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1. Prevalence of HSIL or SCCA in women referred for high-resolution anoscopy

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Abstract. Background: The incidence of anal squamous cell carcinoma (SCCA) in women is increasing. High-resolution anoscopy (HRA) with biopsy identifies anal high-grade squamous intraepithelial lesions (aHSIL), precursors to SCCA. The true prevalence of aHSIL in women either with or without risk factors for SCCA is not known. **Methods:** 250 women at risk for aHSIL or with histologic aHSIL or greater (aHSIL+) who were referred to the UCSF Anal Neoplasia Clinic between 1998 and 2014 were analyzed. Prevalence of aHSIL, defined as the proportion of women with aHSIL within 1 year of their first clinic visit was analyzed according to reasons for referral, immune status, and history of lower genital tract HSIL (LGT-HSIL). **Results:** The median age was 51 years (range 26–80). HIV infection was present in 20% (51/250), 6% (15/250) had solid organ transplants, and 9% (22/250) were immunocompromised for other reasons. The overall prevalence of aHSIL+ was 54% (136/250) including 14 with SCCA. The prevalence of aHSIL+ was 44% (56/126) in women without prior aHSIL+ and 81% (80/99) in women referred for management of aHSIL/possible cancer. None of 25 women referred following radiation for SCCA had prevalent aHSIL. Prevalence in women with a history of LGT-HSIL was 61% (64/105) and 50% (72/145) with no history and was 62% (53/86) in immunocompromised women and 51% (83/164) in non-immunocompromised. **Conclusions:** The prevalence of HSIL+ was quite high across different risk groups even when those with known anal HSIL+ were excluded. This has implications for screening women for anal cancer precursors.

2. Knowledge and acceptability of anal cytology screening among women

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Abstract. Background: Medical providers have initiated anal cytology screening among HIV-positive women to increase early detection of anal cancer caused by HPV. Lack of knowledge of HPV and anticipated screening discomfort may limit patient acceptance. This study investigates attitudes toward anal cytology screening among women. **Methods:** Women in an obstetrics and gynecology clinic at an urban university medical center were invited to complete an anonymous survey assessing their understanding of HPV and level of interest in anal cytology screening. Subjects reported the level of pain, discomfort and embarrassment they expected from screening on a 100mm visual analogue scale (VAS). **Results:** 508 women with mean age 37 years (SD 13) agreed to participate. 425 women reported their race; 49% were Caucasian and 39% were African-American. 426 women reported their ethnicities; 73% were Hispanic and 13% were Haitian. 24% had never heard of HPV and 51% were not familiar with anal cytology screening. While 67% acknowledged regular anal cytology screening would be very helpful to diagnose cancer early, 31% affirmed they were very interested in having an anal cytology test. Among women not interested in anal cytology testing, 48% did not know enough about it and 34% believed it might hurt. On the VAS, mean level of pain, discomfort and embarrassment expected from screening was 58mm (SD 33), 65 mm (SD 31), and 55 mm (SD 35), respectively. **Conclusions:** The limited familiarity with and level of interest in anal cytology screening among women presents an opportunity for medical providers to improve patient education to increase acceptance of screening.

3. Medical students' perception of the acceptability of anal cytology screening among women

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Abstract. *Background:* Medical students receive limited instruction about anal cytology screening for early detection of HPV-related anal cancer. This study investigates medical students' knowledge of HPV and anal cancer risk factors, and their perception of women's attitudes toward anal cytology screening. *Methods:* South Florida medical students were invited to complete an anonymous survey assessing their understanding of HPV and anal cancer risk factors, personal attitudes toward anal cytology screening, and anticipated concerns regarding anal cytology screening among female patients. Subjects reported levels of pain, anxiety and embarrassment they expected women would experience during screening on a 100mm visual analogue scale (VAS). *Results:* 308 students with mean age 25 years (SD 2) from three medical schools agreed to participate (23% response rate). 60% of respondents were female, 78% were Caucasian, and the distribution of first, second, third and fourth-year students was 32%, 27%, 22% and 19%. 34% recognized that 80% of women become infected with HPV by age 50; this improved from 17% of first-year to 47% of fourth-year students. Students believed women may decline anal cytology screening because they don't know enough about it (69%), would be too embarrassed (94%), or believe it might hurt (84%). On the VAS, medical students anticipated women would experience greater mean levels of anxiety (69 mm, SD 22) and embarrassment (74 mm, SD 19) during anal cytology screening than pain (27 mm, SD 22). *Conclusions:* Future medical providers must improve their understanding of HPV and women's expectations regarding anal cytology screening to effectively educate patients and increase acceptance of anal cytology screening.

