefore, we propose that providers consider anal cancer screening in sexually-active, HIV-infected young MSM and transwomen with multiple lifetime sexual partners in demographically similar populations in the southeast United States starting at age 21 years, regardless of history of receptive anal intercourse, anal warts or viral load.

This study was subject to several limitations. The primary goal of this study was to explore the associations of various exposures with ASIL outcomes and so we had relatively small sample sizes. As such, post-hoc tests were presented and interpreted unadjusted. Additionally, there was variation in cytologic screening based on sexual practices and presence of anal warts on visual examination within our clinic, and our loss-to-follow up rate for HRA was high. The reasons for poor adherence to the management plan were likely multifactorial with adolescent behavior; availability of trained providers; lack of standardized management guidelines with resultant variability of provider practices among the most important. Implementing a standardized process for anal cancer screening with scheduled reminders for follow-up would address this limitation. This would allow us to better estimate the prevalence of ASIL in this population and overcome selection bias to produce recommendations that could be generalized to broader populations. Our analyses of disease risk were also limited by information bias due to the retrospective study design as some behavioral variables were inconsistently documented and may be important factors to consider in determining risk for hHSIL. Inconsistent documentation may have also contributed to our low immunization rates. Future prospective, multi-site studies with standardized risk-assessment tools and biological analyses of those persons with CIS and other hHSIL would help identify viral and/or host factors that may affect regression of dysplastic lesions or progression to cancer. In addition, dedicated research in transwomen will be important to elucidate the role of hormonal therapy in disease progression.

Conclusion

Our study population of HIV-infected young MSM and transwomen demonstrated a high prevalence of high-grade squamous intraepithelial lesions, particularly in subjects with high numbers of sexual partners. This highlights the value of early, standardized anal cancer

screening and active surveillance in similar high-risk, unvaccinated and under-vaccinated populations to decrease future risk of anal cancer.

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Abbreviations and Acronyms

AIN	Anal intraepithelial neoplasia
ANOVA	Analysis of variance
ASCUS	Atypical squamous cells of undetermined significance
ASC-H	Atypical squamous cells, cannot exclude HSIL
ASIL	Anal squamous intraepithelial lesions
CIS	Squamous cell carcinoma *in situ*
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HRA	High resolution anoscopy
HSIL	High-grade squamous intraepithelial lesion
LAST	Lower Anogenital Squamous Terminology Standardization Project
LSIL	Low-grade squamous intraepithelial lesion
MSM	Men who have sex with men
STI	Sexually transmitted infection
UD	Undetectable
VFC	Vaccines for children
VL	Viral load

