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Access to Care

1 AWARENESS OF OUTPATIENT ANAL CANCER SCREENING AMONG MEN WHO HAVE SEX WITH MEN LIVING WITH HIV IN CANADA: THE HPV SCREENING AND VACCINE EVALUATION (HPV-SAVE) STUDY

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Background: Men who have sex with men living with HIV (MSMLWH) are disproportionately affected by HPV-associated anal cancer but there are no publicly funded, broadly-available, outpatient screening programs. We assessed awareness of screening strategies for anal cancer among MSMLWH in the HPV-SAVE study, a national anal cancer screening study among MSMLWH in Canada.
Methods: Between 02/2016 to 05/2021, participants were recruited from HIV clinics and invited to complete a questionnaire at study entry which included items related to prior anal cancer screening awareness and experience, which we report using descriptive statistics.
Results: Among the 750 individuals who completed the questionnaire, the majority were over 50 years old (52.4%), white (70.7%) and unpartnered (53.8%). A minority reported awareness of available outpatient anal cancer screening (137/715; 19.2%). Experience with screening included having had a non-specific digital anal exam (493/715; 69.0%), previous anal pap (129/673; 19.2%), or anoscopy (96/649; 14.8%). Previous self-examination for anal lesions was reported by 322 individuals (45.2%), and 97 individuals (13.9%) reported examination by their partner. Most (89.8%) were comfortable discussing anal health issues with their doctor and 92.7% perceived anal cancer screening as important. Following enrolment in HPV-SAVE where participants were educated about anal cancer, 236 individuals (33.1%) reported being more concerned about anal cancer than before enrolment.
Conclusions: Despite being a common malignancy among MSMLWH, few participants had prior experience with formal anal cancer screening. A high proportion of participants reported previous self-examination, suggesting that programs to increase patient-driven anal cancer screening would be well received.

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2 DEVELOPING REMOTE HIGH RESOLUTION ANOSCOPY TRAINING

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Background: Demand for high-resolution anoscopy (HRA) currently surpasses capacity with patients experiencing long delays or lack of access. ANCHOR study results establishing the efficacy of anal HSIL in reducing the risk of anal cancer will likely further increase demand for HRA. Training has typically relied on face-to-face courses with hands-on components and mentoring by experienced providers, but opportunities are limited by the dearth of established HRA clinics. The COVID-19 pandemic created an additional impediment to training due to travel restrictions. In consideration of these challenges, we developed remote access HRA education and training to increase the pool of providers.
Methods: 3 educational components were converted to on-line remote access: the IANS HRA course, live observations (of both mentor and mentee) and recorded observations.
Results: The IANS HRA course with pre-recorded curriculum and live faculty sessions was attended by >200 individuals from 30 countries. For live and recorded observations, internet-meeting software provided two exam views: 1) the HRA using available clinic imaging capture software 2) a phone camera focused on the clinician to observe positioning and equipment handling. Examination metrics were used to evaluate and adjust technique and improve lesion recognition. 35 trainees attended live sessions and received remoted training over a 10-month period.
Conclusions: Live courses and in-person mentoring are ideal but remain expensive and difficult to access. HRA capacity and training may be furthered, by developing these innovative teaching tools. Hands-on training tools also need development. Measurement of metrics pre- and post-training will allow for improvement of these teaching aids.

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Epidemiology and natural history

3 WORRIEDNESS FOR ANAL CANCER AMONG NIGERIAN MSM LIVING WITH HIV

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Background: Anal cancer risk is increasing at a rate of 2.2% annually among men who have sex with men (MSM) living with HIV and may be preventable with treatment of anal precancer. We assessed worriedness for anal cancer among Nigerian MSM living with HIV and their willingness to engage in anal cancer screening.
Methods: Between November 20 and December 14, 2021, a survey was administered to MSM living with HIV who had anal sex in the past year through community outreach and electronic platforms. Worriedness was categorized as not worried (<25%), worried (25%–50%), and very worried (>50%). Data were captured electronically using REDCap, and differences in characteristics by worriedness were assessed with Pearson's Chi-squared test.
Results: Of 800 participants, 451 (56%) were ≥30 years old, 623 (78%) reported 100% ART adherence, and 796 (99.5%) were interested in participating in a future 5-year HPV, precancer, and anal cancer study. Most participants were either worried (53.5%) or very worried (39.5%) about anal cancer. Those very worried about anal cancer reported having ever had receptive anal sex (97%; vs 86% <0.01); less likely to prefer the insertive sexual position (11% vs 28% P <0 .01) compared to those not worried. Furthermore, more of those very worried had heard about anal precancer (28%; vs 18% $P < 0.01$) and participated in anal cancer screening (18%; vs 10% $P < 0.01$) than those not worried.
Conclusions: An unignorable proportion of MSM living with HIV in Nigeria were worried about anal cancer and interested in participating in anal cancer screening.

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4 PREDICTORS OF ANAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS AFTER TWO YEARS OF CYTOLOGICAL AND HISTOLOGICAL FOLLOW-UP IN MEN WHO HAVE SEX WITH MEN LIVING WITH HIV

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Background: Men who have sex with men living with HIV (MSMLWHIV) are at an increased risk of high-grade squamous intraepithelial lesions (HSIL), a precursor to anal cancer. The objective was to assess determinants for cumulative 24-month detection of cytological or histological HSIL in the ANRS EP57 APACHES study (2014–2021).
Methods: MSMLWHIV ≥35 years were recruited from six French hospitals and followed-up at least yearly. At each visit, participants underwent HPV typing, cytology, and high-resolution anoscopy (HRA) with biopsy of suspicious areas. Of note, HSIL was not treated (by protocol). After consensus pathology review, participants were categorized by worse composite cyto-histological (composite-HSIL) diagnosis as <composite-HSIL or composite-HSIL. We assessed determinants for cumulative 24-month composite-HSIL detection using logistic regression, adjusted for age and centre.
Results: In total, 463 participants had ≥2 visits. Cumulative 24-month composite-HSIL detection was 32% (*n* = 149), of which 52%, 35% and 13% were detected at baseline, month-12 and month-24, respectively. No anal cancer was diagnosed during follow-up. The most important predictor for cumulative composite-HSIL detection was baseline high-risk (HR) HPV positivity, most notably HPV16 (adjusted odds ratio [aOR] versus high-risk HPV-negative = 12.8; 95%CI: 6.3–26.0), but also HPV18 in the absence of HPV16 (aOR = 7.7; 95%CI: 3.0–19.7) or other HR HPV in the absence of HPV16/18 (aOR = 4.3; 95%CI: 2.1–8.6). Although few, MSMLWHIV not on combination antiretroviral therapy had higher composite-HSIL risk (aOR = 3.1; 95%CI:1.2–8.0). Other evaluated socio-demographic/sexual-behaviour/HIV-related characteristics were non-significant.
Conclusions: Although repeat cytology and HRA may be required to detect HSIL, partial HPV genotyping is an important HSIL risk stratifier in MSMLWHIV.

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5 THE INCIDENCES AND DISEASE PATTERNS OF HPV RELATED CANCERS IN ENGLAND

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Background: There has been increasing interest in the development of organ sparing treatment for anal squamous cell carcinoma (ASCC) especially in patients with early staging. The patient group most likely to benefit from organ sparing treatment are patients in screening programmes for ASCC, in particular PLWH. Unfortunately, there is little emphasis in the literature on the outcomes of PLWH undergoing organ sparing treatment for ASCC.
Methods: We present a case-series of Stage 1 and 2 ASCC in PLWH and HIV negative patients. Data was extracted from a 20-year retrospective cohort study analysing the treatment and outcomes of patients with primary ASCC in a high HIV prevalence cohort.
Results: 94 patients were included and 57 patients were PLWH. 35 patients received local excision alone as their only treatment for ASCC, they were younger ($P = 0.037$, ANOVA) and were more likely to have either foci of malignancy or well differentiated tumours on histology ($P = 0.002$, Fisher's Exact Test).
There was no difference in 5-year Disease Free Survival and recurrence between treatment groups however, PLWH who had received local excision alone were more likely to recur later compared to patient who received other treatments for ASCC (72.3 months vs 31.8 months, $P = 0.035$, ANOVA).
Conclusions: Local excision may be considered as the sole treatment for Stage 1 tumours that have clear margins and advantageous histology regardless of HIV status. Nevertheless, as a later recurrence is possible in PLWH, PLWH who have local excision alone must have access to an expert long term surveillance programme after treatment.