4. HIV as a risk factor for the progression of high grade anal dysplasia

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Abstract. *Background:* HIV infected (HIV+) persons are at increased risk of invasive squamous cell carcinoma of the anus (SCCA). High-grade squamous intraepithelial lesion (HSIL) is a recognized precursor to SCCA, though its natural history remains poorly understood. Using a population-based cohort with long-term follow-up, we evaluated whether HIV infection is associated with an increased risk of progression to invasive SCCA in individuals with prevalent HSIL. *Methods:* We identified a cohort of 957 subjects with incident, pathologically confirmed HSIL from the Surveillance, Epidemiology, and End Results (SEER) database linked to Medicare claims (1991–2009). HIV infection was identified using relevant ICD-9 codes. We used claims and SEER data to ascertain several outcomes including development of invasive SCCA, colostomy placement, SCCA-specific and all cause mortality. We compared baseline characteristics of HIV+ and uninfected (HIV-) subjects using univariate tests. We then determined risk of outcomes of interest by HIV status using Kaplan-Meier methods, and fitted Cox regression models to adjust for potential confounders, including age, gender, race, income quartile, modified Charlson comorbidity score, condyloma diagnosis and baseline treatment (i.e. surgical or non-surgical excision). *Results:* Our analytic sample included 639 HIV+ and 318 HIV- subjects with a median follow-up of 60 months. HIV+ subjects were younger, more likely to be male, and non-white than HIV- subjects ($P < 0.001$ for all comparisons). HIV+ subjects also had a lesser burden of comorbid illness than HIV- subjects ($P < 0.001$). During follow-up 54 (6%) subjects developed SCCA. There was no significant difference in overall frequency of progression to invasive cancer between the HIV+ and HIV- groups (5% vs 6% respectively, $P=0.5$) or to colostomy (1% for both groups, $P=0.9$). Anal cancer specific mortality was low and did not significantly differ when comparing HIV+ subjects to HIV- subjects (0.2% vs 1%, $P=0.08$). For persons who progressed to SCCA, the median times to diagnosis were 24 months (95% CI 12–36) vs 36 months (95% CI 21–55) in the HIV+ and HIV- groups. Similar results for all outcomes were obtained in adjusted analyses. *Conclusions:* These data suggest that the prognosis of HSIL is similar in HIV+ and HIV- individuals. Our findings may have been limited by the accuracy of HSIL reporting to SEER. More work is needed to determine the specific risk factors promoting HSIL progression to SCCA.

5. Factors affecting recurrence of high grade anal intraepithelial neoplasia – 17 years of observation

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Abstract. Background: Treating high grade anal intraepithelial neoplasia (AIN2+) is thought to reduce anal cancer risk. Recurrence after treatment is common and surveillance is necessary. **Methods:** Data were obtained from clinic records from 1996-2013, containing 121 patients with AIN 2+, with follow-up from 9 months to 17 years (median 5.8 years). A Cox proportional hazards model was fitted to the data, with an outcome of time to recurrence. Intervals were censored at the end of follow-up if no recurrence had occurred. Univariate analyses were carried out for age, gender, HIV status, treatment type (topical vs. laser ablation) and multiple lesions at baseline, before a multivariate analysis including all variables. **Results:** 195 intervals from 121 patients were included in the analyses. 113 patients (93%) were male, and mean age at diagnosis was 37.6 years (range 15.8–67.7). There were 77 recurrences. Mean time to recurrence was 2.1 years. In the univariate analyses, risk of recurrence increased with age (HR=1.03, 95% CI: 1.01–1.05); those of unknown HIV status had a higher risk of recurrence than the HIV-positive cohort (HR=3.40; 95% CI: 1.98–5.85), though numbers were low ($n=12$). In the multivariate analyses both age and HIV status were fully attenuated. **Conclusions:** In our series, AIN2+ was treated: topically (small lesions, patient choice) or with laser ablation. HIV-positivity had no impact on recurrence but HIV-status unknown – perhaps undiagnosed HIV – did. HIV testing is now suggested for unknown-status patients at anoscopy. Reducing AIN2+ recurrence is a major goal of future therapeutic interventions.