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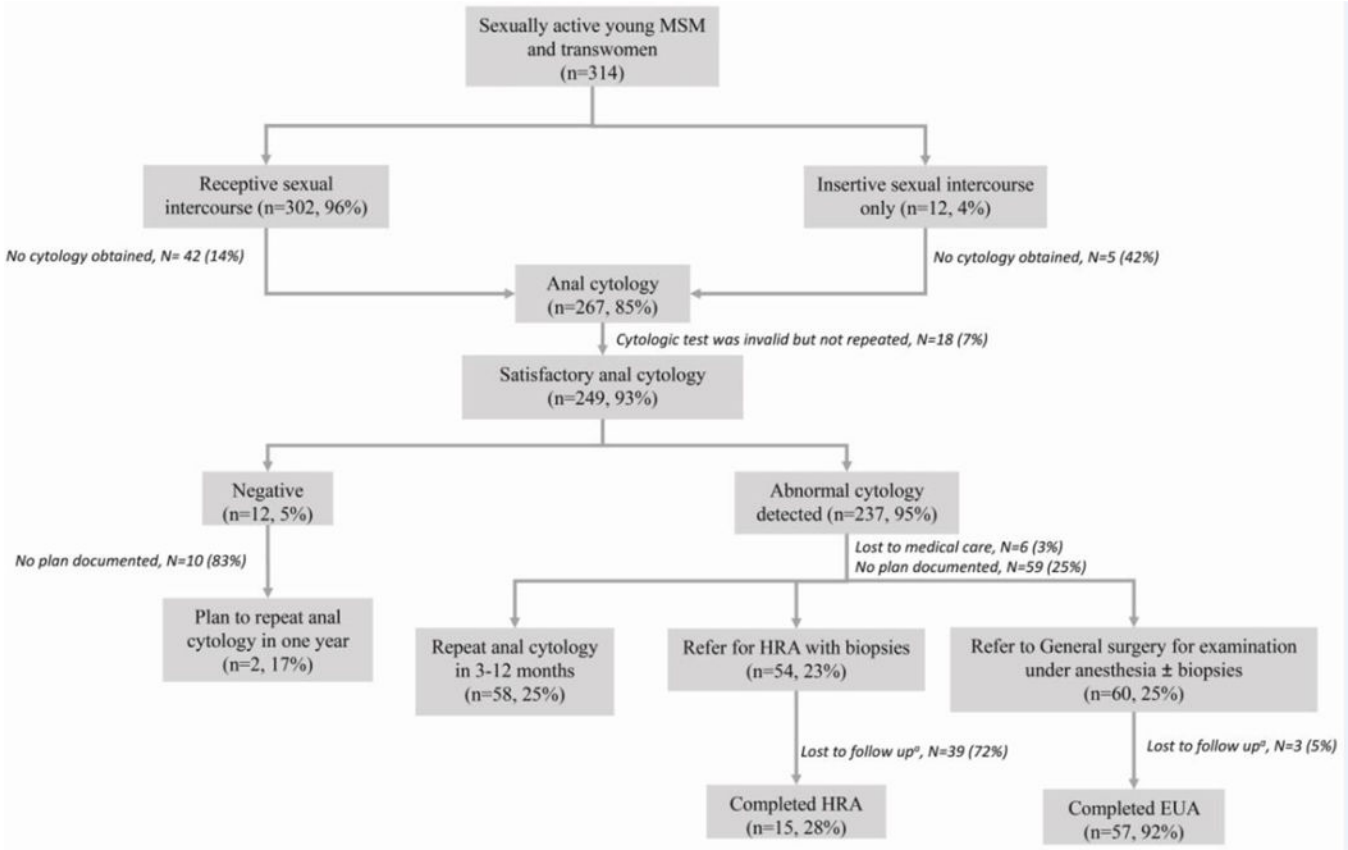

Figure 1:
Anal cancer screening process

Table 1:

HIV-infected young MSM and transwomen in Atlanta, GA 2009–2016, Baseline demographic, behavioral and clinical information

Characteristics, N (%)	N=314
Demographics	
Race	
African American	297 (95%)
Other	17 (5%)
Education, N=305	
High School or Less	164 (54%)
College	141 (46%)
Gender identity	
Cisgender male	307 (98%)
Transwoman	7 (2%)
Gender of sex partners	
Men only	240 (76%)
Men and women	74 (24%)
Housing	
Live with parents/extended family members	157 (50%)
Live with a friend	82 (26%)
Live with a romantic partner	11 (3%)
Live alone	40 (13%)
Homeless	24 (8%)
Behavioral	
Age at coitarche, yr, N=246, Mean ± SD	14.5 ± 3.3
Intercourse practices	
Both Insertive and Receptive	225 (72%)
Receptive only	77 (25%)
Insertive only	12 (4%)
Number of lifetime sexual partners, N=266	
1 to 5	52 (20%)
6 to 10	68 (26%)
11 to 20	38 (14%)
>21	108 (41%)
History of	
Sexual abuse, yes, N=229	75 (33%)
Participation in transactional sex, yes, N=179	35 (20%)
Rectal sexually transmitted infections (STIs), yes, N=303	153 (51%)
Marijuana use, yes	189 (60%)
Marijuana and alcohol use, yes	152 (48%)
Tobacco use, yes, N=218	122 (56%)
Other drug use (cocaine, MDMA etc)	43 (14%)

Characteristics, N (%)	**N=314**
Clinical	
History of external anal warts, N=288	
Yes	130 (45%)
No	158 (55%)
Number of HPV vaccines	
0	272 (87%)
1	19 (6%)
2	7 (2%)
3	16 (5%)

Table 2:

Distribution of results

Anal Cytology, n=249	Frequency (%)	95% Wald CI
Negative	12 (5%)	(2.6%, 8.5%)
ASCUS	103 (41%)	(35.2%, 47.8%)
cLSIL	107 (43%)	(36.8%, 49.4%)
ASC-H	22 (9%)	(5.8%, 13.3%)
cHSIL	5 (2%)	(0.7%, 4.9%)
Anal Histology, n=72	**Frequency (%)**	**95% Wald CI**
Negative	10 (14%)	(7.2%, 24.5%)
hLSIL	20 (28%)	(18.2%, 39.8%)
hHSIL	42 (58%)	(46.1%, 69.6%)

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Table 3:

HIV-infected young MSM and transwomen in Atlanta, GA 2009–2016, Association between anal cytology and demographic, behavioral and clinical factors

Characteristics, N (%)	**ASC-H/cHSIL N=27 (a)**	**cLSIL N=107 (b)**	**ASCUS N=103 (c)**	**Negative N=12 (d)**	***Omnibus P-value***	***Pairwise Comparisons***
Demographics						
Race						
African American	27 (100%)	103 (96%)	92 (89%)	12 (100%)	0.100	
Other	0 (0%)	4 (4%)	11 (11%)	0 (0%)		
Gender of sex partners						
Men only	25 (93%)	84 (79%)	78 (76%)	10 (83%)	0.280	
Men and women	2 (7%)	23 (22%)	25 (24%)	2 (17%)		
Education, n=243						
High School or Less	11 (42%)	54 (51%)	53 (53%)	7 (58%)	0.755	
College	15 (58%)	51 (49%)	47 (47%)	5 (42%)		
Behavioral						
Age at coitarche, mean (SD)	14.9 (3.5)	14.9 (2.8)	14.4 (3.6)	15 (3.9)	0.736	
Intercourse						
Both + Receptive Only	26 (96%)	104 (97%)	102 (99%)	11 (92%)	0.203	
Insertive Only	1 (4%)	3 (3%)	1 (1%)	1 (8%)		
Number of Partners						
1 to 5	7 (33%)	11 (12%)	22 (25%)	1 (9%)	**0.044***	**b ≠ c**
6 to 10	5 (24%)	31 (35%)	18 (20%)	3 (27%)		
11 to 20	4 (19%)	18 (20%)	8 (9%)	2 (18%)		
21 or more	5 (24%)	29 (33%)	41 (46%)	5 (46%)		
Abuse, n=175						
Yes	7 (37%)	19 (25%)	23 (32%)	4 (57%)	0.276	
No	12 (63%)	57 (75%)	50 (69%)	3 (43%)		
Transactional Sex, n=143						
Yes	4 (22%)	14 (26%)	8 (12%)	3 (60%)	**0.038***	**c ≠ d**
No	14 (78%)	41 (75%)	57 (88%)	2 (40%)		
Tobacco Use	8 (30%)	39 (37%)	36 (35%)	6 (50%)	0.670	

Characteristics, N (%)	**ASC-H/cHSIL N=27 (a)**	**cLSIL N=107 (b)**	**ASCUS N=103 (c)**	**Negative N=12 (d)**	***Omnibus P-value***	***Pairwise Comparisons***
Marijuana Use	13 (48%)	71 (66%)	60 (58%)	8 (67%)	0.301	
Marijuana and alcohol use	10 (37%)	56 (52%)	50 (49%)	5 (42%)	0.518	
History of rectal STIs	15 (56%)	59 (57%)	58 (57%)	4 (36%)	0.599	
Clinical						
Age at cytology, mean (SD)	20.9 (2.0)	20.2 (2.0)	20.3 (2.1)	19.8 (2.3)	0.394	
CD4 Counts[a]						
At baseline[b], mean (95% CI)	230 (150 – 327)	257 (205 – 315)	302 (255 – 353)	223 (168 – 286)	0.160	
At cytology, mean (95% CI)	317 (254 – 387)	325 (282 – 371)	389 (345 – 436)	424 (355 – 499)	**0.034***	**a ≠ d, b ≠ c, b ≠ d**
Viral Loads						
At baseline, median (IQR)	46,440 (20,600 – 172,080)	37,080 (12,300 – 155,612)	57,362 (9,580 – 232,760)	36,845 (19,160 – 109,329)	0.854	
At cytology, median (IQR)	40 (40 – 10,563)	153 (40 – 21,220)	109 (40 – 16,418)	40 (40 – 1,000)	0.218	
At cytology, # UD[c] (%)	15 (56%)	43 (41%)	47 (47%)	7 (64%)	0.303	
Number of HPV vaccines						
0	26 (96%)	92 (86%)	86 (84%)	8 (67%)	0.100	
1 or more	1 (4%)	15 (14%)	17 (17%)	4 (33%)		
Anal Warts, n=240						
Yes	9 (35%)	61 (59%)	42 (42%)	4 (40%)	**0.041***	**a ≠ b, b ≠ c**
No	17 (65%)	43 (41%)	58 (58%)	6 (60%)		