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6 INCIDENCE TRENDS FOR HPV-ASSOCIATED ANAL SQUAMOUS CELL CARCINOMA IN THE UNITED STATES, 1999-2018

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Background: Human papillomavirus (HPV)-associated anal cancer cases have increased in the past two decades in the United States (US), with an average annual burden of 7000 cases.
Methods: Using population-based cancer registries covering approximately 97% of the US population, we calculated age-adjusted incidence rates for HPV-associated anal squamous cell cancers (SCC) using SEER*Stat (version 8.3.9). All cancers were malignant, microscopically confirmed, and restricted to the following ICD-O-3 histology codes for SCC: 8050–8084, 8120–8131. We also examined incidence trends from 1999 to 2018 using average annual percentage change (AAPC).
Results: Overall, an average of 5346 incident cases (rate of 1.66 per 100 000 persons) of HPV-associated anal SCCs were diagnosed over the 20-year period. From 1999 to 2018, incidence increased by 2.5% annually, most notably among persons aged 60–69 (AAPC: 4.2) and 50–59 (AAPC: 3.9) years. Incidence also increased among both sexes (female AAPC: 2.9; male AAPC: 1.9), ethnicity groups (non-Hispanics AAPC: 2.7; Hispanic AAPC: 0.8), and among White (AAPC: 2.6), Black (AAPC: 2.3), and American Indian and Alaska Native (AAPC: 1.6) people. Conversely, incidence declined by 1.7% each year among persons aged 30-39 years and remained stable among persons aged 20–29 (AAPC: 1.5; 95% CI: –0.6, 3.7) and 40-49 (AAPC: 0.2; 95% CI: –0.4, 0.7) years.
Conclusions: HPV-associated anal SCC incidence continues to increase overall and among both sexes, ethnicity groups, and most races and age groups; however, incidence declined among persons aged 30–39 years. Ongoing surveillance using population-based registries is needed to monitor trends in the US.

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7 ANAL HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESION (HSIL): U.S. INCIDENCE RATES AND TEMPORAL TRENDS & PREVALENCE BY AGE, 2015–2019

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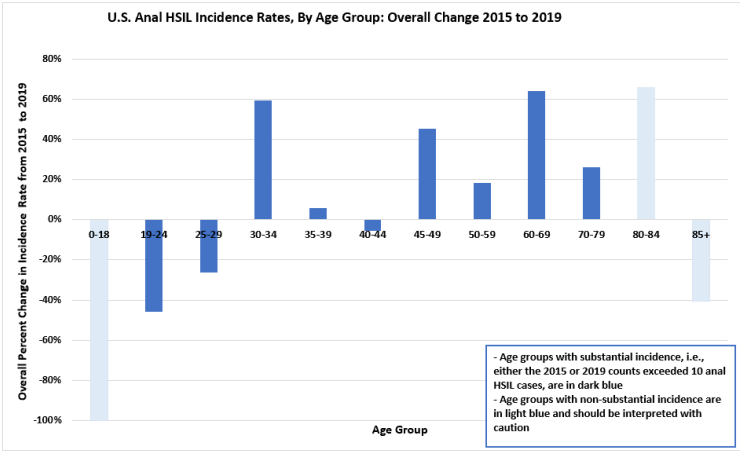
Background: The incidence rate of US anal squamous cell carcinoma (SCC) has more than doubled since 1975. However, anal HSIL epidemiology is incompletely characterized. Recent CDC analyses documented stabilizing AIN3 incidence in US young adults following HPV vaccine introduction but did not assess AIN2 for any age or anal HSIL incidence in middle-aged or older adults. The US anal HSIL epidemiologic burden among ages 0-85+ years was assessed by age category for 2015–2019.
Methods: Health claims algorithms were developed, including diagnostic, biopsy, and treatment codes, to retrospectively identify anal HSIL cases in a U.S.-representative database for all ages of approximately 19 million persons covered annually with commercial or Medicare Part D insurance. Age- and year-specific incidence rates and temporal trends of diagnosed anal HSIL in 2015–2019, and prevalence by age for 2018–2019, were calculated.
Results: Among ages with substantial incidence, change from 2015 to 2019 in incidence rates ranged from a 63.9% increase among ages 60–69 years to a 45.8% decrease among ages 19–24 years. From 2015 to 2019, incidence rates increased among those age 30–39 and 45-84 years and decreased among those age 0–29, 40–44, and 85+ years (Fig.1). Prevalence during 2018–2019 was highest among ages 50–59 years and lowest among ages 0–18 years.
Conclusions: Anal HSIL is rare, but incidence rates of most middle- and older-age groups increased substantially during 2015–2019 while incidence rates of young adults decreased. Evaluating anal HSIL burden by age is important when considering temporal trends and disease screening and treatment approaches.



Change in the Number of Anal HSIL Cases and in the Incidence Rate from 2015 to 2019, by Age Group

Age Group	0-18	19-24	25-29	30-34	35-39	40-44	45-49	50-59	60-69	70-79	80-84	85+
Change in the number of anal HSIL cases	-1	-6	-6	17	5	-1	19	26	58	16	2	0
Change in the incidence rate*	-0.04	-0.56	-0.61	1.35	0.18	-0.24	1.74	0.98	1.81	0.33	0.28	-0.33

*Cases per 100,000 population per year

Fig. 1. US anal HSIL incidence rates, by age group: overall change 2015 to 2019.

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8 SMOKING AND ANAL CONDYLOMAS IN PEOPLE WHO ATTEND THE ANAL NEOPLASIA CLINIC IN PUERTO RICO

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Background: Conflicting evidence exists of the relevance of smoking as a risk factor for anal condylomas. We evaluated this association among a clinic-based population in Puerto Rico.

Methods: This cross-sectional study analysed data from n = 673 individuals who received services at the Anal Neoplasia Clinic of the University of Puerto Rico Comprehensive Cancer Center (2014–2021) and underwent a high-resolution anoscopy (HRA) during their clinical visit. Sociodemographic and clinical variables were collected from medical records. Condylomas were assessed by physicians during the HRA.

Results: Mean age of patients was 46. 2± 12.9 years, 67.9% were men, 74.8% were persons living with HIV, 23.5% were current smokers, and 55.2% reported receptive anal sex (past 12 months). While 8.2% of participants self-reported history of anal condylomas, 15.0% had them on the clinical evaluation. Among these last, 52% had intra-anal condylomas, 27% peri-anal, and 21% had both; additionally, 30.8% of women also had vulvar condylomas and 6.6% of men had penile condylomas. Multivariate logistic regression modelling showed no significant association between current smoking and anal condylomas (OR = 1.44, 95% CI = 0.82–2.52). Higher odds of condylomas were only observed among adults aged <30 (11.39, 95% CI = 5.05–25.70) and 30-39 (OR = 5.02, 95% CI = 2.29–11.03) as compared to individuals aged 50+, with no significant difference for those aged 40–49 (OR = 1.77, 95% CI = 0.76–4.13).

Conclusions: Smoking was not associated to anal condylomas in this high-risk Hispanic population. Differing results with respect to the association of smoking with anal condylomas across studies could be explained by differences in study population, sample size, and research methodologies.

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Pathogenesis, molecular biology and virology

9 MULTI-ZONAL INTRAEPITHELIAL NEOPLASIA: UNDERSTANDING EPITHELIAL TRANSFORMATION (MINUET)

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Background: Certain groups of unvaccinated women are vulnerable to lower anogenital tract neoplasia and rates of anal and vulval squamous cell carcinoma (SCC) continue to rise in women. The presence of high grade squamous intraepithelial lesions (HSIL) in more than one anogenital zone concurrently, is considered to be multizonal intraepithelial neoplasia (MZIN). Since all lower anogenital zones have the potential to progress from HSIL to SCC without treatment, MZIN presents a unique management challenge. Triage of HSIL to prioritise treatment is not an evidenced based process. Further information is needed regarding the molecular nature of MZIN and whether triage can be assisted with biomarkers.
Methods: We conducted a study of MZIN where at least one HSIL lesion progressed to SCC. Biomarkers were studied in specimens from the cancer zone at a date prior to that of invasive SCC in addition to other zones which did not progress to invasive disease.
Results:12 women, with 15 invasive SCCs and 120 samples were analysed. Location of cancers were; anal canal (4), peri-anal (6), vulval (2), vaginal (3). DNA methylation results (currently in progress) will be presented at the IANS conference.
Conclusions: MZIN is a complex phenomenon to manage. Enhanced high resolution multizonal assessment (MZA) is required to identify lesions and allow for their triage. HSIL zones currently go untreated in favour of targeting other areas considered at higher risk of progression to cancer. Biomarkers may in the future enable clinicians managing these complex patients to approach treatment triage in a more objective manner.

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10 REDUCTION OF INTRAEPITHELIAL NK CELLS CHARACTERIZES ANAL DYSPLASIA OF ANY GRADE IN HIV+/HPV+ SUBJECTS

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Background: Natural Killer (NK) lymphocytes play a pivotal role in the response against HPV infected cells and carcinogenesis, through cytotoxic activity ($CD56^{dim}$ NK) and production of proinflammatory cytokines (mainly $CD56^{bright}$ NK).
Methods: 44 HIV+/HPV+ patients undergoing diagnostic HRA gave their consent to collect additional biopsies from at least 1 area of suspected anal dysplasia and biopsies from normal anal mucosa. Flow cytometry evaluation of intraepithelial NK cells subpopulations was performed, after histologic confirmation, on these biopsies.
Results: 44 samples of normal anal mucosa and 65 samples of dysplastic mucosa (9 HSIL and 56 LSIL) were analysed.
Although the frequency of total intraepithelial NK cells, expressed as proportion of total intraepithelial lymphocytes, was similar in healthy and dysplastic mucosa (3.2% vs 2.9%; $P = 0.726$), the proportion of CD16+ NK cells, expressed as part of total intraepithelial NK lymphocytes, was significantly lower in dysplastic tissue when compared to healthy mucosa (39.1% vs 27.3%, $P = 0.006$). Similarly, the proportion of $CD56^{dim}$ NK cells, expressed as part of total CD16+ NK cells, was lower in dysplastic tissue (87.8% vs 69.9%; $P = 0.001$).
HSIL and LSIL showed similar frequencies of total intraepithelial NK cells (0.9% vs 2.9%; $P = 0.110$). On the other hand, lower $CD56^{dim}$ NK cells (62.4% vs 72.9%; $P = 0.015$) and lower $CD56^{bright}$ NK cells (0.08% vs 0.1%; $P = 0.036$) were observed in HSIL when compared to LSIL.
Conclusions: HPV is known to impair innate immune response. Dysplastic anal mucosa is characterized by reduction of NK cells response, which seems to be more pronounced in HSIL than LSIL.