6. Human papillomavirus in multiple sites associated with risk for anal squamous intraepithelial lesions in HIV-seropositive individuals

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Abstract. Background: HIV+ patients have higher prevalence of other viral infections, including HPV, even while on antiretroviral therapy. Infection with high-risk HPV genotypes at multiple sites including cervix, anus, penile head, penile shaft, foreskin, scrotum, and oral cavity may be related to increased risk of anal dysplasia/cancer. The objective was to assess the association of HPV genotypes at different anatomical sites with anal squamous intraepithelial lesions (ASIL) in HIV+ individuals. **Methods:** Cytology specimens were obtained from multiple tissue sites: females with cervical and anal cytologies and oral wash samples; males with anal cytology, oral wash, and exfoliated skin samples (penile head, penile shaft, scrotum, and foreskin from uncircumcised subjects). Demographic and clinical data (gender, ethnicity, age, anal cytology, viral load, nadir CD4) were recorded. Following DNA extraction, HPV was genotyped. Statistical analysis included Chi-square, Fisher's exact, and Wilcoxon nonparametric tests. **Results:** Males were more likely to have ASIL: 28/50 (56%) compared to 1/10 females (10%) ($p=0.013$). For 44 males (88%) with HPV genotype data available, HPV was detectable in at least one site for 33 participants (75%): 27 anus (61.4%), 19 oral cavity (44.2%), 17 penile shaft (38.6%), 13 scrotum (29.5%), and 10 penile head (22.7%). No foreskin specimens tested positive for HPV. ASIL+ males tested HPV+ at more tissue sites than ASIL- males: ASIL+ (2.4 ± 1.8 , $n=25$) versus ASIL- (1.3 ± 1.4 , $n=19$) ($P=0.048$). **Conclusions:** ASIL+ males were likely to have more HPV+ anatomic sites than ASIL- males. Supported by U56CA096254-S1; U54CA143727-S1; U54MD007584; G12MD007601.

7. Characteristics and outcomes of female patients referred to a national anal neoplasia centre

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Abstract. **Background:** Anal neoplasia is recognised precursor to invasive carcinoma. Female patients are at risk of multizone intraepithelial neoplasia. **Methods:** The case notes of 90 female patients referred to our unit were reviewed. Data was collected on demographics, smoking status and past medical history. Baseline clinical and histological findings, treatment and clinical outcomes were recorded. **Results:** The median age of referral was 41 years (19–83). 46 patients (50%) had a diagnosed immunodeficiency including 29 patients (32%) living with HIV. 16 patients (17%) had history of anal neoplasia including high-grade dysplasia ($n=3$) and invasive carcinoma ($n=10$). At first High Resolution Anoscopy examination 54 patients (60%) had anal canal disease, 48 patients (53%) had perianal disease. 51 patients had baseline anal biopsies which demonstrated normal histology ($n=1$), HPV changes ($n=6$), low-grade dysplasia ($n=13$), high-grade dysplasia ($n=29$) and invasive carcinoma ($n=2$). Baseline perianal biopsies from 36 patients demonstrated HPV changes ($n=11$), low-grade dysplasia ($n=7$), high grade dysplasia ($n=17$) and invasive carcinoma ($n=1$). 58 episodes of perianal and/or anal canal disease were treated using laser therapy ($n=41$), laser plus imiquimod ($n=9$), imiquimod only ($n=4$) and excisional biopsy ($n=4$). At first follow up 26 patients (44%) showed resolution of disease, 16 (28%) showed an improvement, 16 (28%) had persistent disease. 2 patients developed invasive carcinoma during treatment. **Conclusions:** Management of anogenital neoplasia in women poses a number of clinical challenges particularly when treating high volume, longstanding disease and in the context of immunodeficiency. Further work is needed to improve cancer prevention in this patient group.

