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Access to Care

I Acceptability of screenings for cancers associated with HPV in transgender populations: a scoping review

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Background: HPV and associated cancers, including anal cancer, may be more common among transgender (trans) populations, especially among those living with HIV. Despite newly emerging research on HIV and HPV co-infections and related cancer risk in trans populations, little has been synthesized regarding the acceptability of screenings for cancers associated with HPV, including barriers and facilitators to screening, in these populations.

Methods: Literature published in English was reviewed following a systematic search of MEDLINE, Embase, Web of Science, Scopus, and CINAHL in November 2022.

Results: Thirty-two articles were included for synthesis, with most originating from the United States ($n = 24$; 75%), and with most employing exclusively qualitative ($n = 11$; 34%) or quantitative research methods ($n = 12$; 38%). Five examined the acceptability of anal cancer screening in trans populations (16%). Facilitators of anal cancer screening included a willingness to undergo future anal Pap testing despite a lack of knowledge regarding anal health. Barriers to anal cancer screening included a lack of knowledge regarding anal cancer ($n = 2$; 6%), a lack of perceived risk of developing anal cancer ($n = 2$; 6%), and a lack of prior anal Pap testing ($n = 2$; 6%).

Conclusions: Despite known barriers to screenings for cancers associated with HPV in trans populations, the option to self-test, clinics and services dedicated to trans people, and provider recommendations are viable facilitators of acceptable screening practices. Further research may elucidate additional needs of trans community members in seeking gender-affirming screening services.

2 Core Outcome Measures in Squamous Intra-Epithelial Precursor Lesions of the Anus (CORSICA)

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Background: There are multiple treatments for anal high-grade squamous intra-epithelial lesions (aHSIL). The evidence for aHSIL treatments is of poor quality, such that the optimal approach cannot be defined. Existing trials in aHSIL have used different ways of measuring the effects of treatment. This makes comparing the results of trials very difficult. Trials have also been poor at reporting how treatment affects patients, e.g., quality of life.

Methods: We are developing a 'core outcome set' (COS) for trials in aHSIL. This is a list of outcomes (treatment effects) that future trials in aHSIL should measure and report on. COS include outcomes that are important to all involved with a particular condition (patients, doctors, trialists).

Results: Using evidence based methodological framework produced by The COMET (Core Outcome Measures in Effectiveness Trials, www.cometinitiative.org) Initiative, the COS will be developed over four stages: 1. A systematic review of the literature to find the outcomes already in use by researchers; 2. A series of semi-structured interviews with patients to establish the outcomes of importance to them; 3. Questionnaire surveys using a method known as a Delphi process to try to agree the outcomes to include in the COS; 4. A consensus meeting to approve the final COS.

Conclusions: We anticipate that utilisation of the COS in future trials will ensure that the outcomes reported are meaningful to those affected, and comparable to determine the optimal approach.

3 Core Outcome Measures in Squamous Intra-epithelial Precursor Lesions of the Anus (CORSICA): systematic review of outcome measures for the treatment of anal high-grade squamous intra-epithelial lesions (AHSIL)

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Background: The evidence for aHSIL treatments is of poor quality, such that the optimal approach cannot be defined. Existing trials in aHSIL have used different ways of measuring the effects of treatment. This makes comparing the results of trials very difficult. Trials have also been poor at reporting how treatment affects patients, e.g., quality-of-life. A 'core outcome set' (COS) for use in future trials can improve this. A systematic review to summarise the outcomes reported in studies evaluating aHSIL treatments is the first stage in COS development.

Methods: Systematic literature searches will identify all studies evaluating treatments for aHSIL. Outcomes and their definitions will be extracted verbatim and categorised into domains.

Results: Initial search of the international clinical trials register identified five phase-3 RCT's currently recruiting or recently published for treatment of aHSIL. A total of 30 outcomes were identified across these trials with seven primary outcome measures of which only two were directly comparable. In addition to the heterogeneity of the outcomes, there was also variation in the definition of outcomes. Only one of these trials proposes to report on quality-of-life. Full systematic review in progress with final results to be available for IANS 2023.

Conclusions: This outcome heterogeneity, when combined with the limited range of reported outcomes, makes it difficult to appraise the available evidence and choose the best outcomes for inclusion in subsequent trials, both of which impact production of meaningful data on which to base treatment decisions. These issues can be addressed through the development of a COS.

4 Factors affecting adherence to and patient comfort during HRA visits

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Background: The UVA Ryan White High Resolution Anoscopy [UVARWHRA] Clinic became operational in December 2017. As of 2020, an estimated 1.3 million people live in the 58% rural region served by our clinic with 14 of the 24 counties designated as Medically Underserved Areas.

Methods: This is a discussion of factors affecting adherence to HRA visits and patient comfort during HRA visits.

Results: Since the inception of the clinic in 2017, 372 HRA procedures have been performed. Transportation and missing work are barriers affecting adherence to follow-up appointments. Patient comfort indirectly affects adherence to follow-up visits. The clinic schedules and pays for transportation. Biopsies and treatment were combined into single visits, thus extending visit intervals. Interventions to address patient comfort include innovative positioning, local anesthetic for biopsies, environmental alterations [iPad with earbuds, eye covers, warm blankets], and various premedication options. The RN coordinator calls patients 1 week prior to their HRA appointment to identify and remove barriers to appointment adherence. She calls the patients 24 hours after the procedure to address any adverse issues. Finally, she calls when the results return to explain the results and plan and answer questions to decrease anxiety regarding future visits.

Conclusions: Ongoing feedback from patients is critical to identifying factors affecting adherence to HRA clinic visits and patient comfort during the HRA procedure in an effort to create innovative solutions. Research is planned utilizing patient surveys to address barriers to adherence and ways to enhance patient comfort during HRA procedures.

5 Navigation as an intervention to increase referral and enrollment rates of persons living with HIV in a cancer-related clinical trial

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Background: Patient navigation (PN) has been associated with improved accrual into clinical trials (CTs). We assessed the effect of PN services for the recruitment of persons living with HIV (PLWH) in ULACNet-101, a CT under the California-Mexico-Puerto Rico (CAMPO) Consortium, at Puerto Rico.

Methods: We provided a training activity on CTs and PN to healthcare professionals (n = 82) at HIV clinics. Follow-up calls assessed 1) challenges faced while referring patients to ULACNet-101 and 2) patient-reported barriers to participation. We analyzed data from 1) pre-screening surveys to determine the effect of the training activity, and 2) the first follow-up survey of professionals to determine barriers to ULACNet-101 participation.

Results: 900 individuals have been screened for ULACNet-101; 324 since the training activity (January 2023), where only 16 pre-screenings were confirmed to have been referred directly by trained professionals. However, 63 individuals pre-screened knew about ULACNet-101 by provider referrals ($n = 29$) and flyers/banners ($n = 34$) from HIV clinics represented in the training activity. The most common barriers reported by trained professionals to refer patients to ULACNet-101 were lack of interest of patients (33%) and lack of time to talk to them (24%). The most common patient-reported barriers were distance to the CT site (55.2%), lack of support (55.2%), and fear of the procedures (55.8%). To overcome barriers, most professionals provided educational material (93.1%) and contact information (89.7%) for CAMPO.

Conclusions: Continued monitoring of recruitment strategies and of barriers will be essential to determine the effect of the training activity on enrollments and achievement of recruitment goals.

6 To improve motivational barriers to retention in high resolution anoscopy, patients and providers recommend social and environmental changes: a sequential mixed methods pilot study in a federally qualified health center

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Background: We explored quality improvement factors that could prevent loss to follow-up in high-resolution anoscopy (HRA) among patients receiving HIV primary care at a community health clinic.

Methods: Using the transtheoretical COM-B (Capability, Opportunity, Motivation, and Behavior) Model, we conducted surveys and interviews with 13 patients who remained engaged in HIV care but delayed their high-grade anal dysplasia monitoring or treatment visits, and 6 HRA providers. Data analysis involved descriptive statistics for surveys and rapid qualitative analysis with consensus coding for interviews.

Results: Patients were racially, ethnically, and economically representative of the lost to follow-up population, and were experienced with HRA (M visits = 4.6, SD = 2.8). Providers included experienced clinicians and medical assistants (M years providing HRA = 6.0, SD = 2.2). Assessments revealed two primary barriers: (A) motivational barriers such as physical pain, discomfort, embarrassment, and anxiety; and (B) opportunity barriers including difficulties with scheduling, inconsistent after-care, and anxiety-inducing exam rooms. Capability barriers, such as limited health literacy about HRA, were less commonly reported and linked to opportunity barriers. Participants recommended potential facilitators, including easier scheduling, standardization of pain management and after-care services, examination room modifications to reduce anxiety, distributing peer-to-peer educational materials, and the introduction of financial incentives.

Conclusions: Interventions should address social and environmental opportunity barriers, not just motivational barriers, to retain HRA patients in community settings. Improving convenience, standardizing pain management, and enabling provider-mediated social support could alleviate capability and motivational barriers. The COM-B Model provides a comprehensive framework for organization-specific, patient-oriented quality improvement for HRA retention.

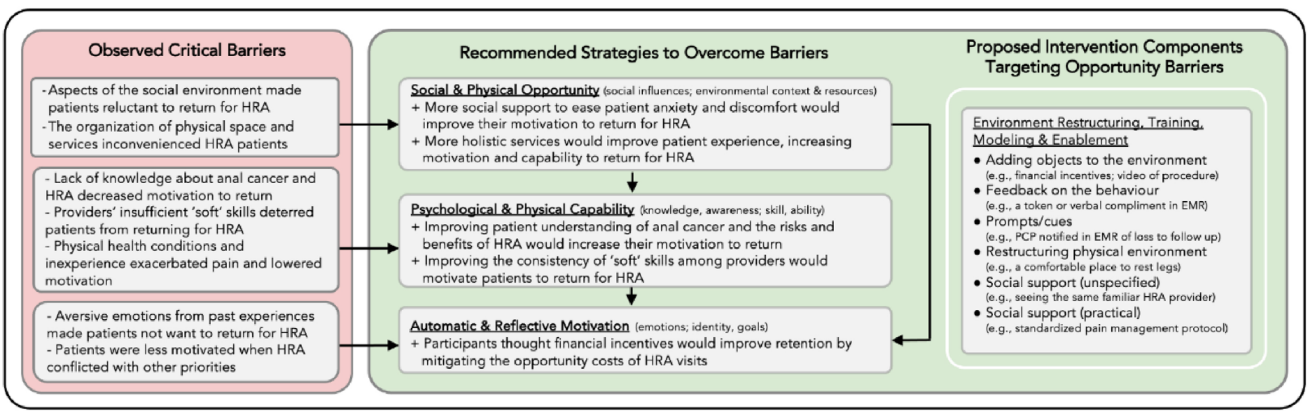

Figure 1. Conceptual model of critical barriers, recommended strategies, and proposed intervention components based on a COM-B analysis

7 Utilization of anal cytology screening among at-risk sexual and gender minority populations in Pennsylvania

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Background: Anal cancer disproportionately affects gay, bisexual, and other men who have sex with men (GBM), as well as transgender women (TGW). Current recommendations suggest anal cancer screening, specifically anal cytology, for high-risk populations, particularly GBM/TGW living with HIV. This study aims to utilize the Andersen Healthcare Utilization Model to identify factors associated with anal cancer screening among GBM/TGW, including predisposing, enabling, and need-related factors.

Methods: Two cross-sectional surveys from the Pennsylvania LGBTQ Health Needs Assessment conducted in 2020 (N = 905) and 2022 (N = 440) were analyzed. Multiple logistic regression analyses were performed to determine the correlates of screening uptake.

Results: The average age of respondents was 39.5 (SD = 13.6) in 2020 and 43.1 (SD = 14.0) in 2021. A minority of respondents reported undergoing screening in the past year (14.9% in 2020 and 13.2% in 2022). Predisposing correlates of screening included Hispanic ethnicity (aOR2020 = 2.18; 95% CI: 1.07–4.46), Black race (aOR2022 = 4.28; 95% CI: 1.60–11.45), and public insurance (aOR2022 = 2.58; 95% CI: 1.36–4.90). Enabling correlates included receiving treatment for a sexually transmitted infection in the past year (aOR2020 = 1.69; 95% CI: 1.14–2.51), current use of HIV pre-exposure prophylaxis (PrEP) (aOR2020 = 2.38; 95% CI: 1.60–3.52 & aOR2022 = 2.41; 95% CI: 1.32–4.37), and HPV vaccination (aOR2022 = 1.84; 95% CI: 1.02–3.31). A previous HIV diagnosis was the only need-based correlate (aOR2020 = 2.18; 95% CI: 1.44–3.30 & aOR2022 = 4.40; 95% CI: 2.45–7.90).