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11 RISK FACTORS FOR ANAL DYSPLASIA AND LINKAGE TO HRA IN TRANSGENDER WOMEN

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[4] Harm Reduction Experts Improving Lives (HIPS)

Background: Studies estimate that transgender women (TGW) have a high prevalence of HPV and anal dysplasia (AD).[1,2] We examined risk factors associated with AD and high-risk HPV(HRHPV) in a sample of TGW.
Methods: We recruited a convenience sample of TGW in DC from 4-12/2021. We collected demographics; serum samples for HIV and hormone levels; and anal swabs for cytology and HPV genotype (ROCHE Cobas). We defined AD as a pathology diagnosis of atypical squamous cells of undetermined significance, low-grade or high-grade intraepithelial lesions. Current gender affirming hormone (GAH) use was defined as self-report of use, or serum oestradiol level higher than 60 pg/mL (oestrogen) and a testosterone level below 264 ng/dL (androgen blocker). If AD+, assistance scheduling off-site HRA was offered. We used Fisher's test to compare differences between risk factors.
Results: Of 41 TGW, most were black (88%), on GAH (61%), and HIV-positive (73%). 19% had received HPV vaccine, and 34% of HIV+ TGW had anal cytology tested in the past. Nineteen (46%) had AD, while 29 (71%) tested positive for HRHPV. HRHPV-positivity was negatively associated with history of HPV vaccination (P = 0.03). AD was associated with Black race (P = 0.05), and with the presence of HRHPV (P = 0.02) (Table 1). HRA was scheduled for 18 (95%) TGW +AD, but only 7 (37%) attended, of whom two (29%) had high grade neoplasia on HRA.
Conclusions: Our findings highlight the high rates of HRHPV and AD in TGW regardless of HIV status, age, or GAH use. In this high-risk population, we found low rates of HPV vaccination or prior anal cancer screening. Despite facilitated linkage to HRA, attendance was limited.

Table 1. Association of risk factors with abnormal anal cytology

Risk factor		Anal cytology		*P*-value	HPV status		*P*-value
		Abnormal n (%)	Normal n (%)		Positive n (%)	Negative n (%)	
Age	21–30	2 (11)	6 (27)	0.25	5 (17)	3 (25)	0.46
	>30	17 (89)	16 (73)		24 (83)	9 (75)	
Current estrogen use	Yes	10 (53)	13 (59)	0.75	18 (62)	5 (42)	0.31
	No	9 (47)	9 (41)		11 (38)	7 (58)	
Current testosterone suppression	Yes	10 (53)	10 (45)	0.75	14 (48)	5 (42)	0.74
	No	9 (47)	12 (55)		15 (52)	7 (58)	
HIV	Positive	16 (84)	14 (64)	0.17	21 (72)	9 (75)	1
	Negative	3 (16)	8 (36)		8 (28)	3 (25)	
High risk HPV	Positive	17 (89)	12 (55)	0.02	N/A	N/A	
	Negative	2 (11)	10 (45)		N/A	N/A	
Race	Black	19 (100)	17 (77)	0.05	26 (90)	10 (83)	0.62
	Non-Black	0	5 (23)		3 (10)	2 (17)	
HPV vaccine status	Vaccinated	4 (24)	4 (18)	0.7	6 (21)	7 (58)	0.03
	Unvaccinated	13 (76)	18 (82)		23 (79)	5 (42)	

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12 RISK OF ANAL HUMAN PAPILLOMAVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS COMPARED WITH IMMUNOCOMPETENT CONTROLS

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Background: Kidney transplant recipients (KTRs) have increased risk of human papillomavirus (HPV)-related anogenital (pre-)cancers, including anal precancer and cancer. In this cross-sectional study, we investigated the prevalence and odds of anal high-risk HPV (hrHPV) in KTRs compared with immunocompetent controls and assessed risk factors for anal hrHPV in KTRs.
Methods: During 2016–2017, we included 247 KTRs and 248 controls from a dermatology department and five nephrology departments in Denmark. From all participants we obtained an anal cytobrush sample which was tested for HPV DNA. Participants completed a questionnaire on lifestyle and sexual habits. We used logistic regression to estimate odds ratios (ORs) of anal hrHPV in KTRs compared with controls and risk factors for anal hrHPV in KTRs. Models were adjusted for age, lifetime number of sexual partners, smoking, and history of receptive anal sex.
Results: The anal hrHPV prevalence was higher in female KTRs (45.5%) than controls (27.2%). Female KTRs had almost three-fold higher adjusted odds of anal hrHPV than controls (ORadjusted = 2.87, 95% confidence interval [CI], 1.57–5.22). In contrast, among men we did not observe increased prevalence or odds of anal hrHPV in KTRs compared with controls (prevalence: 19.4% vs 23.6%; ORadjusted = 0.85, 95% CI, 0.44–1.64). Current smoking, >10 lifetime sexual partners, history of genital warts, and (among men) having had receptive anal sex were risk factors for anal hrHPV in KTRs.
Conclusions: Female KTRs had increased risk of anal hrHPV compared with immunocompetent controls, and almost half of female KTRs had anal hrHPV detected.

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13 RISK ASSOCIATIONS WITH HPV GENOTYPE DIVERSITY AND VIRAL LOAD IN A COHORT OF WOMEN LIVING WITH HIV

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Background: Persistent high risk (HR) Human Papilloma Virus (HPV) infection is associated with squamous intraepithelial lesions (SIL) at various sites and anal cancer risk. People living with HIV are a high-risk population for HR-HPV and progression to cancer. We used nested PCR primers and Next Generation DNA sequencing (NGS) to characterise HPV diversity and viral load (VL) in cervical and anal specimens previously collected in a group of women living with HIV with type and site-specific concordance and associated correlations.
Methods: HPVDetector software was used to detect HPV VL from 59 cervical/vaginal and anal samples from 30 patients. High, intermediate, and low risk HPVs were defined according to literature. We compared HPVs detected using NGS with cytology and commercial HPV assay. Clinical risk factors were included to study how detected HPVs from NGS predict abnormal cytology.
Results: Most anal HPV positive samples validated by the HR-HPV assay had a high number of reads of HPVs, whereas cervical samples did not. HPV VL and CD4 were more likely to predict abnormal cytology. The concordance between HPV VL and other risk factors illustrated that 74% of samples with CD4 <250 had HPV VL >1. HPV status strongly correlated with cytology and HRHPV assay for anal samples ($P = 0.01$, Fisher's exact test).
Conclusions: HIV immunologic control was associated with HR-HPV risk and abnormal cytology in anal specimens. A larger prospective cohort to study associations of CD4 count, risk behaviours, and HR-HPV with the development of abnormal cervical and anal cytology is needed.

Figure 1. HPV genotype diversity and viral load with its associated correlations

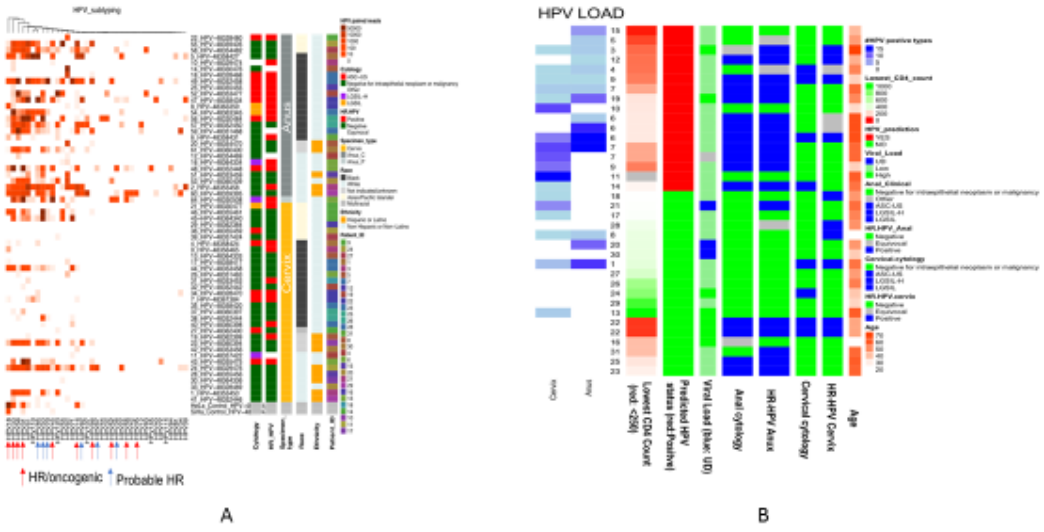

Fig. 1. HPV genotype diversity and viral load with its associated correlations.