8. Pain, discomfort, and embarrassment during high-resolution anoscopy among women: a potential barrier to care?

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Abstract. **Background:** High-resolution anoscopy (HRA) is utilized for microscopic evaluation of the anal canal in patients at increased risk for HPV-induced anal dysplasia. The purpose of this study was to evaluate patients' knowledge about HRA and assess their perceived level of pain, discomfort and embarrassment before and after HRA. Provider perception of patient pain, discomfort and embarrassment was also assessed. **Methods:** HIV-positive women scheduled for HRA at an urban university medical center were surveyed to assess knowledge of HPV and HRA before and after their procedure. Perceived pain, discomfort and embarrassment were evaluated using a 100mm visual analogue scale (VAS). Providers' perception of their patients' level of pain and discomfort was assessed using a similar VAS. **Results:** Of the 55 women surveyed, the mean age was 46 (SD 10), 80% were black, and 60% achieved at least a high school degree. One-third (36%) were not familiar with HRA, and 64% reported limited knowledge. The mean level of anticipated HRA pain differed significantly from actual pain experienced ($P=0.00$). Similarly, anticipated discomfort differed significantly from discomfort reported post procedure ($P < 0.05$). There was no significant difference in embarrassment pre- versus post-HRA. Providers perceived that patients would experience less pain and discomfort than what patients actually reported (pain: $P < 0.05$, discomfort: $P < 0.05$). **Conclusions:** This study demonstrated that patients anticipated greater pain and discomfort than was actually experienced. In contrast, providers anticipated that patients would experience less pain than reported. Consequently, providers need to enhance patient education and address patient concerns regarding anticipated pain and discomfort associated with the HRA procedure.

9. Twenty years of targeted ablation of AIN: what I've learned and where I'm going

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Abstract. Background: In the late 1990's I began targeted ablation of intra anal and perianal high-grade dysplasia (HSIL) in an effort to prevent progression to invasive anal cancer (AC). Initially ablation was carried out with lasers in the operating room and infrared coagulation in office. We transitioned to electrocautery. We are testing radio-frequency ablation (RFA) to try and diminish recurrence. **Methods:** We reviewed our experience of all MSM who had in-office (infrared coagulation or cautery) or surgical (CO₂ laser) intra anal and perianal HSIL and condyloma ablation with ≥ 1 follow-up HRA since March 1998. MSM could be treated by multiple modalities. We began testing RFA intra anal HSIL ablation in 2013 first with hemicircumferential ablation and now circumferential. **Results:** Of 727 MSM (59% HIV-), median follow-up 2.2 (range 0.2–13) years, who underwent HSIL ablation by laser, IRC and/or ECA, median time to recurrence was 6.8 and 6.9 months for HIV-positive and negative patients, respectively. Kaplan-Meier (KM) curves predict recurrence one year post first ablation for HIV+ and HIV- patients of 53% [95% CI: 49–58%] and 49% [95% CI: 43–55%], respectively. At 2 and 3 years recurrence was 68% [95% CI: 63–73%] and 77% [95% CI: 72–82%], respectively for HIV+ patients and 57%. Five HIV+ MSM developed cancer. KM probability of cancer 3 years post ablation was 1.97% (95% CI: 0.73–5.2%). Of 81 MSM (16% HIV-) with perianal HSIL, only 1 HIV-negative patient recurred 8 months post treatment. For HIV-positive patients Kaplan-Meier probability of perianal HSIL recurrence at 1, 3 and 5 years was 38% [95% CI: 26–50%], 59% [95% CI: 47–72%], and 68% [95% CI: 55–81%] post first ablation with no difference for subsequent treatments. Of 231 HIV- MSM treated for anal condyloma, 207 achieved primary clearance but 28% recurred at a median of 12 months. We will also present preliminary safety data on the 24 patients treated with hemicircumferential intra anal RFA and 10 patients treated with circumferential RFA. **Conclusions:** Targeted ablation of AIN seems effective at preventing cancer but HSIL recurrence is high. Circumferential ablation is fairly well tolerated and might decrease recurrence. New methods of treatment might have lower recurrence.