Conclusions: A small percentage of GBM/TGW in Pennsylvania participated in anal cytology screening in the past year. Consistent with existing guidelines, GBM/TGW living with HIV were more likely to be screened. Among GBM/TGW without HIV, engagement in PrEP care was significantly associated with screening, independent of other enabling factors.

Epidemiology and Natural History

8 Evaluation of the association of body mass index with human papillomavirus infection and squamous intraepithelial lesions in the anus in people who receive services at the anal neoplasia clinic in Puerto Rico

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Background: Evidence is limited regarding the association of obesity with anal High-Risk Human Papillomavirus (HR-HPV) infection and High-Grade Squamous Intraepithelial Lesions (HSIL). We aimed to assess the association of Body Mass Index (BMI) with anal HR-HPV and HSIL among Hispanics.

Method: This cross-sectional study evaluated medical records of adults receiving services at the Anal Neoplasia Clinic of the University of Puerto Rico Comprehensive Cancer Center from December 2014–December 2022; 543 records with complete information on HR-HPV and HSIL status were analyzed. Logistic regression models were used to assess associations of interest and estimate Odds-Ratio (OR) with 95% confidence intervals (CIs).

Results: Mean age of participants was 44.10 ± 13.24 years, 65.2% were men, 71.8% were HIV+, 74.4% HR-HPV+, and 37.9% had biopsy-confirmed HSIL. Regarding BMI, 2.9% were underweight, 31.9% normal, 39.0% overweight, 17.3% obesity-class 1, 5.2% obesity-class 2 and 4.2% obesity-class 3. No significant association was observed between BMI and HR-HPV infection in adjusted analysis. Lower odds of HSIL were observed among overweight (aOR: 0.59, 95% CI: 0.39–0.91) and obese-class 2 & 3 (aOR: 0.40, 95% CI: 0.19–0.81) individuals compared to those with underweight/normal BMI, after adjusting for HIV status, smoking, and lifetime receptive anal sex. Although a reduction in the odds of HSIL was observed in persons with obesity-class 1, this finding was not significant (aOR: 0.72, 95% CI: 0.4–1.24).

Conclusion: BMI was not associated with anal HR-HPV infection. Overweight and obese individuals were less likely to have anal HSIL as compared to underweight/normal BMI adults.

9 Factors associated with age of anal cancer onset among people living with and without HIV in the Southeastern U.S.

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Background: Anal cancer (AC) is increasing among younger people globally. The South has the highest HIV incidence rate in the U.S., and people living with HIV have a substantially higher risk of developing AC. We examined age at AC diagnosis among patients treated at the University of Alabama at Birmingham (UAB), and patients in Alabama and Tennessee state cancer registries compared with general U.S. population estimates.

Methods: In a cross-sectional study, using chi-square and linear regression analyses, we examined associations between age at diagnosis, sex, race, BMI, marital status, HIV status, stage, and county-level social vulnerability, among patients with a diagnosis of malignant neoplasm of the anus (ICD-10: C210) or anal canal (ICD-10: C211) in Alabama and Tennessee between 2012 and 2020.

Results: The median age of AC diagnosis was younger in Alabama (61 years) and Tennessee (58 years) compared to the U.S. (63 years). The proportion of younger people (35–44 years) was double in Southeastern states (Alabama: 8.3%, Tennessee: 8.9%, U.S.: 4.7%). Similar patterns were seen across UAB, Alabama, and Tennessee, with males and Blacks being younger at onset. In Alabama, males had a 7-year younger median age of onset compared to females (56 vs 63 years, $P < 0.001$); in Tennessee, Blacks had a 9-year younger median age of onset compared to Whites (51 vs 60 years, $P < 0.001$). HIV infection was significantly associated with younger age of onset.

Conclusions: Southeastern states demonstrate disparities in AC, with males and Blacks being at greater risk of earlier onset compared to other demographics.

10 Molecular epidemiology of anal HPV infections in transgender individuals: deciphering the clinical and immunological determinants of genus-specific HPV colonization and alpha-HPV-related diseases

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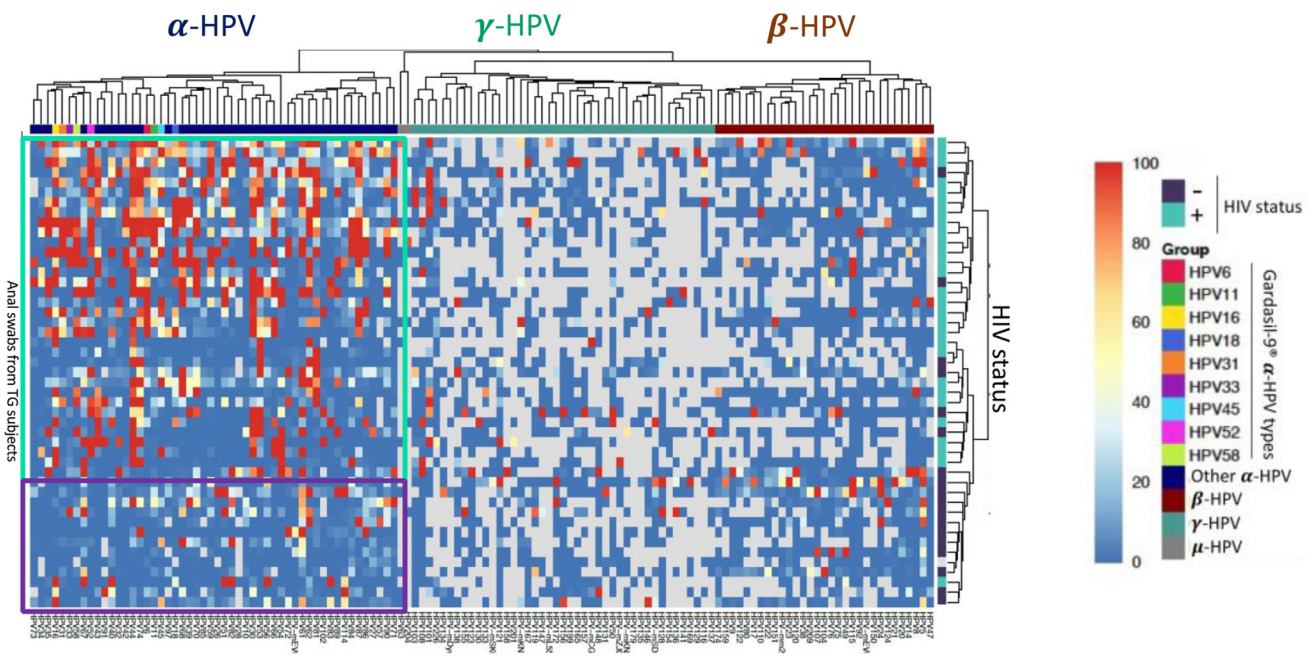
Background: Men-who-have-sex-with-men, bisexual and transgender individuals (TG) are disproportionally affected by HPV infections and HPV-related diseases. We evaluated the prevalence of HPV-types by next-generation sequencing (NGS) in anal swabs of TG to decipher the epidemiological, clinical, and immunological risk factors for HPV-colonization.

Methods: A longitudinal cohort of TG was established in Washington DC. 47 consecutive subjects were selected for HPV-genotyping by a hybrid-capture target-enrichment-NGS allowing the identification of 210 α-, β- or γ-HPV-types. Anal swabs for cytology were also collected. Unsupervised hierarchical-clustering and multivariate distance-matrix-regression was utilized to analyze the associations between genus-specific HPV prevalence and other clinic-epidemiological variables.

Results: The study population comprised mostly TG women (male-sex-assigned-at-birth, 66%), while 15% were non-binary and 8% were TG men (female-sex-assigned-at-birth). Median age was 37 years and 60% were HIV-1-infected (median CD4: 620 cells/μL; 78.5% on ART). Anal cytology was abnormal in 48% and only 19% received an HPV vaccine. α-HPVs largely exceeded the prevalence of β- and γ-HPV in anal swabs. The α-10 HPV44, α-6 HPV30, α-9 HPV16 were the most prevalent HPV-types (66%, 57%, 55%, respectively). The relative abundance (RA) of α-HPV types not included in Gardasil-9® (HPV6,11,16,18,31,33,45,52,58) exceeded the RA of Gardasil-9®-HPV-types in 86% of TG persons. HIV-1 infection was associated with higher prevalence of any α-HPV but did not affect the probability to detect β- or γ-HPV (**Figure**).

Conclusions: Target-enriched-NGS reveals an increased prevalence of α-HPV in HIV-1-infected TG individuals emphasizing the role of specific clinical and immunological determinants of genus-specific anogenital HPV-colonization and consequent α-HPV-related diseases.



11 Persistence and clearance of histological anal high-grade lesions in the ANRS-EP57-APACHES study

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Background: Studies reporting rates of high-grade squamous intraepithelial lesions (HSIL) clearance in untreated population are rare. The objective was to report rate and determinants of histological HSIL clearance in the ANRS-EP57-APACHES study of men who have sex with men living with HIV (MSM-LHIV).

Methods: The ANRS-EP57-APACHES study included 513 MSM-LHIV aged ≥35 years in six hospitals across France between December 2014 and June 2016, followed-up annually until June 2019, and for those with HSIL detected, until June 2021. At each visit, participants underwent cytology, HPV testing, and high-resolution anoscopy (HRA) with biopsy of suspicious areas. Detected HSIL were not treated by protocol. Histological diagnoses underwent blinded panel consensus review. HSIL clearance was defined as the first visit with biopsy-proven regression or HRA-established disappearance.

Results: Overall 95 participants diagnosed with histological HSIL were followed-up up to 76 months (median 36 months, interquartile range 19–56 months) for a total of 340 person-years (PY). At the end of the study, no anal cancer was detected (incidence rate 0/340PY, 95% confidence interval 0–2.5/340PY). Overall, 156 first-detected histological HSIL (from 95 participants) were followed-up for a total of 324PY. 50 (32%) HSIL (33 participants) were persistent for a median duration of 35 months (interquartile range 17–56 months) and 106 (68%) HSIL cleared. HSIL clearance rate was 33/100PY.

Conclusions: Although no anal cancer was detected, our data are compatible with the ANCHOR active-monitoring arm (1.4 anal cancer/340PY, 95% confidence interval 0.9–2.1/340PY). Full evaluation of potential determinants of histological HSIL clearance will be presented.

12 Prevalence of anal HPV infection and anal HSIL among MSM 50 years and older living with or without HIV

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Background: Anal cancer is caused by human papillomavirus (HPV), particularly HPV-16, and is preceded by anal high-grade squamous intraepithelial lesions (HSIL). The incidence of anal cancer is highest among men who have sex with men (MSM) living with HIV (MSMLWH) and increases with age. However, most previous studies of anal HPV infection and anal HSIL were performed on men under 50 years of age, and relatively little is known about HSIL among older MSMLWH or MSM not living with HIV (MSM-Not-LWH).

Setting: We enrolled MSM who were aged 50+ during 2018–2022 in San Francisco, California.

Methods: 129 MSMLWH and 109 MSM-not-LWH participated. All participants had anal HPV DNA testing (Atila Biosystems) and high-resolution anoscopy with biopsy of visible lesions.

Results: Among MSMLWH, 47% (95% CI: 38–56%) had anal HSIL, 71% (62–79%) had oncogenic anal HPV, and 19% (13–27%) had HPV-16. Among MSM-not-LWH, 37% (28–47%) had anal HSIL, 22% (15–32%) had HPV-16, and 57% (47–67%) had other oncogenic anal HPV types. Increasing age was not statistically associated with prevalent HSIL, HPV-16, or other oncogenic HPV infection in MSMLWH or MSM-not-LWH. HPV-16 (OR: 32.7, 95% CI: 12.2–88.0, other oncogenic HPV types (OR: 5.71, 95% CI: 2.72–12.0) were associated with increased odds of anal HSIL, adjusted for age, income, education, and HIV status.