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Screening and diagnostics

14 EVALUATING THE CASCADE OF CARE FOR ANAL CANCER SCREENING WITHIN A RYAN WHITE HIV/AIDS PROGRAM CLINIC

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Background: Care cascades can inform providers about differences in engagement and retention in care among patient populations potentially improving participation by targeting education and designing interventions more effectively. The objective of this study was to assess the uptake and retention of participants along the anal cancer screening algorithm within a single HIV clinic.
Methods: Retrospective procedural and demographic data were collected within a Ryan White HIV/AIDS Program clinic from 18 December 2017 to 29 May 2021. A care cascade was constructed among eligible participants who engaged and were retained in the anal cancer screening algorithm. Engagement was defined as having at least one anal Pap smear. Retention was defined as a follow-up anal Pap smear, and/or high resolution anoscopy, as indicated. Risk ratios (RR) were calculated to reveal characteristics associated with initiation and retention in screening.
Results: Of 821 participants, 312 (38.0%) engaged in screening and 205 (65.7%) were retained in care. Anoreceptive intercourse was positively associated with engagement (RR 2.86, 95% confidence interval (CI) 2.00–4.09, $P < 0.001$), whereas male gender was negatively associated (RR 0.25, 95% CI 0.14–0.43, $P < 0.001$). Abnormal cytology results on Pap smear were associated with retention (RR 1.39, 95% CI 1.03–1.86, $P = 0.03$).
Conclusions: Overall engagement in anal cancer screening is low within our clinic, especially among men, and retention in the screening program is notably better, especially among those with abnormal cytology results. Target populations have been identified to increase engagement, and qualitative studies are underway to understand perceptions and barriers to engagement in anal cancer screening.

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15 THE ANAL CANCER ETIOLOGY AND SCREENING (ACES) STUDY: DESIGN AND BASELINE CHARACTERISTICS

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***Background*:** Recent data showed that treating anal precancerous lesions can prevent cancer. Anal cytology is most widely used for anal precancer detection but has limited reproducibility and sensitivity, and the utility of high-risk HPV testing remains unclear. High-quality studies of biomarkers for anal precancer and cancer detection, such as p16/Ki-67 dual stain (DS) or methylation, are needed. We designed ACES: Anal Cancer Etiology and Screening, a collaboration between the NCI and the Icahn School of Medicine at Mount Sinai.
Methods: ACES will enrol over 1000 individuals referred for anal cytology, high-risk HPV testing, and high-resolution anoscopy at the Mount Sinai Anal Dysplasia Clinic. Routinely discarded anal cytology specimens are biobanked; clinical data is abstracted from electronic medical records. Residual samples are tested for DS, extended HPV genotyping, methylation, and other biomarkers.
Results: Over 260 individuals have been enrolled to date (mean age: 46.9 years), including MSM with HIV (71%), MSM without HIV (18%), and women with HIV (6%). Approximately 80% of individuals had ASC-US or worse cytology and high-risk HPV and HPV16/18 positivity were 75% and 26%, respectively. The prevalence of anal intraepithelial neoplasia (AIN) grade 2 or 3 was 32.7%. In a representative subset with DS testing available (n = 65), the sensitivity and specificity of DS for AIN2+ were 73.7% and 50.9%, respectively.
Conclusions: ACES will enable evaluation of screening tools and novel biomarkers among different subgroups in a clinical setting to generate evidence that informs anal HPV natural history and the possible development of guidelines for anal cancer screening.

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16 AUTOMATED EVALUATION OF P16/KI-67 DUAL STAIN CYTOLOGY IMPROVES DETECTION OF ANAL PRECANCER IN MSM LIVING WITH HIV

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***Background*:** Human papillomavirus (HPV)-related biomarkers such as p16/Ki-67 “dual stain” (DS) cytology have shown promising performance for anal cancer screening. Here, we assessed the clinical performance of automated evaluation of DS cytology using a deep learning approach to detect anal precancer in men who have sex with men (MSM) with HIV.
***Methods*:** 320 MSM with HIV undergoing anal cytology and high-resolution anoscopy (HRA) at Kaiser Permanente Northern California were recruited between 2009 and 2010. High-risk HPV testing and partial 16/18 genotyping (cobas4800) were performed on residual samples. We evaluated the performance of automated DS based on a deep-learning classifier with a pre-determined threshold of 3 positive cells to detect a combined endpoint of histologic or cytologic anal intraepithelial neoplasia grade 2 or 3 (AIN2+). We evaluated automated DS alone compared to manual DS cytology, as well as in combination with different HPV testing strategies.
***Results*:** Automated DS had significantly higher specificity (50.9% vs 42.2%, $P = 0.0004$) and similar sensitivity (93.2% vs 92.1%) for AIN2+ compared to manual DS cytology. Primary HPV testing with automated DS triage had the best performance, with significantly higher specificity compared to automated DS alone (56.5% vs 50.9%, $P = 0.0003$) with the same sensitivity (93.2%). Partial HPV16/18 genotyping with DS triage of other high-risk types had higher sensitivity (96.6%), but worse specificity (47.8%) than automated DS alone.
Conclusions: Compared to manual evaluation, automated DS cytology detects the same number of anal precancers with lower HRA referral, showing promising performance as a standalone test or in combination with primary HPV screening.

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17 CAUSAL HUMAN PAPILLOMAVIRUS (HPV) GENOTYPES OF ANAL CANCERS OCCURRING IN AUSTRALIAN WOMEN

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Background: Anal squamous cell carcinoma (ASCC) rates are rising globally and in the general population the prevalence is unswervingly higher in women compared to men. ASCCs are consistently more likely to be attributed to HPV16 than any other genotypes. However, much of the research into the aetiology and pathogenesis has been focused on men who have sex with men living with HIV. Multiple HPV genotypes are often found in the anal canal, making causal attribution difficult. Laser capture microdissection (LCM) not only allows accurate isolation of a single HPV genotype to a cancerous lesion but also avoids cross contamination of other types infecting surrounding cells.
Methods: 25 anal cancer specimens obtained at diagnostic biopsy were identified from female patients attending a single tertiary hospital. Following histopathological confirmation of anal cancer on tissue sections, all specimens underwent LCM, HPV detection and genotyping.
Results: The mean age of the subjects was 63 years old (range 43 to 94). All 25 LCM specimens tested positive for p16 and β-globin. A single HPV causal genotype was identified in each case. HPV16 was found in 23 (92%) of specimens with HPV18 and HPV31 found in one case each.
Conclusions: LCM convincingly identified a single causal genotype in all specimens of anal cancer from women, with HPV16 the predominant genotype. All cases could have been potentially prevented by the currently available prophylactic vaccine.

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18 A PROSPECTIVE STUDY OF THE PREDICTIVE VALUE OF HIGH-RISK HPV FOR HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESIONS IN A HIGH-RISK POPULATION

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Background: The incidence of anal cancer is rising, largely caused by high-risk HPV (hrHPV). Anal cancer is preceded by high-grade squamous epithelial lesions (HSIL), identifiable by high resolution anoscopy (HRA). There is limited data on the value of testing for high-risk HPV (hrHPV) to detect HSIL, especially in the HIV negative population. We prospectively compared the predictive value of hrHPV for HSIL in our patient cohort.
Methods: HRA's performed at the Homerton Anogenital Neoplasia Service were recorded prospectively over 6 months, including results from anal cytology, hrHPV and histology. The cohort of 248 men and 117 women included 159 HIV positive and 206 HIV negative individuals, all at high risk for anal cancer.
Results: In HIV positive patients, the sensitivity of hrHPV for detecting histologically proven HSIL was 92%, specificity 31%, PPV 44% and NPV 86%. In HIV negative patients, hrHPV detected HSIL with 97% sensitivity, specificity 41%, PPV 39% and NPV 97%. In additional analysis, in cases where histology was not done, we used clinical impression to determine disease status resulting in sensitivity 93%, specificity 39%, PPV 36% and NPV 94% in HIV positive patients. In HIV negative patients, sensitivity 95%, specificity 50%, PPV 31% and NPV 98%.
Conclusions: It is known that hrHPV in MSM LWH has limited utility. Further biomarkers are needed in these high-risk groups. However, hrHPV is potentially a very useful tool for patients in lower risk groups, yet with previous or known HSIL. The NPV may allow longer surveillance intervals for such groups.

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19 GENITAL AND ANAL CYTOLOGY-HPV COTESTING RESULTS AND PREDICTION NOMOGRAM FOR ANAL HIGH-RISK HPC INFECTION IN WOMEN LIVING WITH HIV

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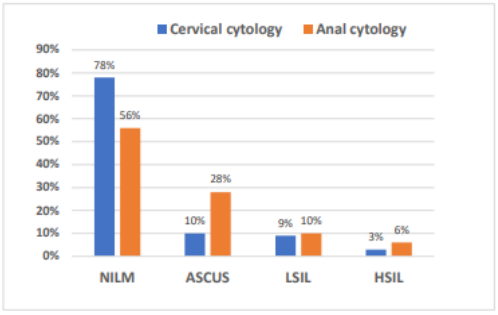
Background: Women living with the human immunodeficiency virus (WLH) are at increased risk for high-risk human papillomavirus (HR-HPV)-associated cervical and anal cancer. There is a strong correlation between cervical and anal HPV disease, indicating the possibility of predicting individual anal cancer risk based on cervical screening results.
Methods: Clinicopathological data were analysed from 381 WLH, including initial anal and cervical/vaginal cytology/HR-HPV cotesting results obtained within 6 months. Rates of and correlation between anal and cervical/vaginal abnormalities were analysed. Significant predictors from logistic regression models were used to create prediction nomograms for anal HR-HPV and HPV16/18 infection.
Results: Median age was 49 years (range: 20–81). Cytological diagnosis of ASCUS or worse (≥ASCUS) was more prevalent in anus than cervix (44% vs 22%). HR-HPV and HPV16/18 were detected in 65% and 27% of participants, more frequently in anus than cervix (61% vs 30% and 25% vs 8%). A nomogram predicting anal HR-HPV infection based on nadir CD4 T-cell count <200 cells/mm^3, cervical/vaginal cytology ≥ASCUS and cervical/vaginal HR-HPV positivity yielded prediction probabilities ranging from 40% (all predictors absent) to 90% (all predictors present).
Conclusions: High prevalence of anal HR-HPV infection and cytological abnormalities among WLH underscore the importance of anal cancer screening independent of preceding or concurrent genital disease. Clinical and cervical/vaginal cytological data can help stratify the risk of anal disease via prediction nomograms, although further prospective validation is warranted.