10. Causative human papillomavirus genotypes in anal squamous cell carcinoma: HIV-positive versus HIV-negative patients

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Abstract. Background: Human papilloma virus (HPV) DNA is detected in 84–96% of anal cancers. Earlier studies suggested that in HIV-positive patients frequently HPV types other than HPV-16 and/or multiple HPV genotypes are found. We compared HPV genotype distribution of anal cancers between HIV-positive and HIV-negative patients, using laser capture microdissection (LCM) in addition to whole-tissue section (WTS) typing. **Methods:** Stored biopsies of anal cancer were retrieved from 10 HIV-negative males and females, and 20 HIV-positive males. HPV genotyping was performed using the SPF10-LiPA25 system. In case the WTS PCR contained multiple HPV genotypes, invasive growth regions were sampled by LCM to establish the causative HPV type. **Results:** HPV DNA was detected in 90% of anal cancers (9/10 HIV-negative, 18/20 HIV-positive). In HIV-negative patients the WTS showed single HPV-16 infections in 78% (7/9). 2 lesions (22%) showed multiple HPV genotypes (16-83, 16-89). Additional LCM revealed HPV-16 as causative infection. In contrast, in HIV-positive patients only 44% (8/18) showed single HPV-infections: HPV-6 (1/18), HPV-11 (1/18), HPV-16 (5/18), undetermined HPV genotype (1/18). Multiple HPV genotypes (2-7 genotypes/WTS) were detected in the majority of HIV-positive patients (56%, 10/18). LCM indicated a single HPV-infection for each lesion: HPV-16 (6/18), HPV-18 (1/18), HPV-45 (2/18), HPV-51 (1/18). **Conclusions:** 100% of HPV-positive anal cancers in HIV-negative were caused by HPV-16, against 61% in HIV-positive. The majority of anal cancers among HIV-positive patients showed multiple HPV-infections, with LCM always indicating a single causative HPV type. These results confirm the 'one lesion, one virus' concept for anal cancer.

11. Raising awareness about anal cancer clinical trials among PLWHA and health care professionals in Puerto Rico

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Abstract. *Background:* We have implemented coordinated efforts aimed at increasing capacity, infrastructure and community engagement, with the goal of raising awareness among persons living with HIV/AIDS (PLWHA) and health care professionals (HCP) in Puerto Rico (PR) about anal cancer screening and clinical trials (CT). *Methods:* Activities have included the development of printed educational materials on anal cancer and CT targeted to PLWHA. Training activities on HPV and anal cancer for HCP are being executed through seminars and an online short-course. A 6-item pre- and post-test is given to HCP in each intervention to assess change in knowledge. *Results:* Overall, 15 community activities have been completed to disseminate our educational materials. We established collaborations with 8 community-based organizations to share these materials through their web pages and social media. Regarding the face to face intervention, 70% ($n=216$) answered the survey. From these, 74% were interested in collaborating in a CT. An increase in the knowledge test scores on anal cancer was observed after the educational activities. Regarding the online course, 96 HCP have been registered and 23 (24%) have completed all its modules. *Conclusions:* Our multilevel interventions have increased interest among PLWHA as well as significantly increase the knowledge among physicians in anal cancer and CT topics. Due to the creation of the first Anal Neoplasia Clinic (AMC certified) in the island, our previous educational efforts with both PLWHA and HCP set the stage for future recruitment efforts in CTs in PR, which will help define standard of care on the prevention of anal cancer.

12. Towards an anal cancer screening risk stratification algorithm

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Abstract. *Background:* Anal high grade squamous intra-epithelial lesions (HSIL) are highly prevalent among homosexual men and have a lower rate of progression to cancer than the cervical equivalent. There is currently no published proof of effectiveness of anal HSIL treatment, recurrence rates are typically 50% at one year and side effects are common. Targeting treatment towards those at highest risk of progression may be a preferable approach. *Methods:* In the prospective Study of the Prevention of Anal Cancer (SPANC), community recruited homosexual men aged ≥ 35 undergo five visits involving anal cytology, HPV DNA testing and high resolution anoscopy with biopsy. A clinical algorithm was developed which utilised detection and persistence of high risk (HR) HPV types, anal HSIL and lesion size. At study completion, participants were stratified into low, moderate, elevated and highest risk of subsequent anal cancer development. *Results:* 488 participants had been enrolled into the study by December 2014 (median age 49, 29% HIV positive) and 87 had completed 5 study visits. Using the clinical algorithm, 32% of these participants were in the low risk stratum (no HR HPV or HSIL at any visit), 13% moderate, 46% elevated and 9% highest risk (persistent large volume HPV16

and/or HSIL). **Conclusions:** Repeated testing can identify a small subset of homosexual men with persistent anal HSIL and HR HPV. This subset of men is likely to be at greatest risk of progression to anal cancer and thus may benefit most from closer monitoring and potential treatment of their HSIL.