[a] CD4s regression modeled as square root of CD4, presented squared for interpretation purposes

[b] Baseline indicates at the time of HIV diagnosis

[c] UD: Undetectable

Table 4:

HIV-infected young MSM and transwomen in Atlanta, GA 2009–2016, Association between anal histology and demographic, behavioral and clinical factors

Characteristics, N (%)	**hHSIL, N=42 (a)**	**hLSIL, N=20 (b)**	**Negative, N=10 (c)**	***Omnibus P-value***	***Pairwise Comparisons***
Demographics					
Race					
African American	38 (91%)	20 (100%)	9 (90%)	0.403	
Other	4 (10%)	0 (0%)	1 (10%)		
Gender of sex partners					
Men only	33 (79%)	17 (85%)	6 (60%)	0.340	
Men and women	9 (21%)	3 (15%)	4 (40%)		
Education					
High School or Less	19 (45%)	13 (65%)	5 (50%)	0.345	
College	23 (55%)	7 (35%)	5 (50%)		
Behavioral					
Age at coitarche, mean (SD)	14.8 (3.5)	14.2 (2.7)	13.1 (4.6)	0.587	
Intercourse					
Both + Receptive Only	42 (100%)	20 (100%)	10 (100%)	NA	
Insertive Only	0 (0%)	0 (0%)	0 (0%)		
Number of Partners					
1 to 5	6 (17%)	5 (31%)	1 (10%)	**0.017***	**a ≠ c, b ≠ c**
6 to 10	7 (20%)	3 (19%)	7 (70%)		
11 to 20	7 (20%)	1 (6%)	2 (20%)		
21 or more	15 (43%)	7 (44%)	0 (0%)		
Abuse, n=54					
Yes	14 (40%)	2 (20%)	6 (67%)	0.144	
No	21 (60%)	8 (80%)	3 (33%)		
Transactional Sex, n=34					
Yes	8 (38%)	1 (11%)	0 (0%)	0.171	
No	13 (62%)	8 (89%)	4 (100%)		

Tobacco Use	14 (33%)	7 (35%)	5 (50%)	0.610
Marijuana Use	23 (55%)	10 (50%)	6 (60%)	0.868
Marijuana and alcohol use	21 (50%)	7 (35%)	6 (60%)	0.371
History of rectal STIs	23 (55%)	10 (56%)	7 (77%)	0.434

Characteristics, N (%)	**hHSIL, N=42 (a)**	**hLSIL, N=20 (b)**	**Negative, N=10 (c)**	***Omnibus P-value***
Clinical				
Age at histology, mean (SD)	22.0 (1.9)	21.9 (2.7)	22.5 (1.9)	0.718
CD4 Counts[a]				
At baseline[b], mean (95% CI)	213 (152 – 284)	307 (193 – 447)	251 (47 – 617)	0.389
At biopsy, mean (95% CI)	391 (338 – 447)	417 (322 – 524)	378 (193 – 626)	0.874
Viral Loads				
At baseline, median (IQR)	27,790 (7,150 – 68,980)	50,710 (21,480 – 131,893)	31,015 (1,630 – 258,180)	0.478
At biopsy, median (IQR)	40 (40 – 480)	40 (40 – 40)	145 (40 – 2,415)	0.484
At biopsy # UD[c] (%)	27 (66%)	15 (79%)	4 (50%)	0.316
Number of HPV vaccines				
0	40 (95%)	16 (80%)	10 (100%)	0.092
1 or more	2 (5%)	4 (20%)	0 (0%)	
Anal Warts (external or internal)				
Yes	36 (86%)	16 (80%)	8 (80%)	0.737
No	6 (14%)	4 (20%)	2 (20%)	

[a]CD4s regression modeled as square root of CD4, presented squared for interpretation purposes

[b]Baseline indicates at the time of HIV diagnosis

[c]UD: Undetectable