Conclusion: The prevalence of oncogenic anal HPV, anal HPV-16, and anal HSIL remain very high in older MSMLWH and MSM-not-LWH. With recent evidence showing that treating anal HSIL prevents anal cancer, all MSM aged 50+ should be considered for anal cancer screening.

13 Prevalence of anal HR-HPV infection and abnormal cytohistology in MSM using prep compared to MSM living with HIV

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Introduction: The use of Pre-Exposure Prophylaxis (PrEP) in HIV-negative MSM created a new Sexual Minority Group; MSM-using-PrEP. The aim of this study was to determine the prevalence of anal HR-HPV infection and abnormal anal cytohistology in MSM using PrEP and MSMLWH. Preliminary data are reported here and final results are expected in coming months.

Methods: MSM-using-PrEP and MSMLWH were enrolled in this mono-centric study during consultations. Patient characteristics, sexual behavior and demographics were collected using a questionnaire, completed on the day of the anal swab testing. Patients with HR-HPV infection, abnormal cytology or both were subsequently sent for High Resolution Anoscopy (HRA).

Results: At present, we enrolled 150 MSM-using-PrEP and 107 MSMLWH. Quality of anal swabs was sufficient in respectively 95% ($n = 143$) and 81% ($n = 87$). HR-HPV prevalence in MSM-using-PrEP was comparable with HR-HPV prevalence in MSMLWH; respectively 74% ($n = 106$) and 75% ($n = 65$) tested positive for at least one HR-HPV ($P = 1.000$). No significant difference in abnormal cytology was seen; 53% ($n = 76$) of MSM-using-PrEP and 58% ($n = 51$) of MSMLWH had either ASC-US, ASC-H, LSIL or HSIL ($P = 0.6$). Until today, 58 MSM using PrEP and 31 MSMLWH underwent HRA. Biopsies were performed in 43 MSM-using-PrEP and 25 MSMLWH. Preliminary results on histology of lesions show presence of anal HSIL in 19% ($n = 11$) and 32% ($n = 10$) respectively ($P = 0.706$).

Conclusions: MSM-using-PrEP have a similar risk of HR-HPV infection and abnormal anal cytohistology as MSMLWH, which is higher than what has been reported in HIV-negative MSM not using PrEP.

14 Projections in anal cancer incidence and burden in the United States, 2001–2035

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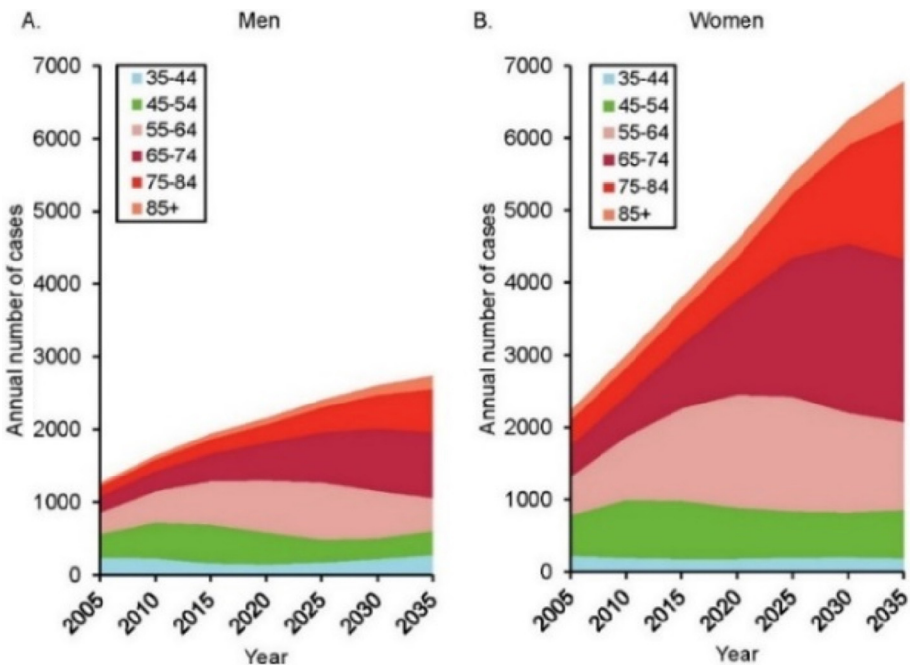
Background: Squamous cell carcinoma of the anus (SCCA) incidence has been rising rapidly (~3%/year) in the United States (US), with a pronounced increase (~5%/year) occurring among older adults (≥65 years). To inform public health response, we estimated how SCCA incidence patterns and burden (annual number of cases) will change over the next few decades.

Methods: Using the National Program of Cancer Registries and Surveillance Epidemiology End Results data, we analyzed SCCA incidence and burden during 2001–2020. Further, using age-period-cohort modeling, we estimated age-specific SCCA incidence and burden by sex in the US through 2035.

Results: SCCA incidence among older adults (aged 65–74, 75–84, and ≥85 years) is projected to rise, reaching 5.0, 4.9, 4.3 (per 100 000) in 2031–2035 among men vs 3.7, 3.8, 3.4 in 2016–2020 and 11.2, 12.6, 8.0 among women in 2031–2035 vs 8.2, 6.8, 5.2 in 2016–2020, respectively. In contrast, among men and women aged <65 years, SCCA burden is expected to decline, likely due to declining SCCA incidence rates among recent birth cohorts. As a result of increasing incidence and rising number of older adults, the SCCA burden is expected to rise, reaching ~2700/year among men and ~7000/year among women in 2031–2035, with most cases aged ≥65 years (61% in men and 70% in women in 2031–2035; from 40% and 46% in 2016–2020).

Conclusion: The projected rise in SCCA burden among older adults is an emerging concern and could have important implications to guide future research to improve early detection and clinical care among older adults.

Figure: Recent and projected burden (annual number of cases) of squamous cell carcinoma of the anus among men and women in the United States: 2005–2035.



15 Racial and ethnic differences in high-risk HPV genotype distribution among people living with HIV in the ACES cohort

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Background: Fewer anal cancer cases are attributable to HPV16 among people living with HIV (PLWH; ~67%) compared to without HIV (~86%). Additionally, evidence suggests that cervical cancers in Black women are more likely attributable to non-HPV16 high-risk types versus other racial and ethnic (R/E) groups. We assessed R/E differences in anal HPV positivity and partial genotyping among PLWH in a diverse high-resolution anoscopy (HRA)-referral population.

Methods: In the Anal Cancer Etiology and Screening (ACES) study, participants were referred for HRA at the Mount Sinai Anal Dysplasia Clinic. Clinical data were abstracted from electronic medical records. Clinical testing at the HRA visit included anal cytology and HPV testing for HPV16, HPV18, and pooled 12 other carcinogenic types (cobas® 4800). Among PLWH, high-grade squamous intraepithelial lesion (HSIL) prevalence, HPV prevalence and genotype differences by R/E were assessed with a multivariate logistic regression model adjusting for age and vaccination status.

Results: 606 PLWH had samples and data collected between 2020–2023. Black individuals had the highest HPV-positivity and Hispanic individuals had the highest HSIL prevalence. Black individuals with HSIL had the highest HPV16-positivity; yet, among those with ≤LSIL, they had the highest non-HPV16/18 high-risk HPV-positivity (Table 1). Overall, there were no significant R/E differences in HPV prevalence, partial genotype distribution, or HSIL prevalence adjusted for age and vaccination status.

Conclusions: While there were no differences in partial genotype distribution among PLWH in adjusted models, our findings suggest potential interesting differences in HPV genotype distribution by R/E and disease status that warrant further exploration.

Table 1. Racial and ethnic differences in HSIL prevalence, HPV prevalence and partial genotyping, overall and stratified by histology (HSIL vs ≤LSIL) among PLWH in the ACES cohort. n/N (%)[1].

		Black	Hispanic/Latinx	White
HSIL prevalence		65/178 (36.5)	82/197 (41.6)	61/187 (32.6)
HPV prevalence	HSIL	140/177 (79.1)	135/196 (68.9)	130/188 (69.2)
	≤LSIL	59/65 (90.8)	74/82 (90.2)	54/61 (88.5)
		80/113 (70.8)	61/115 (53.0)	74/126 (58.7)
HPV16	HSIL	31/140 (22.1)	39/135 (28.9)	26/130 (20.0)
	≤LSIL	22/59 (37.3)	26/74 (35.1)	12/54 (22.2)
		9/80 (11.3)	13/61 (21.3)	13/74 (17.6)
HPV18	HSIL	13/140 (9.3)	11/135 (8.2)	16/130 (12.3)
	≤LSIL	3/59 (5.1)	6/74 (8.1)	4/54 (7.4)
		9/80 (11.3)	5/61 (8.2)	11/74 (14.9)
Other HR-HPV type	HSIL	96/140 (68.6)	85/135 (63.0)	88/130 (67.7)
	≤LSIL	34/59 (57.6)	42/74 (56.8)	38/54 (70.4)
		62/80 (77.5)	43/61 (70.5)	50/74 (67.6)

[1]Missing or insufficient data excluded. Results similar when restricted to men living with HIV only.

16 The effects of sociodemographic risk factors on HPV related cancer trends in England between 2014–2020

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Background: High-risk Human Papillomavirus (hrHPV) strains are responsible for approximately 4% of all cancer worldwide. hrHPV is responsible for 40%, 70%, 50%, 100% and 90% of vulval, vaginal, penile, cervical and anal cancers, respectively. There has been a reported rise in a number of these malignancies, however studies looking at data in England are limited.

Methods: Demographic data from the Clinical Outcomes and Services Dataset (COSD) was presented at IANS 2022, this is a larger and more up-to-date dataset. Data was extracted for all patients over the age of 25 years diagnosed with anal, penile, cervical, vulval and vaginal cancer in England between 2014–2020. Outcomes included ethnicity, social deprivation, staging and performance status.

Results: Cervical, vulval, female anal, penile, male anal and vaginal cancers made up 44.9%, 19.5%, 14.7%, 9.9%, 7.4% and 3.6%, of all HPV cancers, respectively. There was an increase in number of new diagnoses/year between 2014–2022 for most hrHPV cancers, which was more marked when age was accounted for. There was a significant ($P < 0.05$) relationship between: staging and ethnicity for cervical and vulval cancer; staging and deprivation for cervical and vaginal cancer; deprivation and performance status for male and female anal cancer; and age and deprivation for anal, cervical, penile and vulval cancer.

Conclusions: hrHPV cancer trends and the relationship between different socioeconomic risk factors are important to understand in order to comprehend the effect of HPV cancer prevention strategies as well as understand how to better improve services targeting the screening and treatment of such conditions.

17 The patch cohort: high-risk HPV persistence and anal dysplasia at 12 months among transgender individuals

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Background: Transgender women (TGW) with HIV have a high prevalence of high-risk HPV (HR-HPV) and anal cancer. We examined anal dysplasia (AD) and HR-HPV persistence among TG persons to inform preventive strategies.

Methods: Using a convenience sample of TG persons in Washington DC, we collected baseline and 12-month demographics, sera, and anal swabs for cytology and HR-HPV genotyping (ROCHE-Cobas). We defined AD as a cytology diagnosis of ASCUS or greater; and current gender affirming-hormonal treatment (GAHT) as self-reported use, or serum estradiol >60 pg/mL (estradiol) and a testosterone level below 264 ng/dL (androgen blocker). Factors associated with HPV and/or AD persistence by month-12 were examined using Fisher's exact test.

Results: Of 98 enrolled TG persons, 89 had anal cytology results at baseline, and 42 reached the 12-month follow-up visit by June 2023. At baseline, only one transgender man (6%) had HR-HPV (other than HPV-16/18) and AD; while among 76 TGW with adequate anal cytology, 37(48%) had AD, and 55 (71%) had HR-HPV. Among 12 TGW with HPV-16 at baseline, 7(58%) had persistent HPV-16 at 12-months, which was not associated with history of HPV-immunization ($P = 0.19$) or HIV-1-infection ($P = 0.42$). Of 18 TGW with AD at baseline, 12 (67%) had persistent AD at 12-months, without any significant association with HPV-immunization ($P = 0.19$) or HIV-1-infection ($P = 0.42$). Of note, 11 (92%) TGW with persistent AD and 7 (100%) TGW with persistent HPV16 were HIV+.