13. Results from a screening pilot for anal HSIL in women with a history of cervical, vaginal and vulval hpv related disease (WHCVVHD)

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Abstract. Background: Rates of anal cancer are generally higher in women than in men. WHCVVHD have elevated risks of developing anal cancer and we hypothesized that high rates of anal HSIL would be found in these women. **Methods:** WHCVVHD attending a colposcopy clinic completed a brief survey. An anal swab was taken for ThinPrep (Hologic) cytology and HPV testing using MagNA pure 96 system (Roche), followed by HPV linear array (Roche). **Results:** Of 102 women approached, 75 (74%) consented. All had a history of cytopredicted cervical HSIL. Mean age 34.1 years (range 18–76). 29 (40%) of 73 disclosed a lifetime history of anal intercourse. Two (2.8%) were HIV positive. 15 (20%) cervical Paps were HSIL or ASC-H at time of anal sampling. 43 (57.3%) anal swabs were cytologically negative and 5 (6.7%) non-negative (3 ASC-US, 1 LSIL and 1 ASC-H). The rest, 27 (36%), were technically unsatisfactory. Any High Risk (HR) HPV was found in 13 (17.3%) anal and 26 (34.6%) cervical swabs. HPV16 was found in 6 (8%) anal and 10 (13.3%) cervical swabs. Concurrent HR HPV infections were found in 8 (10.6%) sample pairs. Anal HR HPV DNA was found in 6 cases where cervical Paps were negative. **Conclusions:** Anal cytological abnormalities were uncommon and technically unsatisfactory anal Pap tests frequent among WHCVVHD. Anal HR HPV detection was found more commonly than cytological abnormalities, frequently with shared genotypes between the two sites. Future screening programs in WHCVVHD may have additional challenges to those developed for homosexual men.

14. Anal superficially invasive squamous cell carcinoma (SISCCA) treatments and outcomes

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Abstract. Background: Human papillomavirus (HPV) causes high-grade dysplasia (HSIL), the anal cancer (AC) precursor. SISCCA is defined as ≤ 3 mm depth of invasion and ≤ 7 mm horizontal spread. AC with concomitant HSIL is often treated with chemotherapy and radiation (CRT). **Methods:** A retrospective chart review was performed of patients with histology diagnosis of “minimally invasive” AC between 2004 and 2014. All specimens were reviewed to confirm SISCCA. Charts were analyzed for treatment and response. Patients with invasion close to SISCCA (1–5 mm invasion but 7–10 mm lateral spread) were also included. **Results:** Of 96 minimally invasive AC's identified 25 had SISCCA and close to SISCCA. 19 were HIV+ MSM; median age 57 years. Initial biopsy yielded HSIL in 40% but suspicion led to excision and AC diagnosis. Treatment was excision in 13 and CRT in 12. None treated with excision had AC recurrence. Two treated with CRT recurred at 1.5 and 1.74 years. Kaplan-Meier (KM) curves predict HSIL recurrence at 2 years of 80.0% and 30.7% in those treated with excision and CRT, respectively; $P=0.003$. Two patients, both treated with CRT, died of non-AC causes at 2.2 and 1.7 years. KM curves predict no difference in cancer recurrence between excision versus CRT; $P=0.229$. Of 6 patients with lesion size slightly >SISCCA, 2 were treated with excision and 4 with CRT; all without AC recurrence. **Conclusions:** Superficially invasive AC must be fully excised to ensure it meets the definition of SISCCA as most will not. SISCCA at first is often diagnosed as HSIL and excision confirms the diagnosis. Although the numbers are small, SISCCA might be amenable to local excision. Excision did not increase risk of AC recurrence but increased risk of HSIL recurrence.