Figure 1: **Anal and cervical/vaginal screening results.** Data presented as percentage of participants in each category.

A. Cytological diagnoses (47 inadequate samples were excluded).



B. High-risk HPV testing results

Others: HPV31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68

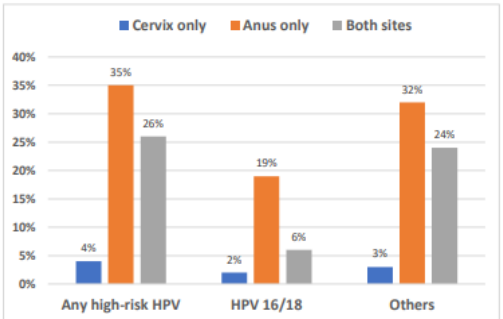


Fig. 1. Anal and cervical/vaginal screening results. (*a*) Cytological diagnoses. (*b*) High-risk HPV testing results.

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Figure 2: Nomogram predicting anal high-risk HPV infection.

To calculate the probability of anal high-risk HPV infection, add the score of each risk factor and then determine the probability based on the total score axis.

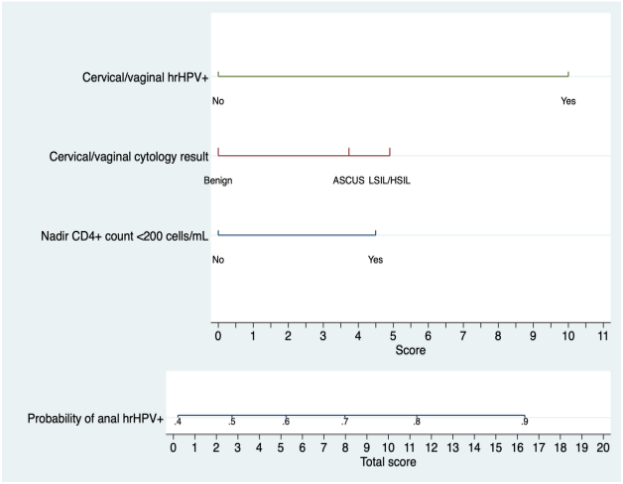

Fig. 2. Nomogram predicting anal high-risk HPV infection.

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20 PREDICTORS OF ANAL DYSPLASIA IN PEOPLE WITH HIV

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Background: Anal cancer is an important co-morbidity with rising prevalence among people with HIV. Anal cancer screening involves performing anal Pap smears followed by high resolution anoscopy (HRA) if cytology is abnormal. Here, we sought to understand predictors of dysplasia in our clinic population.
Methods: Demographic, social and clinical data from participants ≥30 years old with at least one anal Pap smear performed during the study period (12/18/2017–5/29/2021) were collected. A subgroup analysis was performed on those that received at least one HRA. Logistic regression produced adjusted odds ratios (aOR) for each variable of interest.
Results: Of 317 participants, 48% (n = 152) had abnormal cytology. Of those who underwent HRAs, 62% (n = 84/136) had high-grade dysplasia. Having prior sexually transmitted infections (aOR 2.39), and detection of human papillomavirus (HPV) 16 (aOR 2.75) and other high-risk HPV strains (aOR 3.00) were significantly associated with abnormal cytology whereas history of anoreceptive intercourse (aOR 4.62), HPV 16 (aOR 4.13) and other HPV strains (aOR 5.66) were significantly associated with high-grade dysplasia on HRA.
Conclusions: Nearly half of those screened for anal cancer had abnormal cytology and nearly three quarters of those that received HRAs had high-grade dysplasia, highlighting the high prevalence of anal dysplasia in people with HIV. HPV 16 and other high-risk strains were associated with abnormal cytology and high-grade dysplasia whereas socioeconomic factors and markers of HIV severity and chronicity showed no significant association. Cytology seems to underestimate the severity of dysplasia. More research is needed to understand the correlation between these findings on histopathology.

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21 SCREENING AND EARLY DETECTION TO PREVENT ANAL CANCER (SEPAC): PROTOCOL AND PROGRESS REPORT

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Background: Limitations of methods for anal pre-cancer screening have prevented their implementation, even among high-risk populations such as men-who-have-sex-with-men (MSM) living with HIV. High-resolution anoscopy (HRA) and biopsy, the gold standard for the detection of anal high grade squamous intraepithelial lesions (HSIL), are too expensive/impractical for primary screening. We aim to develop a screening strategy based on liquid-based cytology (LBC) and a biomarker panel, with HRA confirmation for those who screen positive. Delayed by the COVID-19 pandemic, the study is recruiting at six London sites.
Methods: The study will determine the sensitivity/specificity of a panel of biomarkers to detect persistent HSIL among MSM with HIV aged >40 (n = 1000). All will have anal LBC followed by HRA. Participants with HSIL on HRA/biopsy have repeat examination at 6/12 to define presence of persistent HSIL. LBC samples will be assessed for cytology, p16/Ki-67 dual-staining, hrHPV, HPV16-E2/E6 ratio, DNA methylation of host/HPV genes. Topographic records and images, and histology will be secondarily reviewed for QA. Baseline clinical data and pre/post screening quality of life will be recorded.
Results: To date, n = 98 enrolled and screened; of those with first screen results (n = 85), 29 (34%) had HSIL on biopsy; 48 (56.5%) were negative. One case of early anal cancer was detected. 7(8%) have had repeat examination due to inconsistent initial cytology/histology results. Two participants have withdrawn.
Conclusions: SEPAC is expected to provide further evidence to support the design and implementation of practical screening programmes in selected populations at increased risk of anal cancer.

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22 THE VALUE OF HIGH RESOLUTION ANOSCOPY (HRA) IN THE EARLY DIAGNOSIS OF ANAL CANCER IN A HIGH-RISK COHORT

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Background: 12% of anal squamous cell carcinomas (ASCC) in the UK are diagnosed at stage 1. Currently no national screening programme exists for anal cancer. At the Homerton Anogenital Neoplasia Service (HANS), high resolution anoscopy (HRA) is performed to diagnose and treat high grade anal intraepithelial neoplasia (AIN), a precursor to cancer. In some, ASCC is found on referral for AIN; in others it develops while undergoing AIN management. We reviewed all ASCC diagnoses to establish if HRA offers added value in the early diagnosis of ASCC in a high-risk cohort.

Methods: We used cross-sectional analysis of all new ASCC diagnoses between 2018 and 2021. Patient records, histology and radiology results were reviewed to define anal cancer stage per AJCC TNM classification. Our results were compared to national anal cancer statistics published by Cancer Research UK. ***Results:*** 53 ASCC diagnoses were made, of which 66.0% were stage 1 (14 prevalent, 21 incident), 20.8% stage 2 (9 prevalent, 2 incident) and 11.3% stage 3 (5 prevalent, 1 incident). None were stage 4; one cancer was unstageable. By comparison, 5836 cancers were diagnosed in the UK between 2013 and 2017. 12.0% were stage 1, 22.8% stage 2, 33.0% stage 3 and 8.46% stage 4; 23.8% were unknown or unstageable. Pearson Chi-squared statistic (χ^2) was 150.26 with $P < 0.001$ indicating statistical significance. ***Conclusion:*** Our findings suggest a benefit of using HRA in the early diagnosis of ASCC, particularly in high-risk cohorts. Further research is needed to assess feasibility of HRA as a national screening tool.

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23 HOST CELL DNA METHYLATION ANALYSIS ON MINIMALLY INVASIVE ANAL SWABS FOR THE DETECTION OF HGAIN AND ANAL CANCER IN HIV+ MSM

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***Background*:** Testing for host cell DNA methylation markers on anal biopsies has been preclinically validated as a valuable approach to identify HGAIN at risk of progression to cancer.[1] Here, we studied the applicability of these DNA methylation markers in anal swabs to detect underlying HGAIN at risk for progression to anal cancer.

Methods: We prospectively collected anal swabs and paired biopsies of 223 HIV+MSM in screening for anal cancer and 20 patients diagnosed with anal cancer. DNA methylation analysis of six markers and HPV testing was performed on all samples. The accuracy of DNA methylation analysis in anal swabs to detect histological HGAIN at increased cancer risk, based on a positive methylation test on biopsies, was determined by logistic regression analysis.

***Results*:** For the detection of methylation-positive histological HGAIN in cytology samples, the AUC of each individual methylation marker ranged from 0.56 to 0.64. The AUC increased to 0.74 when methylation analysis was combined with hrHPV testing. All anal swabs of cancer patients showed high methylation levels.