Conclusions: HR-HPV and AD were common in TGW and uncommon in TG men. The rate of persistent HR-HPV and AD at 12-months were elevated, particularly in HIV+TGW.

Table 1: Baseline Characteristics of transgender individuals in the PATCH cohort

Baseline Characteristics		
	N (%)	
N	Total = 98	TGW = 80
Male Sex assigned at birth	80 (82)	NA
Age <35	41 (42)	41 (51)
Gender affirming hormone use:		
• Estradiol use	28 (29)	28 (35)
• Androgen blocker use	25 (25.5)	25 (31)
• Testosterone use	2 (2)	0 (0)
Tobacco use	57 (58)	49 (61)
Anal receptive sex within the last 12 mo	62 (63)	60 (75)
Recalled getting HPV vaccine	22 (22)	19 (24)
HPV 16 positive	20 (20)	20 (25)
HPV 18 positive	9 (9)	9 (11)
Other high-risk HPV positive	53 (54)	52 (65)
Any HR HPV positive	56 (57)	55 (69)
Anal cytology:		
• Normal	51 (52)	39 (49)
• ASCUS	22 (22)	21 (26)
• LSIL	15 (15)	15 (19)
• HSIL	1 (1)	1 (1)
HIV Positive	54 (55)	54 (68)
HIV Viral Load >200 copies/mL	20 (36)	
CD4 count <200	3 (5)	
Median CD4 count	467.5	
Prescribed ART	47 (85)	

Table 2: Anal dysplasia and HPV clearance at month 12 among transgender women.

Changes in AD and HPV status at 12 months follow up compared to baseline		N (%) Total=37
Anal cytology	AD to normal	6 (16.2)
	Normal to AD	8 (21.6)
	Persistent AD	12 (32.4)
	Persistent normal	11 (29.7)
HPV-16	Persistent positive	7 (18.9)
	Persistent negative	25 (67.6)
	Cleared infection	5 (13.5)
	Acquired infection	0
HPV-18	Persistent positive	2 (5.4)
	Persistent negative	35 (94.6)
	Cleared infection	0
	Acquired infection	0
Other HR-HPV	Persistent positive	19 (51.4)
	Persistent negative	11 (29.7)
	Cleared infection	5 (13.5)
	Acquired infection	2 (5.4)

Multi-zonal/Multi-site Disease

18 Exploration of biomarkers in multizonal intraepithelial neoplasia: understanding epithelial transformation (MINUET)

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Background: Rates of lower anogenital tract (LAGT) squamous cell carcinoma (SCC) have risen steadily in women over recent years. All LAGT zones are susceptible to HPV-related dysplasia. In some women, high-grade squamous intraepithelial lesions (HSIL) occur in more than one LAGT zone concurrently, designated multizonal intraepithelial neoplasia (MZN). All HSIL have the potential to progress to SCC without treatment making timely assessment and management of MZN challenging. Although DNA methylation (DNAme) has been useful in prognosing other LAGT HSIL, few studies have assessed this approach in MZN. Investigation of MZN is needed to determine if biomarkers can assist in MZN triage.

Methods: We conducted a study on 12 women with MZN where at least one LAGT HSIL progressed to SCC. DNAme of host gene EPB41L3 and late regions of HPV16, 18, 31, 33 was assessed in biopsies: from the cancer zone prior to progression to SCC and at the time of SCC; and from other LAGT zones not progressing to SCC.

Results: 123 multi-timepoint samples from 12 women were analysed, including 15 invasive SCCs in the anal canal ($n = 4$), peri-anus ($n = 6$), vulva ($n = 2$) and vagina ($n = 3$). DNAme profiling of SCC with respect to time and zone was performed. Preliminary analysis suggests that DNAme increases with disease severity in all LAGT zones, except the peri-anus.

Conclusions: MZN is under-researched yet complex to manage clinically. DNAme has previously been useful to predict disease progression, suggesting its usefulness in triaging cases of MZN. Identification of biomarkers and their application in the triage of HSIL may improve the objectivity of MZN treatment.

Pathogenesis, Molecular Biology and Virology

19 Significance of programmed cell death ligand 1 (PD-L1) expression patterns in pathogenesis of anal high-grade intraepithelial lesion and anal squamous cell carcinoma

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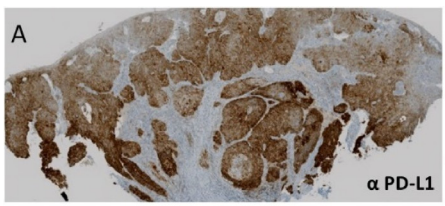
Background: Activation of the PD-L1/PD-1 axis leads to dysfunction of tumor infiltrating immune cells (TIC) in the tumor microenvironment (TME) and can occur due to an inflammatory process. This study examined PD-L1 expression patterns in anal epithelial cells (EC) and immune cells (IC) to understand their role in pathogenesis of anal high-grade squamous intraepithelial lesions (HSIL) and squamous cell carcinoma (SCC).

Methods: Samples: Fresh-frozen paraffin-embedded samples from 49 people with HIV (PWH) (27-SCC, 11-HSIL,) and 47 HIV-negative people (25-SCC, 11-HSIL,) were studied. Sections were stained with hematoxylin and eosin. PD-L1 expression was determined by immunohistochemistry using anti-PD-L1 (SP263) antibody.

Results: 52% of SCC samples expressed PD-L1 in tumor cells (TC), 4.5% of HSIL samples expressed PD-L1 in EC. HIV status did not affect PD-L1 expression in TC (52% HIV-negative SCC, 48% HIV-positive SCC). IC PD-L1 expression was observed in HSIL (54.5%), and SCC (90.4%) samples. TC PD-L1 expression showed three patterns: diffuse (7.7%), focal (11.5%) and patchy (36.5%) (Fig 1). TIC PD-L1 expression correlated with increased IC infiltration (r = 0.5; 95%CI, 0.3–0.7; $P < 0.0001$).

Conclusions: The increase in EC PD-L1 positivity from HSIL to SCC may contribute to enhanced immunosuppression and may be associated with progression from HSIL to SCC. In majority of anal SCC PD-L1 expression pattern in TC was non-diffused. The TIC PD-L1 expression was associated with increase in stromal IC infiltration. These findings potentially suggest that inflammatory molecules secreted by IC may trigger inducible PD-L1 expression in both TC and TIC indicating an immune-reactive anal TME.

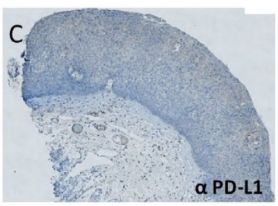


SCC

Fig 1A: PD-L1 expression pattern –diffuse

SCC

Fig 1B: PD-L1 expression pattern, non–diffuse



HSIL

Fig 1C: absence of PD-L1 expression in epithelial cells

20 Spatial mapping of immune cells in barrier tissues of immunocompromised patients affected by human papillomavirus-related disease

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Background: Inborn errors of immunity (IEI) are rare, genetic disorders that compromise the immune responses, leading to increase susceptibility to infections, immune dysregulation and increased risk of malignancy. GATA2 deficiency, an IEI caused by heterozygous mutation of the hematopoietic transcription factor GATA2, is characterized by an increased susceptibility to skin and mucosal HPV-related diseases. GATA2 deficiency is treated with hematopoietic stem cell transplantation (HSCT), which results in resolution of HPV-related diseases.

Methods: We assessed myeloid and lymphoid cell populations in biopsies of lesional and non-lesional verrucous lesions and anogenital condylomas from GATA2 deficiency patients pre- and post- HSCT via confocal microscopy, characterizing the immunological landscape resulting in regression of HPV- related disease at epithelial surfaces.

Results: Our preliminary data show that following HSCT, long lived Langerhans cells, recruited dendritic cells and other myeloid cells help orchestrate the innate and adaptive immune response during the critical early period of immune reconstitution post-HSCT.

Conclusions: After HSCT, innate immunity and myeloid reconstitution play a central role in regression and clearance of HPV related skin lesions in GATA2 deficiency patients. Further imaging and functional studies will help elucidate the role that different immune cell types play in lesion regression, allowing us to devise better strategies for effector cell-based therapies or vaccines for humans. (Funded by the National Institute of Allergy and Infectious Diseases and the National Cancer Institute).

Screening and Diagnostics

21 An anal pap screening quality improvement project at a federally qualified health care center

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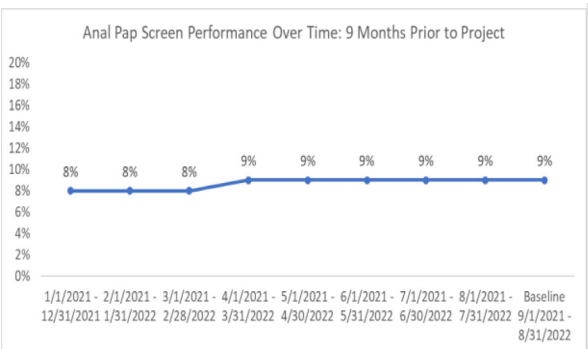
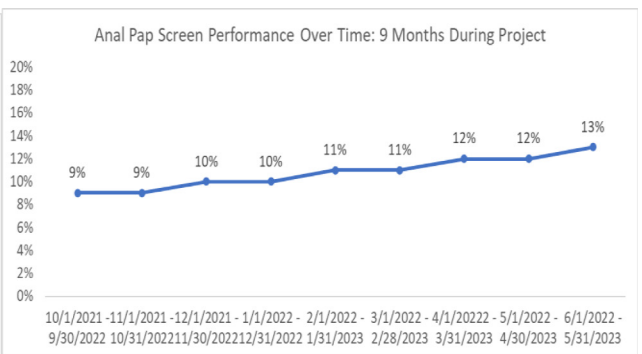
Background: The aim of this study was to evaluate the effectiveness of adding an anal pap care gap to visit planning reminders as standard of care for selected patient populations.

Methods: Using a population health platform that reads data from our electronic medical record and generates a variety of reports, including individualized provider visit planning reports, we added anal pap reminders for patients at risk of HPV related anal dysplasia who were due for an anal pap. This care gap appeared in each provider's daily visit planning report with the goal of performing the anal pap during the routine visits. The initial care gap query was launched in August 2022 and then modified in September 2022. We retrospectively examined the rate of screening nine months before and nine months after the addition of the anal pap reminder to the visit planning reports.

Results: Prior to implementation of the care gap measure, 9% of eligible patients were screened with an anal pap. This rate remained stagnant for over a year. With the start of the care gap measure, the rate of screening increased to 13% of eligible patients. The greatest increase, 7% to 10%, occurred in MSM and AMAB PLWH over the age of 30 years old.

Anal Pap Screen Care Gap Population
Patients with a medical visit in the past 12 months
Anyone living with HIV and a history of HSIL or warts
MSM and AMAB living with HIV at age 30
Women and non MSM living with HIV at age 40
Perinatally acquired HIV
MSM not LWH at age 40





Conclusions: These early results suggest that implementation of visit planning reminders can increase the rate of anal pap screenings in patients at risk for anal dysplasia. Further research is needed to determine the long-term sustainability of this care gap model.

22 Anal cancer screening results from 18-to-35-year-old men who have sex with men living with HIV

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Background: Men who have sex with men living with HIV (MSM LWH) are at highest risk for human papillomavirus (HPV)-associated anal cancer. No consensus exists on the optimal age to start screening for anal cancer. This study aimed to assess prevalence and severity of anal HPV disease in young MSM LWH under the age of 35 which is the currently proposed screening threshold.

Methods: 1255 MSM LWH <35 with anal cytology screening between 2014 and 2020 were analyzed. 916 were co-tested for high-risk HPV (HR-HPV). 467 underwent high-resolution anoscopy (HRA) and biopsy. Cancer registry data were queried. Predictors of abnormal cytology (i.e. ≥ASCUS) and histological high-grade squamous intraepithelial lesion (HSIL) were evaluated using unadjusted logistic regression.