15. Acceptability of anal cancer screening in women living with HIV: results from the EVVA study

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Abstract. *Background:* Routine anal cancer screening in women living with HIV (WLHIV) could potentially prevent invasive cancer in this population. However, acceptability of screening tools is necessary for screening program success and has never been verified in WLHIV. *Methods:* EVVA (Evaluation of HPV, HIV, and AIN in women) is a cohort study of 150 WLHIV in Montreal (Canada), involving biannual cervical/anal HPV testing and cervical/anal cytology over 2 years. A systematic HRA is performed at baseline and 2 years, and an acceptability questionnaire is completed at 2 years or withdrawal. *Results:* Of 150 women enrolled, 59 had completed the acceptability questionnaire at time of analysis. Of those, 78% (46/59) considered routine anal cancer screening in WLHIV an absolute necessity (95% CI: 65-88%). Pain during anal cytology and digital rectal exam (DRE) was similar to cervical cytology (median grade: 1/10). HRA was considered more painful by 83% (49/59) of participants (median grade: 6/10). Yearly cervical cytology was considered very acceptable by 85% (50/59). Anal cytology was considered very acceptable yearly by 77% (44/59), and every 2–5 years by 93% (54/59). DRE was considered very acceptable yearly by 80% (45/59) and every 2 years by 93% (53/59). HRA was considered very acceptable every 2 years by 75% (43/59) and every 5 years by 90% (52/59). Pain was the main reason for low acceptability responses. Psychological effects were mentioned. *Conclusions:* Most participating WLHIV considered screening necessary and very acceptable. Pain management can be improved and potential adverse psychological effects of screening should be explored.

16. Towards the development of robust quality assurance (QA) metrics for high resolution anoscopy (HRA)

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Abstract. *Background:* QA is critical in delivery of high quality clinical services and scientific studies. It is important in HRA, being a new and technically demanding procedure, with no widely recognised QA metrics. We developed and evaluated a number of QA metrics within the Study of the Prevention of Anal Cancer, a longitudinal study of the natural history of anal human papillomavirus infection and anal cellular abnormalities in community-recruited HIV positive and negative homosexual men. *Methods:* By December 2014, over 480 participants had been enrolled and 1400 HRAs performed. QA data measured: 1) technical expertise and 2) patient experience. Based on similar approaches in cervical colposcopy, we selected a variety of metrics to establish baseline standards and to track performance of anoscopists.

Results:

QA Metric	Overall ^A	P-value ^B
1. Unsatisfactory anal cytology on first attempt	9.2%	0.114
2. Anoscope insertion time	12.6 mins	<0.001
3. Proportion of HRAs reported as visually “normal”	25.4%	<0.001
4. Number of biopsies per HRA	1.85	<0.001
5. Proportion of cytology HSIL when HRA reported as normal	2.7%	0.040
6. Proportion of participants reporting pain ^C from cytology swab	8.9%	0.004
7. Proportion of participants reporting pain ^C from HRA	14.2%	0.021
8. Proportion of participants reporting bleeding ^D from HRA	4.8%	0.056

^AOverall mean or proportion.

^BP-value is for heterogeneity among anoscopists.

^CPain scores of “Quite a lot” and “Very much” were included, but not “Not at all”, “A little”, “A fair bit” or “Did not have”.

^DBleeding scores of “A lot” included but not “Not at all”, “Just a little” and “Some blood”.

Conclusions: These metrics are used to measure individual anoscopist’s performance and provide feedback. They established group standards and are essential in monitoring changes following interventions such as the introduction of new anal cytology collection techniques.