***Conclusions*:** Testing for DNA methylation markers on anal swabs is feasible and detects all anal cancers. Combined with hrHPV testing an AUC of 0.74 was obtained for the detection of histological HGAIN at risk of progression to anal cancer. Further exploration of methylation markers specifically for cytological material is to be considered.

Reference

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24 DNA METHYLATION ANALYSIS TO PREDICT REGRESSION OF HIGH-GRADE ANAL INTRAEPITHELIAL NEOPLASIA IN HIV+ MEN (MARINE): A COHORT STUDY PROTOCOL

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***Background*:** Anal cancer precursors, or high-grade anal intraepithelial neoplasia (HGAIN), are highly prevalent in human immunodeficiency virus-seropositive (HIV+) men who have sex with men (MSM). Around 30% of lesions regress within one year, but current histopathological assessment is unable to distinguish between HGAIN likely to regress and HGAIN likely to persist or progress to cancer. We aim to assess if host cell DNA methylation markers can predict regression of HGAIN, thus determining the need for immediate treatment, or active surveillance. This could reduce overtreatment and the associated anal and psycho-sexual morbidity.
***Methods*:** This is a multicentre, active surveillance cohort study in Amsterdam, the Netherlands, in 200 HIV+MSM diagnosed with HGAIN. Participants will not be treated, but closely monitored during 24-months of follow-up with six-monthly visits including cytology, and high-resolution anoscopy (HRA) with biopsies. The primary study endpoint is histopathological regression of each baseline HGAIN lesion at the end of the study. Regression is defined as ≤low grade AIN in the exit biopsy at 24 months. Regression proportions in lesions with low versus high methylation levels (*ASCL1, ZNF582*), other biomarkers (HPV genotype, HPV-E4, p16INK4A, Ki-67 and immunological markers) at baseline will be compared. Main secondary endpoints are the histological and clinical outcome (i.e., the number of octants affected by HGAIN) of each baseline HGAIN lesion and overall HGAIN disease (i.e., all lesions combined) after each visit. The health-related quality of life of the study group will be compared to that of a control group of 50 HIV+MSM receiving regular HGAIN treatment.

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25 HPV TESTING DIFFERENTIATES METASTATIC ANAL CANCER IN THE LUNG FROM PRIMARY LUNG CANCER

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Background: For patients with anal cancer, the development of a squamous cell carcinoma in the lung may indicate a new lung primary or metastasis of anal cancer (stage IV). Although the distinction is clinically important, it may not be straightforward on histologic grounds. In contrast to primary lung squamous cell carcinomas, most anal cancer are HPV-related such that HPV testing could be useful in establishing tumour relationships.
Method: The pathology database was searched for patients diagnosed with anal cancer from 2010 to 2020. Chart review was performed. HPV testing including real-time PCR and high-risk RNA in-situ hybridization (ISH) was performed on the lung tumours when tissue blocks were available.
Results: Among 610 anal cancer patients, 16 (2.6%) developed histology-proven lung metastases. The mean age was 63 (range 32–84). Eleven (69%) were male. Six (38%) were HIV positive. Four patients had synchronous anal and lung tumours; and 12 developed lung tumours after anal cancer (median interval 2.2 years, range 1–4). All patients received chemotherapy and radiation. Five died of the disease. Of the four patients with sufficient tissue for PCR and ISH, all were found to have lung cancers that were positive for high-risk HPV (HPV 16, n = 3; HPV 73, n = 1).
Conclusions: For patients with anal cancer who develop a squamous cell carcinoma in the lung, HPV analysis provides a useful tool in establishing tumour relationships. In such patients, we found that a squamous cell carcinoma in the lung most likely reflects a metastasis and not a second malignancy.

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26 PERFORMANCE OF 2 DIFFERENT HIGH-RISK HPV ASSAYS TO PREDICT HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS (HSIL) ON HIGH-RESOLUTION ANOSCOPY (HRA)

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***Background*:** Anal high-risk (HR) HPV-testing could be useful when screening for HSIL. The Cobas assay (Cobas) (Polymerase Chain Reaction (PCR) and Nucleic Acid Hybridization test) was compared to the Hybrid Capture 2 MRNA (HC2mRNA) (a Transcription-Mediated Amplification test for HR HPV mRNA) to determine ability to predict HSIL on HRA.
Methods: Data was abstracted from records of patients with HR HPV-testing, cytology and HRA between June 2020 and June 2021. An HRA without biopsy was considered negative for HSIL.
Results: 625 patients were eligible and 96.4% were male, 77% were HIV-negative with a median age of 47 (range 23–87) years. 303 (48.5%) had Cobas (61.1% were HR+). 323 (51.5%) had HC2mRNA (65.6% were HR+). HSIL was found in 84 (50.6%) Cobas HR+ and 6 (5.6%) HR HPV- participants yielding sensitivity: 93.3%; specificity: 55.5%; PPV: 50.9%; NPV: 94.4%). HSIL was identified in 116 (49.8%) HC2mRNA + and 15 (12.7%) HR HPV- patients yielding sensitivity: 88.5%; specificity: 47.2%; PPV: 50.2%; NPV: 87.2%) ($P = 0.013$). For HIV-negative patients HC2mRNA sensitivity, specificity, PPV and NPV were 86.2%, 46.9%, 48.8% and 85.2%, and for Cobas 92.8%, 55.3%, 53.8% and 93.3%, respectively ($P = 0.007$). For HIV-positive patients, sensitivity, specificity, PPV and NPV for HC2mRNA was 93.5%, 48.8%, 56.9% and 91.3% and for Cobas 88.9%, 51.7%, 36.4% and 93.8%, respectively ($P = 0.029$). Each assay performed significantly different when stratified by HIV status.
Conclusions: Cobas could be a superior screening tool as compared to the HC2mRNA with higher sensitivity, specificity and NPV to predict HSIL.

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27 HIGH RESOLUTION ANOSCOPY SEPARATOR: A NEW TOOL TO IDENTIFY ELUSIVE LESIONS

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Background: High resolution anoscopy is the gold standard in the screening of anal cancer and its precursor. Recently, ANCHOR study was prematurely suspended because it demonstrated that detecting and treating HSILs prevents anal cancer. In order to detect every HSIL it is imperative to observe the entire transition zone. Counting with the proper device would help to achieve this goal.
Methods: Motivated by some particularly difficult exams in patients with big haemorrhoids or mucosal folds, we decided to design a separator to allow a thorough evaluation of the transition zone, and to simplify the complete treatment of the detected lesions.
We performed a 3D print of a removable separator which has the same curvature of the anoscope surpassing it in 1 cm. A generic 3D printer with fused deposition modelling technology with polylactic acid was employed.
Results: After using the device in 10 HRAs for 2 months, we found it easy to be used and effective to expand the folds, allowing us to see the entire transition zone, reducing the patient's discomfort caused by the manipulation of the anoscope. There were no complications related to its use.
Conclusions: HRAs are more challenging than colposcopies because of the anatomical differences between the cervix and the anus. This emphasises the need for specific tools for performing HRAs. The separator can help to see the anal canal entirely and potentially reduce the risk of failing to detect elusive HSILs. Studies are needed to determine the effectiveness of the HRA separator on a larger scale.

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28 RECTAL HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESION (HSIL) - THREE CASES AND A MANAGEMENT PLAN

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Background: High grade squamous intraepithelial lesions (HSIL) are premalignant, driven by infection with oncogenic human papillomavirus (HPV). The anal squamocolumnar junction (SCJ) is the usual proximal limit for such lesions as HPV does not readily infect the columnar mucosa. Rectal squamous metaplasia can occur, however. We present three cases of rectal HSIL and suggest a management strategy for this rare situation.
Methods: Three cases were collated and followed prospectively.
Results: 2 males (M1, M2) and 1 female (F) patient were included, median age 46 (32–54) median follow up 35 months (33–38) and all had inflammatory bowel disease (IBD). Both males were men who have sex with men (MSM) and living with HIV (LWH). M1 had ulcerative colitis (UC), M2 indeterminate proctitis and F was post-colectomy for UC with innate IgA and Natural Killer cell deficiency.
The SCJ varied: from 20 cm of the rectal stump in F to 10 cm in M2. All three patients had concurrent anal HSIL. Management: regular 4 monthly endoscopic surveillance with narrow band imaging, acetic acid spray and biopsy plus high resolution anoscopy (HRA) and anal HSIL ablation for all patients. No invasive disease has yet been found. Argon beam and laser ablation have been trialled as treatment – abandoned due to stenosis and immediate recurrence.
Conclusions: IBD combined with immune suppression seem to predispose to proximal migration of the SCJ and subsequent HSIL. Joint endoscopic and HRA surveillance is recommended. Treatment modalities remain unproven.