Results: Median age was 28 years (range, 18–34). 21% received one or more doses of HPV vaccine. Abnormal cytology rate was 65%. HR-HPV and HPV16 prevalence were 87% and 30%. HRA-guided biopsy results were benign (10%), LSIL (43%), and HSIL (47%). No cases of prevalent or incident anal cancers were detected. Similar findings were observed across age subgroups (18–24, 25–29, and 30–34), except for a higher AIN 3 prevalence in the 30–34 group (19%, $P = 0.01$). Abnormal anal cytology was significantly associated with HR-HPV positivity. Histological HSIL was associated with HR-HPV infection and cytological diagnosis of LSIL or worse.

Conclusions: The absence of anal cancer in a large cohort of young MSM LWH <35, despite high rates of anal high-risk HPV infection and HSIL, supports an age-based anal cancer screening strategy for MSM LWH.

23 Anal cancer screening results from HIV-negative women with history of genital precancer or cancer: preliminary findings of the SWAN study

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Background: Women with a history of HPV-associated genital high-grade squamous intraepithelial lesions (HSIL) and cancer are at increased anal cancer risk. The prevalence of anal HPV and the severity of associated lesions in this population is unknown. To evaluate clinical performance of screening for anal cancer in this population and anal HSIL (aHSIL) prevalence, we launched the Screening Women for Anal Neoplasia (SWAN) study (NIH R01CA256660). Herein, we describe the initial findings from the first 44 participants.

Methods: We enrolled HIV-uninfected women with a history of cervical, vaginal or vulvar HSIL or cancer aged 45 or older in a longitudinal screening protocol. At baseline, participants underwent contemporaneous anal cytology (AC) and high-risk HPV (hrHPV) testing as well as high-resolution anoscopy (HRA). We calculated the prevalence of abnormal anal testing and histologically confirmed anal HSIL.

Results: The mean age was 55 years (range 45–71). Participants were mostly white (47%) with 39% Hispanic ethnicity; 7% were Black. More than half (53%) were past or current cigarette smokers, and 69% reported a history of receptive anal sex. Nearly half (45%) had a history of CIN2 lesions, while 39% had prior CIN3 and 4 participants had invasive cervical cancer. On anal exam, nearly a third (31%) had anal hrHPV infection; 6% had HPV16 anal infection. On baseline HRA examination 13.6% (95% CI: 5.2%–27.4%) had histologic aHSIL.

Conclusions: Preliminary results from the SWAN Study indicate substantial aHSIL prevalence among HIV-uninfected women with a history of genital HPV-associated neoplasia/cancer despite a substantial proportion of less severe genital neoplasia.

24 Anal cancers in previously screened versus unscreened patients: tumor stage and treatment outcomes

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Background: The utility of targeted screening for anal squamous cell carcinoma (SCC) remains unclear. This study aimed to determine whether screening high-risk patients detects SCC at an earlier stage compared to the routine practice of not screening.

Methods: This cohort study included patients with a pathologic diagnosis of invasive anal squamous cell carcinoma between 2002 and 2022 at a quaternary care center in Canada. Patients diagnosed through a high-risk screening program were compared to those who did not undergo screening. The primary outcome was clinical stage at presentation, categorized as T1N0M0 vs other.

Results: A total of 612 anal squamous cell carcinoma patients were included, with 26 of those patients diagnosed through screening. Screened patients had greater odds of presenting with T1N0M0 tumors compared to unscreened patients (18 [69.2%] vs 84 [14.3%]; adjusted odds ratio 9.95; 95% confidence interval 3.95–25.08). A propensity score matched sensitivity analysis found similar results (odds ratio 11.13; 95% confidence interval 4.67–26.52; $P < 0.001$). Screened patients had greater odds of treatment with wide local excision alone, as opposed to any combination of chemotherapy, radiation, and surgery (3 [12.5%] vs 18 [3.2%]; odds ratio 4.38; 95% confidence interval 1.20–16.04). There were no significant differences in treatment failure or overall survival between groups.

Conclusions: Screening for anal squamous cell carcinoma amongst high-risk populations detects cancers at an earlier stage. Patients with screen-detected cancers also had a greater likelihood of being candidates for wide local excision alone, which may have spared them the morbidity associated with chemoradiotherapy or abdominoperineal resection.

25 Anal HR-HPV genotyping as a strategy for detection of precursor lesions of lower genitourinary tract malignancies

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Background: Women living with HIV (WLWH) are especially vulnerable to anogenital HPV infections, although there is limited information regarding the potential role of the anal canal as a reservoir for HR-HPV infections contributing to cervical precancers. We aim to investigate the presence of HR-HPV in the anal canal and its association with cervical HR-HPV and cervical lesions among WLWH.

Methods: We have commenced a prospective 24-month study of 600 WLWH living in Santo Domingo, Dominican Republic. To date, we have enrolled 325 non-pregnant women attending STI clinics. Women were referred to a screening clinic (IDCP) where they provided informed consent and underwent a comprehensive assessment, including a questionnaire, medical examination, clinician collection of samples from cervix and anus, and vaginal self-sampling. We used the ScreenFire HPV assay, an isothermal assay providing HPV genotype data in four risk-based groups. The study is part of two NCI-sponsored networks: US-Latin American-Caribbean HIV/HPV-Cancer Prevention Clinical Trials Network (ULACNet) and the HPV-AVE Consortium (PAVE).

Results: Preliminary data from 250 WLWH were analyzed. Anal samples were more likely to be HR-HPV positive compared to cervical or vaginal samples (40.3%, 36.5%, 45% positive, respectively: *P*-value 0.035). Among HR-HPV positives, HPV16 was detected more frequently in anal samples than cervical or vaginal samples, although differences were not statistically significant. Hierarchical HPV genotyping analysis is shown in Table 1.

Conclusions: In WLWH, HR-HPV is commonly found in the anal canal, suggesting that this may play a role as HR-HPV reservoir even after management of cervical lesions.

Table 1. Estudio Oportunidad: ScreenFire HPV results by sample type* for 250 WLWH.

	Cervix		Vaginal		Anal	
	n	%	*n*	%	*n*	%
Negative	155	63.5%	126	55.0%	74	71.6%
Positive	89	36.5%	103	45.0%	71	40.3%
HPV16	20	8.2%	23	10.0%	23	13.1%
HPV18/45	12	4.9%	16	7.0%	22	12.5%
HPV31/33/35/52/58	28	11.5%	36	15.7%	29	16.5%
HPV39/51/56/59/68	29	11.9%	28	12.2%	31	17.6%

*Multiple infections are counted once, in highest HR-HPV risk category (hierarchical analysis).

26 Attitudes towards anal cancer screening among people living with HIV living in Puerto Rico

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Background: While people living with HIV (PLWH) are at increased risk of anal cancer, lack of awareness and education greatly hinders screening efforts. This study aims to describe attitudes regarding anal cancer screening tests and diagnosis among PLWH.

Methods: Between November 2020 to December 2021, 212 PLWH completed a telephone-based interview assessing medical, sexual history, socio-demographic, lifestyle variables, alongside attitudes and knowledge pertaining to anal cancer screening. Descriptive statistics and Chi-square test were used for the analysis.

Results: Overall, 67.5% of participants were male and 67.5% ≥50 years. Most, 81.3%, were concerned about developing anal cancer. While 60.4% of the population had heard of anal pap test, 52.2% had an anal pap test in the past, 47.6% had no prior knowledge about the test, 96.7% expressed willingness to undergo future screening, 65.9% reported being worried about the test results, and 75.5% expressed fear of a diagnosis. Meanwhile, 40.0% of participants expressed discomfort with current screening methods, with higher observed among those with lower education (51.6% vs 30.4%, $P < 0.05$). Furthermore, 27.8% of participants referred to not knowing which doctor to consult regarding their anal health concerns. Additionally, 97.2% expressed interest in learning more about the anal pap test, while 96.7% desired further information about anal cancer.

Conclusions: These findings highlight the urgent need for increased education and awareness regarding anal cancer screening in PLWH, where stigma is high. Improving primary prevention and early detection of anal dysplasia among high-risk populations in Puerto Rico could mitigate the rising rates of anal cancer.

27 Bridging the gap: assessing perceived motivators and barriers in anal cancer screening among people with HIV

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Background: Anal cancer screening with Papanicolaou smears and biopsies and ablation via high-resolution anoscopy (HRA) are becoming increasingly more accessible however uptake remains low in many settings. We sought to explore what factors influence the decision to pursue anal cancer screening among people with HIV (PWH).

Methods: PWH currently receiving care at our Ryan White HIV/AIDS Program clinic ≥35 were eligible to participate. We recruited by convenience sampling via in-person clinic advertising and an internal mobile platform. Interview questions were developed using the health belief model.

Results: Twenty-six interviewees were included (8 women, 1 transgender woman, 14 men who have sex with men and 3 men who have sex with women). Nine had never engaged in anal cancer screening, 6 had undergone Papanicolaou smears without HRA and 10 had undergone both a Papanicolaou smear and HRA. Perceived barriers included stigma, lack of awareness, negative experience with HRA, and sexual trauma. Perceived motivators included perceived risk (i.e. HIV status, co-morbidities and sexual practices) and perceived benefits (i.e. trust in clinic staff and personal investment in health).

Conclusion: Eliciting patient perspectives can be a powerful tool in evaluating and improving on a screening program's performance. Our findings highlight that in order to increase engagement and retention in screening services is it important to: (1) increase awareness using destigmatizing messaging, (2) provide anticipatory guidance when counseling people on HRA procedures and (3) be willing to modify and adapt screening protocols for patients who face significant barriers such as sexual trauma.

28 Clinical prediction model for anal high-grade squamous intraepithelial lesion (HSIL) screening

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Background: Anal high-grade squamous intraepithelial lesion (HSIL) screening tools include anal cytology (inconsistent performance) and high-risk HPV testing (low specificity). This study aimed to develop a clinical prediction model to facilitate anal cancer screening.

Methods: Patients' medical records from two institutions were reviewed to identify candidate predictors of HSIL. A prediction model was built using elastic net regression, and internally validated with five-fold cross-validation. A third institution provided data for external validation. The initial candidate predictors were age, sex, immunosuppressant use, HIV status, prior genital HPV-related disease requiring treatment, anal cytology, anal high-risk HPV infection, and interaction terms (HIV status*high-risk HPV infection) and (HIV status*history of genital HPV-related disease). The area under the curve/receiver operating characteristic (AUROC) was calculated.

Results: Among 536 patients included in the model development, 382 (71%) were HIV-positive, 168 (31%) were women, and mean age was 49.2 (SD 12.1). The prevalence of HSIL was 21% (114/536). The predictors selected for the model were: age, sex, immunosuppressant use, prior genital HPV-associated disease, anal cytology, anal high-risk HPV infection, and the two interaction terms (HIV status*high-risk HPV infection) and (HIV status*history of genital HPV-related disease). The AUROC in the test set was 0.80 (95%CI: 0.69–0.90). The external validation set consisted of 242 patients, of whom 224 (93%) were male, 159 (66%) were HIV-positive, and mean age was 50.5 (SD 13.5). The prevalence of HSIL was 37% (90/242). The AUROC in the external validation dataset was 0.73 (95%CI: 0.67–0.80).

Conclusions: This clinical prediction model demonstrated a promising performance and included objective and easily obtained predictors.

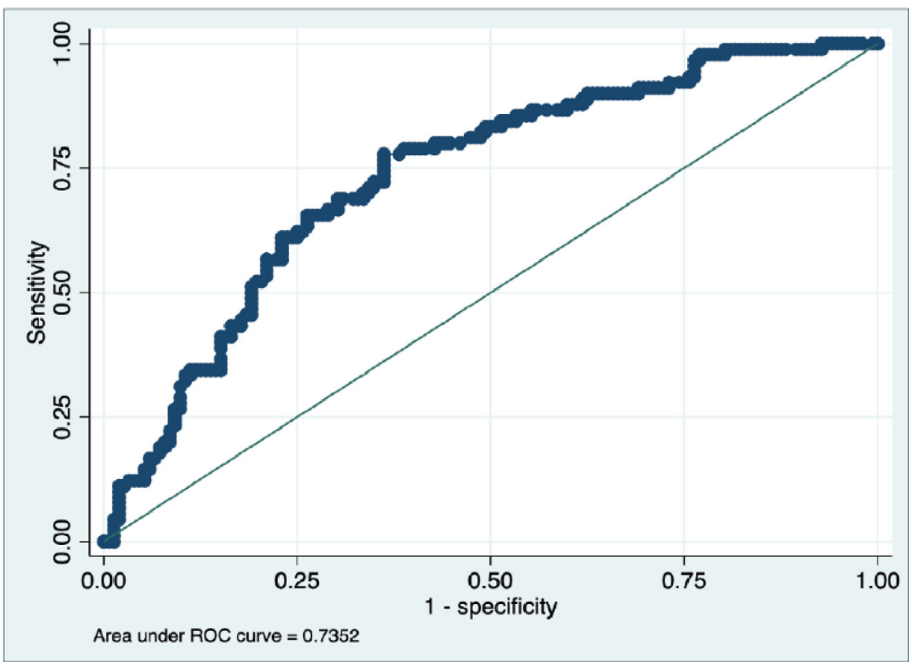

Fig. 1. ROC curve in external validation dataset.