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29 ANAL DYSPLASIA SCREENING IN PEOPLE WITH HIV YOUNGER THAN 35

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Background: Anal cancer is a growing source of frequent cancer morbidity for people living with HIV (PWH). Evolving guidelines recommend initiating anal cancer screening for PWH at age 35. With new evidence supporting the cancer prevention benefits of anal high-grade squamous intraepithelial lesion (HSIL) treatment, we analysed the outcomes of anal dysplasia screening for PWH <35 years.
Methods: Between January 2014 and August 2020, we identified initial anal cytology and high-risk HPV (hrHPV) test results for all PWH <35 years who underwent screening in our health system. We then collected information on subsequent high-resolution anoscopy (HRA)-guided biopsies and linked cancer registry entries (to identify any anal cancer diagnoses) for this cohort. Using these data, we compared screening and HRA outcomes according to demographics, CD4 count, HPV vaccination status and age subgroups.
Results: 1389 PWH <35 underwent anal dysplasia screening during the study period. Most (>90%) were 25–34 years of age and the vast majority were men (93%) of whom 98% were men who have sex with men. Only 28% received at least one dose of HPV vaccine before their initial screening cytology. Most subjects (66%) had cytologic abnormalities of ASCUS or greater (11% had HSIL cytology). 75% of cytology samples were contested for hrHPV with 85% of tests positive for any hrHPV type and 43% positive for HPV 16 and/or 18. Of subjects with abnormal screening cytology 62% underwent subsequent HRA which yielded anal HSIL in 44% (histologic HSIL rate in the overall screening cohort was 21%). Women had substantially less histologic HSIL than men (8% versus 22%; $P = 0.001$). There was no significant difference in the proportion of persons diagnosed with histologic HSIL by age subgroup (<25, 25–29, 30–34; $P = 0.7$). CD4 count at initial screen was not associated with severity of cytologic abnormalities, hrHPV infection or HSIL diagnosis. History of HPV vaccination was associated with lower rates of HPV 16/18 infection (38% in vaccinated versus 45% in unvaccinated, $P = 0.02$) but did not impact rates of overall hrHPV infections or eventual HSIL diagnoses. No incident cancers were diagnosed during the follow-up period.
Conclusions: High-risk HPV infection, cytologic abnormalities, and associated histologic HSIL were all common in PWH under age 35. With emerging evidence regarding the benefits of anal HSIL treatment, the role of screening should be further investigated in this population.

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30 GERMAN EXPERIENCE WITH HIGH RESOLUTION VIDEO-PROCTOSCOPY (PROCTOSTATION) IN ANAL SCREENING IN MEN WHO HAVE SEX WITH MEN (MSM)

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Background: Patients at risk for developing anal intraepithelial neoplasia are enrolled in screening programs. Cythopathological examinations and high-resolution anoscopy are a part of it. High-resolution anoscopy is a laborious, time-consuming method. To significantly reduce the examination time, the so-called Proctostation was developed, which includes a camera attachment on a proctoscope with up to 39× magnification.
Methods: From May 2021 to October 2021, we performed 99 HRA examinations with the 'Proctostation'. The examination was performed after three percent acetic acid application using a moist thick gauze swab in the anal canal after 3 min. We performed biopsies in case of abnormal findings.
Results: The average age of the men who have sex with men (MSM) was 48 years, 59/99 were HIV-infected. In 72% of the patients, suspicious epithelial changes were found, which bioptically showed AIN of various grades in addition to condylomata acuminata. In 14/99 (10 /59 HIV infected) of these patients, we were able to detect AIN grade 1 (LSIL) and in 8/99 (7/59 HIV infected) patients AIN grade 2 or 3 (HSIL). Average time for the diagnostic procedure was 12 min.
Conclusions: HRA is an important and highly sensitive examination for early detection and therapy of anal dysplasia. The 'Proctostation' simplifies and accelerates the procedure with similar results as in existing HRA studies, which were performed with a colposcope. In addition, the video function and an image comparison tool proved helpful in the follow-up.

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31 RE-AUDIT OF HIGH RESOLUTION ANOSCOPY OUTCOMES ACCORDING TO IANS STANDARDS JAN–MAR 2021

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Background: Our HRA service was re-audited in relation to IANS standards.
Methods: Data was collected over 3 months and included all HRAs and multizonal anogenital assessments. Pathology results, biopsy number and site, and anoscopy duration were then analysed by clinician, sex of patient, HIV status, and new versus follow-up status.
Results: Of 206 patients, 46% of patients were female, 7% were heterosexual men, and 42% were HIV-positive. Biopsy rates met the standard (>1/HRA) – 2.44 biopsies per HRA for new patients, and 3.08 biopsies per patient for all areas. Follow up patients had 1.22 biopsies/HRA.
HRAs took an average of 13 min. One third took longer than 15 min (IANS suggest <10% exceed 15 min).
One quarter of patients had perianal biopsies, meeting the 5% minimum target.
Pick-up rates of high-grade lesions per biopsy varied considerably by clinician (0–48%). Overall, 27% of patients had HSIL. In new patients, half of all biopsies showed HSIL.
All anoscopists hit the target of >= 50 HRAs per year.
Conclusions: All clinicians demonstrated adequate caseload and biopsy rates but widely differing HSIL prevalence. This may be due to differing case-mix but could be due to differences in HRA performance. Time taken for anoscopy in our clinic exceeds the standards, and comparison with other centres is warranted. Separating HRA and vulval/vaginal biopsies enabled better comparison between clinicians. Perianal biopsy rates much higher than the 5% standard likely reflects our multizonal disease population. Further audits should include complications and adequacy of view.

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Sexual Health

32 EXPERIENCE OF IMPLEMENTING AN HIV PREEXPOSURE PROPHYLAXIS (PREP) PROGRAM INTO AN ANAL DYSPLASIA-FOCUSED OFFICE

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Background: Condomless anal intercourse is associated with HIV seroconversion and anal HPV disease. Our practice is an anal dysplasia-focused office which implemented a PrEP program.
Methods: Data was collected from individuals prescribed PrEP from 2014 to 2019. Patients prescribed PrEP ≥360 days were included in additional analysis as 'PrEP patients'. Reasons for PrEP patients starting and stopping PrEP were recorded by manual chart review.
Results: 235 Patients received a PrEP prescription and 114 patients were prescribed PrEP ≥360 days. Among PrEP patients >99% were men who have sex with men, mean age was 35 years. 41 (35.9%) were discontinued care, 39 (34.2%) remained on PrEP managed by the practice, 13 (11.4%) discontinued, and 21 (18.4%) switched PrEP management to their primary care provider (PCP). Among individuals with a known reason for starting PrEP (N = 75), 13 (17.3%) were encouraged by our practice, problems getting a prescription from primary care were cited among 5 (6.7%) patients, 24 (32.0%) requested PrEP including two who established care specifically for sexual rather than anorectal health. 5 (6.7%) individuals converted from postexposure prophylaxis, and 15 (20%) noted that they chose PrEP management from us rather than their PCP. The mean duration of maintaining PrEP prescriptions among PrEP patients was 2.62 years. No seroconversions were reported despite high rates of bacterial STIs among PrEP patients.
Conclusions: With continued underutilisation of PrEP, anal dysplasia clinics should consider offering this service to their patients when appropriate.

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Treatment

33 JUST CUT IT OUT!? SURGICAL EXCISION IS SAFE AND EFFECTIVE IN TREATMENT OF HIGH GRADE ANAL INTRAEPITHELIAL NEOPLASIA: RESULTS FROM A RETROSPECTIVE COHORT STUDY

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Background: The incidence of anal carcinoma is increasing worldwide. Evidence is building up showing that treatment of the precursor lesions, anal intraepithelial neoplasia (AIN), decreases the progression rate to anal carcinoma.
Topical or ablative approaches are considered minimal invasive but are limited by high recurrence rates requiring multiple interventions and consecutive patient discomfort. Local surgical excision may be a valuable alternative, but data regarding efficacy and safety are rare.
Methods: Evaluation of efficacy, safety and recurrence rate in a surgically treated prospective cohort of patients with high-grade AIN (AIN HSIL) at a tertiary referral centre. Patients received clinical follow-up including high-resolution anoscopy over a period of at least 5 years.
Results: In 70 patients (50% male, mean age 53 years) a lesion containing AIN HSIL was resected between 2012 and 2021. In 13 patients (18%) a recurrence was observed (8 patients/11% AIN HSIL, 89% LSIL or Condylomata) during a median follow-up of 44 months (range 0–88). Recurrence occurred after median 33 months (range 0–67). Persisting functional problems were observed in seven patients (10%) and consisted mainly of soiling.
Conclusions: Local surgical excision is effective in achieving low recurrence rates as compared to topical or ablative treatment options. Long-term morbidity is low. Especially in recurrent disease after conventional therapy, excision may be a valuable option in experienced hands, achieving an excellent oncological result with minimum patient discomfort.

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34 IS LOCAL EXCISION ALONE FOR EARLY ANAL SQUAMOUS CELL CARCINOMA (ASCC) EFFICACIOUS IN PEOPLE LIVING WITH HIV (PLWH)?

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Background: The rate of cervical squamous cell carcinoma (SCC) is decreasing worldwide, however the incidence rates of other less common HPV-related perineal malignancies are increasing. Ethnicity and socioeconomic deprivation are known to be contributing factors in the prognosis of cervical SCC, less is known about their role in other HPV-related perineal malignancies.
Methods: Incidence rates of HPV-related perineal malignancies in England between 2013 and 2017 were extracted from the Clinical Outcomes and Services Dataset (COSD). Data was broken down for ethnicity, stage, treatment and socioeconomic score.
Results: Cervical SCC remains the most common HPV-related malignancy but its incidence has decreased by 5.8%. It is associated with higher levels of social deprivation.
The incidence rates of vulval and penile SCCs have remained stable (3.05 cases per 100 000 women vs 3.14 cases per 100 000 men).
Vaginal SCC is the least common malignancy (0.49 cases per 100 000 women) but its incidence has increased by 15.6%.
Anal SCC incidence has increased by 29.0% in women and 14.5% in men, with increasing numbers of men presenting with early-stage disease (106.9% increase) and increasing numbers of women with metastatic disease (121.5% increase). Ethnicity and social deprivation were independent factors in the staging and treatment of patients with anal SCC.
Conclusions: Although, the cervical screening programme is reducing the incidence of cervical SCC, rates of rarer HPV-related perineal malignancies are increasing. Moreover, the rates of metastatic disease in women with anal SCC are concerning. Ethnicity and socioeconomic status appear to be factors in the presentation patterns of HPV-related perineal malignancies.