29 Core Outcome Measures in Squamous Intra-Epithelial Precursor Lesions of the Anus (CORSICA): development of a disease measurement tool

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Background: Existing trials in anal high-grade squamous intra-epithelial lesion (aHSIL) have predominantly used disease response outcomes based on histological and cytological changes to measure the effects of treatment. Several limitations to this approach have been identified.

Methods: We aim to develop a disease measurement instrument capable of describing disease burden such that it can be used to evaluate disease response to treatment in addition to histological and cytological based measurements further strengthening the quality of disease response outcomes. To account for variations in diagnostic practice, the approach will be applicable to both a HRA and non-HRA setting.

Results: The disease measurement instrument will be developed over 4 stages: 1. A meeting of AIN experts to determine a longlist of lesion measurement items capable of capturing disease burden; 2. A series of disease assessments will be undertaken in participants known to have aHSIL to assess disease burden using the measurement items identified in stage 1; 3. Data analysis to determine the best performing measurement items and comprise a disease measurement instrument; 4. Pilot-testing of the proposed disease measurement instrument.

Conclusions: An acceptable, feasible, reliable and reproducible method of disease measurement would add further granularity to outcomes relating to disease assessment. It could be utilised in aHSIL treatment trials to improve the quality of disease response outcomes and in clinical practice as a modality for communicating disease extent or evaluating response to treatment.

30 Determining optimal anal cancer screening algorithms for men who have sex with men with HIV: a modelling study

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Background: The objective of this study was to determine optimal anal cancer screening algorithms (by evaluating harms, benefits, and efficiency) over the lifetime of men who have sex with men (MSM) with HIV aged ≥35 years.

Methods: We developed a mathematical modeling framework of anal HPV, high-grade squamous intraepithelial lesion (HSIL), and anal cancer natural history among persons with HIV. The framework was parameterized using the best available natural history and HSIL treatment data (guided by several meta-analyses and the ANCHOR trial) and validated independently to ensure the accuracy of model predictions. Screening algorithms were evaluated in terms of lifetime anal cancer incidence and resource needed (number of tests, high-resolution anoscopies [HRAs] and biopsies, and treatments) to prevent a single anal cancer case.

Results: In the absence of screening, the estimated lifetime anal cancer incidence among MSM living with HIV was 4375/100 000. Annual cytology prevented 2376 cases/100 000 (54% reduction). Longer screening interval decreased the number of tests, HRA-directed biopsies, and HSIL treatments, but resulted in higher anal cancer incidence. Lifetime reduction in anal cancer incidence and corresponding screening outcomes (i.e., number of screening tests, HRA-directed biopsies and HSIL treatments) greatly varied based on the choice of primary screening test, triage strategy, and screening interval.

Conclusions: Our study provides initial guidance on the harms/benefits of different screening algorithms among MSM with HIV, which is necessary to inform guidelines. Future findings will provide efficiency frontiers, optimal screening intervals based on age and screening outcomes, cost-effectiveness ratios, and outcomes among other risk groups.

Table. Cumulative anal cancer incidence (per 100 000) and resource utilization (number of tests, HRA-directed biopsies, and HSIL treatments) for different anal cancer screening and triage strategies for MSM with HIV (aged ≥35 years).

Primary Test	Triage*	Cumulative (lifetime) anal cancer incidence (per 100,000)			Resource utilization to prevent a single anal cancer case											
					Number of cytology tests			Number of HPV tests			Number of HRAs and Biopsies			Number of HSIL(s) treatments		
		Screening interval			Screening interval			Screening interval			Screening interval			Screening interval		
		1-yr	2-yr	3-yr	1-yr	2-yr	3-yr	1-yr	2-yr	3-yr	1-yr	2-yr	3-yr	1-yr	2-yr	3-yr
None	None	4375			0			0			0			0		
Cytology	None	1999	2478	2874	914	584	501	0	0	0	498	337	297	163	149	147
Cytology	HR HPV	2018	2528	2847	922	599	492	506	347	292	331	241	209	153	142	134
HR HPV	None	1850	2330	2616	0	0	0	861	542	428	522	343	279	158	149	139
HR HPV	Cytology	2036	2560	2812	571	392	317	928	610	481	333	245	205	154	145	132
CT (HR-HPV)	None	1818	2281	2595	851	529	423	851	529	423	679	431	349	166	155	146
Cytology	HPV16/18	2389	2766	3101	1092	687	590	622	406	355	235	169	155	128	115	114
HPV16/18	None	2176	2574	2844	0	0	0	987	614	492	339	223	185	128	119	112
HPV16/18	Cytology	2391	2789	3058	385	259	219	1094	697	570	235	171	149	128	117	110
CT (HPV16/18)	None	1852	2302	2648	861	534	436	861	534	436	585	375	310	164	151	143
Cytology	HPV16	2595	2936	3228	1219	768	656	704	457	396	209	153	140	116	106	105
HPV16	None	2414	2807	3027	0	0	0	1106	705	558	301	205	169	116	112	105
HPV16	Cytology	2598	2946	3230	343	231	203	1220	773	656	210	153	140	117	106	104
CT (HPV16)	None	1864	2298	2671	865	534	441	865	534	441	563	361	304	162	148	142

Acronyms: CT, co-testing with cytology; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesions; HR, high-risk; HRA, high-resolution anoscopy; MSM, men who have sex with men; yr, year
* Triage is an additional step interposed between screening and diagnosis to further stratify individuals with positive primary screening results according to risk for the disease state

31 Expert opinions on the management of anal neoplasia: a Delphi consensus study

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Background: Anal cancer is preceded by high grade squamous intraepithelial lesions (HSIL). Guidelines for which populations to screen, details of neoplasia screening and treatment, and long-term management related to HSIL are inconsistent.

Methods: Using a Delphi method to determine consensus regarding key aspects of anal neoplasia screening and management. This approach uses two rounds of a questionnaire that are sent sequentially to participants. In round one, the experts responded to quantitative and qualitative questions. Answers were aggregated as agreement, neutral and disagreement and the distributions were compared using Pearson's Chi-Square test.

Results: Experts agreed (>80%) on populations to screen such as persons living with HIV, men who have sex with men not living with HIV, and persons with a history of anal condyloma, incidental neoplasia, or current HPV disease. High-risk (HR)-HPV testing and cytology results accompanied by HR-HPV tests were agreed upon as the primary screening tools for referral to high-resolution anoscopy (HRA). Consensus on the best procedure to detect neoplastic lesions was HRA with a colposcope in an office setting without sedation. Lesions indicative of high-grade, particularly with diagnosis of HR-HPV, were recommended for treatment. Treatment practices favored ablative vs topical therapy. Regular screening for at risk individuals as well as those at risk of recurrence after treatment was recommended.

Conclusions: Findings from this study present a preliminary consensus of experts' opinions regarding the optimal screening and treatment modalities and can serve as a tool to help address the lack of detailed guidelines for anal neoplasia screening and management.

32 High-resolution anoscopy intensive training in Mexico

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Background: We report the experience of a high resolution anoscopy (HRA) intensive training course in Mexico City.

Methods: From March to August 2022, men who have sex with men living with HIV (MLWH) patients of Condesa Clinics in Mexico City, were evaluated, as part of an HRA training course 2 physicians. Training was conducted by two experienced anoscopists: the first week, professors directly supervised HRA procedures. In the following weeks HRAs were performed by themselves, using remote supervision and online feedback. Finally, trainees were directly evaluated using metrics including: median of collected biopsies, inadequate histology, and anal high-grade squamous intraepithelial (HSIL) identified according to specific HPV-type status. All detected HSIL was referred for standard clinical care.

Results: Trainee 1 (T1) performed 112 HRAs and Trainee 2 (T2) 74. At the end of the training T1 collected a median of 2 biopsies per procedure, and T2 a median of 3. HSIL detection for T1 was 44% at the beginning and 36% at the end, T2 identified 38% and 60% at the end. The concordance between histology and cytology is the most popular metric for HRA performance, however, the ratio between prevalence's of HSIL and HPV16/18/31/33 seems to be also a good metric for improvement.

Trained by period $n = 186$				
Characteristic	**T1 ($n = 112$)**		**T2 ($n = 74$)**	
	P1[1] ($n = 59$)	**P2[2] ($n = 53$)**	**P1 ($n = 34$)**	**P2 ($n = 40$)**
Median number of biopsies	2	2	2	3
HSIL identified by histology	44%	36%	38%	60%
Prevalence HPV 16/18/31/33[3]	63%	55%	59%	75%
Concordance HSIL histo/cyto[4]	55% (5/9)	33% (1/3)	25% (1/4)	100% (6/6)
Ratio %HSIL /% HPV16/18/31/33	44/63 = 69	36/55 = 65	38/59 = 64	60/75 = 80

[1]P1: Period 1 (from March to mid-June).
[2]P2: Period 2 (from mid-June to August).
[3]According to the literature, these are the HPV types most frequently associated with lesions.
[4]Number of histology HSIL cases detected among the cytology HSIL cases detected.

Conclusions: An intensive HRA training in a short period of time may be feasible as an efficient learning experience for physicians to improve detection of anal HSIL. We consider that specific HPV-type status may add value to standardizing metrics according to HSIL-risk in each particular training population.

33 Initial anal cancer screening among sexual and gender minority males living with HIV in Nigeria

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Background: Although treatment of high-grade squamous intraepithelial lesions (HSIL) prevents anal cancer,[1] implementation of screening and treatment programs for anal HSIL is at early stages in low- and middle-income countries (LMIC).[2–4] We describe implementation of HSIL screening with high-resolution anoscopy (HRA) and reception of this program at an HIV-care facility among sexual and gender minority males living with HIV (SGMLH) in Abuja, Nigeria.

Methods: Since May 4th, 2023, 37 SGMLH have enrolled in an ongoing anal cancer screening study. HRA was performed with biopsy of suspicious lesions. Participant experiences were captured electronically on a scale from 0 (strongly disagree) to 10 (strongly agree) using REDCap. Ratings were further categorized into low (0–4), moderate (5–7), and high (8–10) agreement.

Results: Median age was 32 (interquartile range [IQR]:30–36) years, 47% had a sexual debut ≤18 years, and 100% were on antiretroviral therapy. Prevalence of HSIL and LSIL was 17% (6/36) and 31% (11/36), respectively. Forty-six percent had previously experienced HRA.[3] For overall satisfaction with screening, 0%, 5%, and 95% reported low, moderate, and high agreement. Median pain was rated a 2 (IQR:1–4) on a scale of 0–10, with 0 being no discomfort during the procedure. One hundred percent reported that they would return for annual screening and would strongly recommend the procedure to friends.

Conclusions: The initial detection of HSIL, high levels of satisfaction, low reports of pain, and re-engagement of persons not naïve to HRA offer promising insights into the implementation of HSIL screening and treatment programs among SGMLH in LMIC.

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34 Performance of p16/Ki-67 dual stain cytology to detect anal precancer in the Anal Cancer Etiology and Screening (ACES) study

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Background: Accurate and effective tests for anal cancer screening are needed. Here, we evaluated p16/Ki-67 dual stain (DS), a promising biomarker for detection of anal high-grade squamous intraepithelial lesions (HSIL).

Methods: The Anal Cancer Etiology and Screening (ACES) study was designed to evaluate the performance of biomarkers for anal cancer screening. Participants were referred for high-resolution anoscopy (HRA) at the Mount Sinai Anal Dysplasia Clinic. Routine anal cytology and high-risk HPV (hrHPV) testing were performed at the HRA visit. DS testing was performed using residual ThinPrep specimens by the manufacturer. DS clinical performance for HSIL detection was compared to other testing strategies. Clinical data were abstracted from electronic medical records.

Results: 488 individuals with samples, collected from 2020–2023, were included, with a mean age of 48 years. The majority of individuals were White (38%), Hispanic/Latinx (31%), or Black (25%), and male (87%) of whom, 82% were men who have sex with men living with HIV. hrHPV and DS positivity were 73% and 49%, respectively. DS compared with hrHPV testing had lower sensitivity (76% vs 87%), but higher specificity (65% vs 35%) for detection of HSIL. DS triage of positive hrHPV results, improved specificity from 65% to 72%, with a slight reduction in sensitivity (76% to 70%) compared to DS alone.

Conclusions: DS alone and in combination with hrHPV testing improves specificity compared to hrHPV alone, but with decreased sensitivity. These approaches warrant further evaluation as settings with limited HRA capacity require triaging only the highest risk patients for referral.

35 Pilot study of sampling methods for anal microbiome among Hispanic adults

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Background: Approximately 20% of all cancers are thought to be associated with infectious agents with yet undiscovered mechanisms. Knowledge of the stability of the anal microbiome and how distinct it is to the fecal microbiome is limited. We aimed to compare the composition and diversity of fecal-associated and anal mucosal-associated biofilm microbiota in a sample of adults in Puerto Rico.

Methods: Eighty samples were self-collected from men and women aged ≥21 years (n = 20). Four time points were established for each participant: pre-defecation anal swab, fecal-sample, 1–5-hour post-defecation swab and 1-day post-defecation swab. Genomic DNA was extracted and 16S rRNA gene was sequenced to characterize the microbiota using the QIITA platform and QIIME2.

Results: Clear differentiation was observed between anal swabs versus fecal-samples (beta diversity). Samples collected before defecating were similar to samples collected 1-day post-defecation. Diversity decreased as time after defecation increased. Post-defecation swabs had higher diversity than pre-defecation, but less diversity than fecal-samples. The phyla *Euryarchaeota* was more abundant in fecal-samples while the abundance of Proteobacteria and Fusobacteria increased significantly on the anal biofilm. Genera such as *Prevotella*, *Porphyromonas* and *Fusobacterium* were significantly more abundant in the anal biofilm while *Bifidobacterium*, *Roseburia* and *Faecalibacterium* were more abundant in the stool.

Conclusions: Differences in anal and fecal-samples were observed; collecting anal-swab samples 1-day after defecation showed a more distinct microbiome. Anal sampling evidenced that the anal biofilm contains bacterial groups that are low in prevalence in stool, supporting its use to study differences in anal microbiome across populations.

36 Save the bottoms!!! Acceptability and feasibility of an anal dysplasia screening unity at LGBTQ+ focused community events

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Background: Anal swab (or "anal pap") protocols for cytology and dysplasia screening remain poorly implemented, especially among individuals in high-risk populations. Men who have sex with men (MSM) have previously demonstrated willingness to perform anal self-swab in both the clinic and at home, with specimen adequacy similar to that of clinicians. The objective of this study was to assess feasibility and acceptability of self-swabbing to screen for anal dysplasia at a temporary screening unit at a large LGBTQ+ focused community event.

Methods: A temporary anal dysplasia screening unit was set up, consisting of two 10x10-foot tents, at the Twin Cities Pride Festival (June 24–25, 2023). On-site anal dysplasia screening via self-swab was offered to MSM ages 18+ who were assigned male sex at birth. Clinician-performed testing/assistance was available upon request. The primary endpoint for this preliminary analysis was uptake of self-screening.

Results: Over one hundred individuals (n = 101) underwent on-site screening. Most participants were white, lived within 30 miles of Minneapolis, with a mean age of 40 (range 18–79 years). Fifteen individuals were transgender/non-binary. Ninety-seven tests were self-performed. Limitations to higher-volume screening were sufficient space and personnel to perform intake activities, not lack of interest by potential participants.

Conclusions: On-site anal self-swab for cytology at LGBTQ+ community events is feasible and acceptable to MSM and is a potential mechanism to increase anal dysplasia/cancer screening in this high-risk population. Cytologic examination is ongoing at the time of abstract submission. Participants screening positive (ASCUS+) will be invited for High-Resolution Anoscopy.

37 Scattering-based light sheet microscopy imaging of fresh anoscopic biopsy specimens: a prospective descriptive study characterizing anal lesions

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Background: Current anal cancer screening and prevention rely on high-resolution anoscopy (HRA) with biopsies, which is a procedure with a steep learning curve for providers and considerable morbidity for patients. Scattering-based light-sheet microscopy (sLSM) is a novel imaging modality that our group is developing for potential in-vivo visualization of anal lesions, to guide and reduce the quantity of biopsies. We previously optimized sLSM parameters in formalin-fixed paraffin-embedded anal tissue. Here, we describe sLSM features associated with benign findings, low-grade squamous intraepithelial lesions (LSIL), and high-grade squamous intraepithelial lesions (HSIL) in fresh anal and rectal tissue.

Methods: Fresh biopsy specimens were prospectively collected from consented patients undergoing HRA. Prior to formalin fixation, images were acquired using a rapid, semi-automated ex-vivo sLSM imaging setup. sLSM images were compared to final histologic diagnoses to determine characteristic features of anal lesions.

Results: Normal squamous and transformation zone epithelium is characterized by bright nuclei of similar size with denser clustering towards the base. Normal colorectal mucosa is characterized by large, bright tubular structures representing intestinal glands. LSIL is characterized by nuclei with greater variability in size and shape, and hexagonal cellular borders can be more apparent. HSIL is characterized by large, crowded nuclei spanning the full thickness of the epithelium.

Conclusions: sLSM produces images of fresh anal tissue with characteristic features that may distinguish between areas of benign, LSIL, and HSIL.

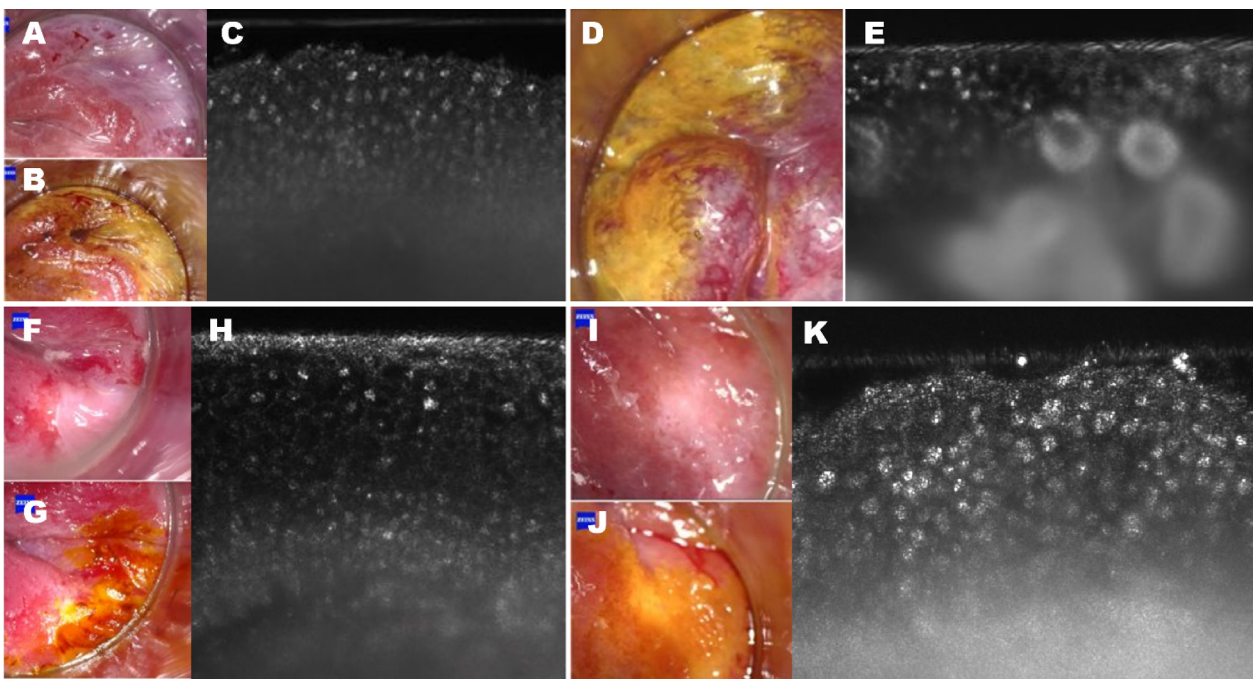

Fig. 1. HRA photos with corresponding sLSM images. Per final histology, A–C: normal squamous epithelium, D, E: colorectal mucosa, F, G: LSIL and I–K: HSIL.

38 The accuracy of anal self- and companion examinations compared with a health care provider digital anal rectal examinations

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Background: Self-assessment of and competency with anal health may reduce barriers to anal cancer screening with a health care provider (HCP). Our objective was to assess the accuracy of anal self- and companion examinations (ASE/ACE) when compared with an HCP-performed digital anal rectal examination (DARE).

Methods: Cisgender and transgender gay and bisexual men and transgender women were enrolled in Chicago and Houston and then taught about anal anatomy and how to perform an ASE/ACE to detect any abnormality. An HCP then performed a DARE and recorded details of each anal canal and perianal abnormality. Thereafter, participants performed the ASE or ACE and recorded their result as normal or abnormal. ASE/ACE concordance, sensitivity and specificity were assessed.

Results: Of 717 people completing a baseline ASE/ACE, 36% were living with HIV, and the median age was 40 years (IQR, 32–54 years). HCPs recorded 245 individuals with ≥1 lesion. Median diameter of primary lesion was 3 mm (range, 1–10 mm). Concordance, sensitivity and specificity between HCP and participant was 73% (95% CI = 70–76), 60% (95% CI = 54–66) and 80% (95% CI = 76–84), respectively. Concordance increased as anal canal lesion size increased (p_{trend} = 0.02). Increasing age was associated with decreasing concordance (P = 0.004). A total of 93.4% agreed/strongly agreed they would report concerning lesions to HCPs, and 35% preferred ASE/ACE to HCP examination.

Conclusions: Individuals may detect perianal and anal canal lesions of ≤10 mm in diameter. For individuals reluctant to undergo HCP-performed DARE or facing other barriers, educational programs and self-discovery of a lesion may support screening programs.

39 The association between host and viral genome methylation and anal precancers/cancers: comparing home-based self-sampling and clinician sampling in the prevent anal cancer study

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Background: Anal cancer is a common cancer in sexual minority men (SMM) with increased risk for HIV+ve individuals. The increasing incidence of anal cancer makes the choice of appropriate triage strategy for high-risk groups a pressing need. We investigated the potential of our DNA methylation classifier to identify anal intraepithelial neoplasia grade 2 or higher (AIN2+/AIN3+) using clinician sampling and home-based self-sampling from SMM in the Prevent Anal Cancer (PAC) Study.

Methods: DNA methylation of host gene EPB41L3 and late regions of HPV16, 18, 31, 33 were assessed in self- and clinician-collected anal canal exfoliated cell samples taken at baseline and 12 months from 206 SMM from the PAC study. For baseline there were 165 clinician samples with 80 histology results; and 106 self-samples with 47 histology results. There were 75 paired baseline samples and 36 paired 12-month samples.

Results: The methylation classifier performed similarly in paired clinician and self-collected samples showing statistically significant correlation ($n = 111$, $P < 0.001$). In baseline samples, our DNA methylation classifier showed significant separation between <AIN3 and AIN3+ for clinician ($n = 80$, $P < 0.05$, AUC 0.6685) and good separation for self-collected samples ($n = 47$, AUC 0.6378). Higher methylation levels were observed in HIV+ve compared with HIV-ve participants. A significant difference in methylation score was seen for self and clinician samples in participants with persistent hr-HPV infection vs non-persisters ($P < 0.05$, AUC 0.7301 and 0.6394 respectively).

Conclusions: Our methylation classifier could potentially be useful as a biomarker of anal disease and tool for screening of high-risk populations.