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35 THE VIABILITY OF LASER METHODS FOR HSIL ABLATION

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***Background*:** As understanding of anal high grade squamous intraepithelial lesions (HSIL) broadens, the need for evidence regarding treatment increases. Whilst electrocautery is acknowledged in the literature, we studied laser ablation to establish if this option has equivalent outcomes.
***Methods*:** A retrospective cohort study from December 2014 to 2019 of 278 male patients with proven high-grade squamous intraepithelial lesions (HSIL) who received laser treatment was performed. The primary outcome was length of disease-free survival before recurrence.
***Results*:** The study is ongoing. This abstract reports the outcome for 65 patients undergoing treatment for 96 lesions. 54 (83%) were MSM, 47 (72%) HIV positive and 24 (37%) were active smokers. 50 lesions (52%) were AIN3 and 46 (48%) AIN2, p16 positive or without p16 in earlier cohort years. 25 (27%) were treated with CO2 and 70 (73%) with diode laser; 25 (26%) were performed under general anaesthetic and 71 (74%) under local. The total median disease-free survival was 400 days (range 52–1603); with recurrence earlier in the AIN2 group (557 days) versus AIN3 (720), $P < 0.02$.
***Conclusions*:** Whilst study numbers at present are low, we are able to demonstrate the validity of the use of laser for HSIL treatment, and its concurrence in efficiency and outcome to electrocautery ablation. Laser may be a therapeutic option for anal HSIL eradication in future.
The earlier recurrence in the AIN2 group is interesting and as the patient cohort increases, we may understand this further. In particular, examining p16 and potential treatment bias between the two groups.

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36 ANAL CANCER TREATMENT AND OUTCOMES – A SINGLE CENTER 10 YEAR EXPERIENCE

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***Background*:** Anal cancer is a rare type of cancer, however the incidence is increasing in The Netherlands with 269 new patients and approximately 60 deaths in 2019. Standard of care for locally advanced stage consists of chemoradiotherapy (CRT) with mitomycine C (MMC) and 5-fluoro-uracil (5-FU or capecitabine) or radiotherapy (RT) alone for early tumours. Large randomised trials are scarce, therefore we report our single centre results.
***Methods*:** Retrospective analysis, with inclusion period from 2009 to 2019 of patients with carcinoma or high grade dysplasia of the anus treated with (C)RT with curative intent. Primary endpoint was locoregional recurrence (LRR) at 3 years. Secondary endpoints were overall survival (OS), disease-free survival (DFS), colostomy-free survival (CFS) and toxicity.
***Results*:** 184 patients were included, one patient was treated with RT alone. Median follow-up was 57.4 months (range 0–139 months). LRR at 3 years was 9.0%. OS at 3 and 5 years were 79.7% and 72.6%, DFS 72.5% and 65.4% and CFS 74.0% and 67.8%, respectively. Most frequent reported short-term toxicity was perianal dermatitis (grade ≥ 3 71.1%), followed by inguinal dermatitis (grade ≥ 3 55.4%) and proctitis (grade ≥ 3 9.8%). Long-term toxicity reported was proctitis (grade ≥ 3 32.0%), dyspareunia (grade ≥ 2 5.4%) and erectile dysfunction (grade ≥ 2 4.3%). In one patient grade 5 toxicity was reported (not healing perianal wound).
***Conclusions*:** In this study almost one out of 10 patients developed LRR. Despite combined modality treatment with chemotherapy and radiotherapy, treatment of patients with anal cancer could be improved.

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37 RADIOFREQUENCY AS TREATMENT IN A PATIENT WITH A HSIL

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Background: The SIL is the precursor of the ASCC, with a low incidence, however in high-risk groups (MWSM, especially with HIV) it's comparable to the incidence of colon cancer.
The treatment is the directed destruction of HSIL with electrocautery, having an efficacy of 74–84%. A novel technique has been developed, being circumferential or hemicircumferential radiofrequency ablation, with promising results.
Methods: A 60-year-old woman (HIV-) with history of moderately differentiated epidermoid anal canal cancer diagnosed 4 years previous to her current condition. She had transrectal bleeding, therefore a HRA and a colposcopy were made, finding an HSIL in the anal canal and HPV in cervix. An exploration was made and resected a condilomatous 3 × 3 × 2 cm lesion 1 cm away from the anal margin. The diagnosis was epidermoid anal cancer, she received RT and QT.
10 months after her follow up an HRA was made, finding an HSIL, therefore we used electrocautery as treatment. 1 year after the HRA showed HSIL again. The disease recurred so we used radiofrequency ablation. Finding in the posterior portion of anal canal fibrosis and condilomatous aspect lesions, we used Halo Flex of Barrx Medical (Medtronic).
Results: The patient had a satisfactory evolution. Posteriorly the patient continued her follow up, 1 year after the procedure we found in her HRA an LSIL in anal margin, but no recurrence of HSIL.
Conclusions: Even though there are few studies of the detection and treatment of this lesions, experts support routine HRA in patients with high risk.

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38 THE EFFICACY OF TOPICAL DIHYDROARTEMISININ TO TREAT ANAL DYSPLASIA IN MICE

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***Background*:** Anticancer activities of the artemisinin family of compounds have been observed across a wide variety of cancers, including treatment of cervical dysplasia, caused by human papillomavirus (HPV). We evaluated the efficacy of topical Dihydroartemisinin (DHA) in a mouse model of papillomavirus-induced anal dysplasia.
***Methods*:** *K14E6/E7* mice, that express HPV16 oncoproteins in their epithelium, were randomised into groups: control, DHA only (78 mM daily), 7,12-Dimethylbenz(a)anthracene (DMBA) (carcinogen) only (0.12 μmole weekly), and DHA with DMBA. DMBA, was utilised to ensure progression from dysplasia to cancer within a 20-week period. Treatments began at 25 weeks-of-age, when mice reliably develop high-grade anal dysplasia. Mice were treated topically at the anus for 20 weeks and monitored for anal tumour development. Anuses were harvested for histopathological examination by gastrointestinal pathology. Data analysis included Wilcoxon and Log-rank tests for tumour-free survival and Fisher's exact test for histologic grade.
***Results*:** Zero mice in the control or DHA only groups developed overt tumours or histologic evidence of cancer. In the DMBA only group, 77% (10/13) of mice demonstrated overt anal tumours and microscopic cancer compared to 67% (8/12) with overt tumours and 92% (11/12) with microscopic cancer in the DHA with DMBA group. When comparing treatment groups to their respective controls, there was no statistically significant difference in tumour-free survival (*P*-values = 0.71, 0.90) or final anal histology (*P*-values = 1.0, 0.59).
***Conclusions*:** Treatment with topical DHA did not prevent progression from high-grade anal dysplasia to anal cancer in an HPV-induced mouse model of anal carcinogenesis.

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39 ANAL SQUAMOUS CELL CARCINOMA (ASCC) TREATED BY EXCISION ALONE RESULTS IN HIGHER RATES OF HSIL, AND HIGH-RISK HPV GENOTYPES WHEN COMPARED TO CHEMORADIOTHERAPY

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Introduction: Treatment of ASCC includes excision, chemoradiotherapy, or a combination of both. We sought to evaluate the role of HRA in detecting HSIL and HRHPV during follow-up.
Methods: HRA was added to standard follow-up protocols for people receiving ASCC treatment Nov 2003 to Sep 2021. Clinical databases were examined.
Results: Of 79 patients, 59 (75%) had intra-anal ASCCs. Nearly half (n = 36, 47.4%) were stage I, 18 (23.7%) stage II, and 22 (29.0%) stage III. Most (n = 65, 83.3%) were male, and 44 (57.1%) were HIV-positive. Median age was 60 years at first visit.
26% were treated with excision alone, and 74% chemoradiotherapy. Median time from diagnosis to first HRA was 325.5 days (IQR: 208–1074). At first visit, 13 (16%) patients had histologic HSIL, of whom (n = 7, 38.9%) had undergone excision alone vs 6 (11.8%) who had chemoradiotherapy (P = 0.016). Excision alone patients were more likely to have other HRHPV detected (56.3% vs 26.1%, P = 0.031), and borderline more likely to HPV16 (37.5% vs 15.6%, P = 0.077), but no association was found with HPV18 (6.3% vs 9.1%, P = 0.717).
When HSIL was not detected at first visit, those undergoing excision alone were significantly more likely to develop new HSIL compared to those who received chemoradiotherapy (60.0 vs 4.74 per 100 person-years, HR=12.35, 95% CI: 2.31–65.90, P = 0.003). None of these abnormalities were identified by other specialists during follow up.
Conclusions: Chemoradiotherapy was associated with greater clearance of HSIL and HRHPV, compared to excision alone. HRA provided more comprehensive follow-up data than existing standard protocols.