40 The potential role of reflex anal cytology testing in gay and bisexual men (GBM) who screen positive for high-risk human papillomavirus (HRHPV)

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Introduction: Anal HRHPV-based anal cancer screening in GBM is associated with high sensitivity, but high HRA referral rates and low specificity. We explored the reflex use of liquid-based cytology (LBC) in HRHPV positive men in predicting persistent anal HSIL in a cohort of GBM in Sydney, Australia.

Methods: Men in the Study of the Prevention of Anal Cancer (SPANC) underwent annual HRHPV testing, cytological and HRA guided histological assessments. Persistent HSIL was defined by histological HSIL at both baseline and the 12-month follow-up visit. We examined an HRA referral threshold of HPV16 positivity at baseline, or persistent non-16 HRHPV detection at both visits, with or without reflex LBC.

Results: Among a total of 617 participants, 439 (71.5%) who attended the 12-month follow-up visit and had valid HPV, cytological, and histological results at both visits were included. Median age was 50 years (IQR: 44–57), and 157 (35.8%) were HIV-positive. Among them, 149 (33.9%) tested HPV16 positive at baseline and an additional 154 (35.1%) had persistent non-16 HRHPV. Guided by HRHPV screening alone, the theoretical referral rate, sensitivity and specificity for detection of 12-month persistent HSIL (n = 84, 19.1%) was 69.0%, 98.8%, and 38.0%, respectively (Table). Adding reflex LBC (any abnormality) resulted in lower referral (50.3%), improved specificity (58.9%) and only slightly lower sensitivity (89.3%).

Conclusion: The reflex use of anal cytology in GBM testing positive for anal HRHPV led to only slight reduction in sensitivity (by <10%), with a close to 20% lower referral rate and a 20% higher specificity.

Table. Anal cancer screening performance using HRHPV testing and anal cytology in the SPANC study.

	HPV16 at baseline (n = 149)			HPV16 Neg (n = 290)			Overall (n = 439)		
	Screen+ n (%)	Sens (%)	Spec (%)	Screen+ n (%)	Sens (%)	Spec (%)	Screen+ n (%)	Sens (%)	Spec (%)
HRHPV testing	149[1] (100.0)	100.0	0.0	154[2] (53.1)	97.0	52.5	303 (69.0)	98.8	38.0
Cyto screening	114 (76.5)	90.2	30.6	151 (52.1)	90.9	52.9	265 (60.4)	90.5	46.8
Cyto as reflex	114 (76.5)	90.2	30.6	107 (36.9)	87.9	69.6	221 (50.3)	89.3	58.9

[1]Participants who tested HPV16 positive at baseline.
[2]Participants who tested to have persistent type-specific non-16 HR-HPV infection at both baseline and 12-month follow-up visit.

41 Towards simplified anal cancer screening: biomarker discovery by genome wide methylation analysis on anal swabs

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Background: Only a subset of people at increased anal cancer risk is currently screened due to limited capacity and expertise of high-resolution anoscopy. Hence there is an urgent clinical need for an objective minimally-invasive screening test on anal swabs. We previously showed that testing for DNA methylation markers on anal biopsies can accurately detect high-grade anal intraepithelial neoplasia (HGAIN) at risk of progression to anal cancer (i.e., advanced HGAIN). This study aimed to develop a methylation test applicable to anal swabs to detect advanced HGAIN by genome wide methylation analysis on anal swabs.

Methods: Genome wide methylation profiling was performed on anal swabs of 36 cases (i.e., AIN3), 34 controls (i.e., <AIN1), and 7 anal cancer patients using EPIC arrays (Illumina). Candidate methylation markers were selected using logistic regression penalized with adaptive multi-group ridge penalties using co-data and derived with an empirical Bayes approach (ecpc). Most promising markers were subsequently evaluated by quantitative methylation specific PCRs (qMSPs).

Results: Ecpc yielded 50 candidate markers with a combined area under the curve of 0.80. Sixteen CpGs corresponding to 10 genes showed significant differences between disease categories. For 2 of those genes, qMSPs have been developed showing significant differences between cancers versus controls ($P < 0.0079$). qMSP development and evaluation of other candidate markers is currently ongoing.

Conclusions: We successfully performed methylation profiling on anal swabs, resulting in the identification of 10 new candidate markers for anal cancer screening. First qMSP results indicate a good marker potential, but further evaluation is to be awaited.

42 Women and anal dysplasia assessment (WANDA): a pilot study of anal cancer screening in women with a history of HPV-related lower genital tract cancers

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Background: Almost all anal cancer is caused by HRHPV and women with prior lower genital tract cancers (LGTC) are at disproportionate risk. This pilot study aims to examine the uptake and results of an anal cancer screening program in women with prior LGT cancer.

Methods: Women diagnosed with LGTC, ≥18 years were enrolled at 2 sites in Sydney, Australia from February 2021 to February 2023. Participants underwent a digital anorectal examination (DARE), a lower vaginal/vulvar, cervical/upper vaginal and anal swab for HPV and p16/Ki67 testing and completed a questionnaire on the acceptability of anal cancer screening. Participants with positive results were referred for a high resolution anoscopy (HRA).

Results: Of 52 enrolled participants, 6 provided demographic information only. Median age was 46.5 (IQR: 36.0–58.5), 58.8% were Australian-born. Most had prior cervical cancer (82.4%), 11.8% vulval and 5.9% vaginal cancer. Seven (15.2%) had anal HRHPV (4 HPV16). Eight (17.4%) had positive p16/Ki 67 staining, with invalid results for 25 (54.4%). From 8 of 9 HRA referrals, 4 had normal histology, 1 LSIL and 3 HSIL (2 HSIL-AIN2, 1 HSIL-AIN3). Forty-one (89.1%) participants completed questionnaires. The majority (92.5%) reported that being screened was reassuring (97.5%) and was positive for their health (95.1%).

Conclusion: Approximately one in 5 women had prevalent anal HRHPV and/or p16/Ki67. The fact that half of the p16/Ki67 tests were unsatisfactory compromises the use of this test in screening. Anal cancer screening was viewed as a beneficial process by almost all participants.

Competing interest: AEG has received honoraria and research funding from CSL Biotherapies and honoraria and travel funding from MSD. RJH has received honoraria and travel funding from CSL Biotherapies and MSD. All other authors declare that they have no conflicts of interest.

Sexual Health

43 Radiation dose to the anterior vaginal wall and patient-reported sexual dysfunction among women treated for anal squamous cell carcinoma: daily use of a vaginal dilator allow for favorable dosimetry

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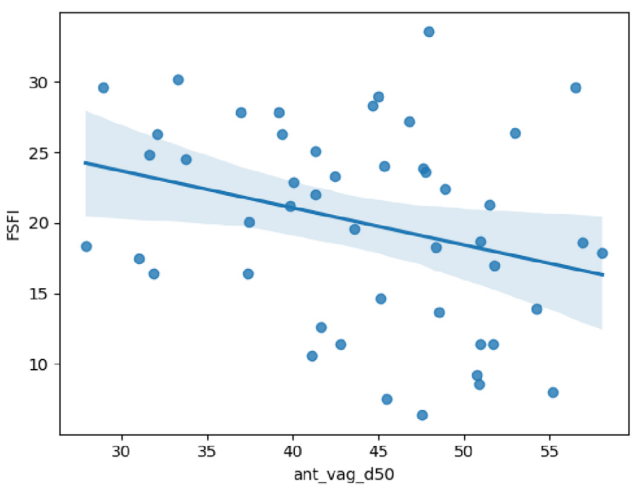
Background: Sexual dysfunction (SD) is common for women after radiation for squamous cell carcinoma of the anus (SCCA). We aimed to evaluate use of a daily vaginal dilator (VD) to spare radiation to the anterior vaginal wall (AVW), and to correlate patient-reported long-term SD with radiation dose to the AVW.

Methods: Women treated for SCCA with chemoradiation between 2006–2018 were included. Use of daily VD was recorded. The Female Sexual Function Index (FSFI) was collected from women who were alive without evidence of disease >2 years post-radiation. SD was defined as FSFI score <26.55. Doses to the AVW were recorded. Multiple regression models were used to identify factors associated with FSFI. Youden index analysis estimated an AVW dose cutoff to predict SD.

Results: Ninety women of 184 women (49%) completed the survey, and 51 (56.7%) were sexually active with valid FSFI scores. Forty-one women (80%) had SD. Univariate analysis showed higher dose to 50% (D50%) of the AVW correlated with worse FSFI (β −0.262; $P = 0.043$), worse desire FSFI subscore (β −0.056; $P = 0.003$) and worse pain FSFI subscore (β −0.084; $P = 0.009$). Higher age correlated with worse pain FSFI subscore (β 0.067; $P = 0.026$), but only AVW D50% was significant on multivariable analysis (β −0.087; $P = 0.009$). Youden index analysis showed AVW D50% >48.35 Gy predicted increased risk of SD.

Conclusion: Dose to the AVW correlates with worse FSFI for women treated with radiation for SCCA. Using a VD during treatment to displace the AVW and keeping AVW D50% <48 Gy may reduce the risk of SD.



Treatment

44 2012–2022: a ten year monoinstitutional experience in the treatment of anal squamous cell carcinoma (SCC)

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Background: Squamous Cell Cancer (SCC) of the anal canal is relatively rare, comprising 2–4% of colorectal malignancies, with an annual incidence of approximately 1 case per 100,000 people globally. The standard treatment for SCC has been a chemo-radiotherapy protocol known as the NIGRO Protocol, which has shown significant improvements in local disease control, 5-year survival rates, and patients' quality of life in stages I–II–III.

Methods: The objective of this retrospective study conducted at the "Fondazione IRCCS Istituto Nazionale dei Tumori di Milano" was to analyze the therapeutic strategy employed and evaluate clinical and radiological responses, local disease control, overall patient survival, and late treatment toxicity. The study included patients aged 18 or above with locally advanced SCC (Stage II–III) who received concurrent radio-chemotherapy and had a follow-up period of at least 12 months.

Results: Out of the 110 patients who completed treatment between 2012 and 2022, 87% achieved a complete radiological response, 7% had a partial response, 3% had stable disease, and 3% experienced disease progression. The median follow-up period was 47 months, with a median Relapse-Free Survivor of 44 months and a median Overall Survivor of 50.5 months. The most common late toxicities observed were faecal incontinence in 26% of patients and dyspareunia in 13% of women.

Conclusions: These findings are consistent with existing literature, confirming that radio-chemotherapy remains the standard treatment for SCC. Leveraging artificial intelligence to retrospectively analyze such data could enhance clinical and radiological descriptions of patients, enabling personalized treatment approaches and potentially reducing late treatment toxicity.

45 Semi-structured interview study of patients undergoing endoscopic treatment of anal squamous intraepithelial neoplasia

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Background: HIV-positive men and women, men having sex with men, women diagnosed with cervical dysplasia and immune-suppressed patients all have a higher risk of developing anal cancer compared with the normal population. Most patients with ASIL in Sweden are treated surgically with a risk of late effects i.e. discomfort, bleeding, pain, incontinence and stenosis. We have developed a gentle method to treat ASIL using high-resolution flexible endoscopy. To gain a deeper understanding of the physical, psychological and sexual aspects experienced by patients, we conducted interviews with patients treated endoscopically for ASIL.

Method: The study employed qualitative methodology where semi-structured interviews were analysed using qualitative content analysis. Fourteen men and women diagnosed with ASIL and previously treated with flexible endoscopy gave written consent to be interviewed. Treatment was given during 2021–2022 and interviews were conducted during 2022–2023. Eligible patients were 18 years or older.

Results: Prior to treatment, patients experienced mild burning sensations, bleeding and had noted changes at the anal verge. Post treatment using high-resolution flexible endoscopy patients described minor bleeding, tolerable pain and no problems having sex. Some used lidocaine gel when defecating but most reported no discomfort. However, in connection with treatment, patients described feelings of worry when discussing the risk of relapse or the possibility of developing anal cancer. Finally, the procedure was well tolerated by the patients.

Conclusions: Our findings indicate that high-resolution flexible endoscopy is a gentle method, well tolerated by patients with ASIL, giving only minor physical symptoms. However, patients expressed thoughts and feelings of worry.

	Included, *n*
Number of patients (%)	14 (100)
Male sex (%)	8 (57)
Age, mean ± SD (years/±)	45.1 ± 12.3
Interview time, mean (min)	15.59