17. Effects of HRA-triage bias on estimates of AIN progression and regression rates in a 3-state Markov model

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Abstract. Background: The study aim is to compare AIN progression and regression rates in a cytology inception cohort to estimates based on the sub-cohort referred for ≥ 1 HRAs. **Methods:** A cytology-based retrospective cohort was assembled including the anal cytology histories and invasive anal cancer (IAC) outcomes of all HIV-infected adults under care between 2001 and 2012. A 3-state Markov model (<HSIL \leftrightarrow HSIL \rightarrow IAC) was estimated separately for all patients and for the sub-cohort undergoing ≥ 1 HRAs with biopsy. Cytology was adjusted for misclassification. State transition rates (per person-year) and covariate hazard ratios were estimated using the R package *msm*. **Results:** Of 2804 eligible patients in the inception cohort, 629 (22%) were in the HRA sub-cohort and 2175 (78%) in the non-HRA sub-cohort. Patients in the HRA sub-cohort were more likely to have baseline CD4<350, viral load >400, and to have HSIL at baseline and thereafter. They also had more anal cytology examinations (median 6 vs. 3) and longer follow-up (median 5.5 vs. 3.6 years). State transition rates were overestimated in the HRA sub-cohort relative to inception cohort, but the degree of discordance varied by transition: for <HSIL to HSIL (0.44 vs. 0.04); for HSIL to <HSIL (0.56 vs. 0.17); and for HSIL to IAC (0.014 vs. 0.011). Beneficial covariate effects on the <HSIL to HSIL transition were concordant ($p<0.05$) for time-updated HIV viral load, CD4 count, and antiretroviral therapy. **Conclusions:** The observed effects of HRA-triage bias may be relevant to estimates of AIN state transitions from other cohorts subject to referral bias.

18. High resolution anoscopy is comparable in sensitivity to cervical colposcopy

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Abstract. Background: Optimal methods for determining anal intraepithelial neoplasia remain to be established. **Methods:** A prospective study at RPH Sexual Health Clinic performed high resolution anoscopy (HRA) on 110 males and 9 females with prior anal cytological abnormality. Directly observed cytology provided 123 paired conventional and ThinPrep (TP) cytology samples. Seventy-eight biopsies (63%) were performed. **Results:** The median age was 46 (range 19–75) years and 86% were high-risk HPV positive. Of the males 97% were MSM/BSM and 55% (61/110) were HIV-positive, and 26% had visible anal warts.

Cytology	Unsatisfactory %	Negative %	ASCUS %	HPV effect %	AIN 1 %	AIN 2 or 3%
Conventional	0%	12	33	7	9	40
ThinPrep	4%	15	28	11	11	29

Conventional cytology detected 19 more cases of high-grade intraepithelial neoplasia (IN), and TP detected 5 additional cases of high-grade IN compared to conventional cytology. Assuming histology is the gold standard, the sensitivity of conventional cytology for detection of high-grade IN was 61%; (95%CI 45–75), specificity 63% (95%CI 44–79) $P=0.042$; for TP the sensitivity was 54%; (95%CI 39–69), specificity 84% (95%CI 67–95) $P=0.001$. HRA missed up to 4% of cases of high-grade IN but high-grade disease was detected by cytology in 96% of the biopsy samples. **Conclusions:** Conventional cytology had a higher sensitivity to detect high-grade IN, and TP higher specificity. Detection of high-grade IN is complex and both cytology methods were equivalent. HRA with tissue biopsy should be regarded as the ‘gold standard’ with comparable sensitivity to cervical colposcopy.

19. Observational data base of anal dysplasia in persons living with HIV/AIDS [PLWH] in an HMO

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Abstract. Background: PLWH have increased risk for HPV-related squamous cell cancer of the anus. Screening PLWH for anal dysplasia can reduce morbidity and mortality. Accumulating evidence and clinical experience support screening for and treatment of precancerous lesions. **Methods:** KPNW started an anal dysplasia screening program using anal cytology, HRA w/ bx’s and ablation of bx proven HGAIN as a routine component of the primary care HIV services. The Anal Dysplasia Clinic [ADC] follows and treats members with any abnormal findings. Treatment includes use of intra anal imiquimod, trichloroacetic acid, efudex and infra-red coagulation. When indicated patients are referred to rectal surgery for excision and fulguration. **Results:** 70% of eligible members have been screened for anal dysplasia. 52% of the 2,519 screenings performed were abnormal. There have been 495 referrals since 04/20/2011. To evaluate the success of early detection and treatment, stages of precancerous lesions found in each biopsy are tracked. 1,609 biopsies were examined from 403 patients. There has been an overall decrease in HGAIN in patients that received multiple biopsies. 60% of the 99 patients were successfully treated with IRC and another 14% were treated with intra anal imiquimod. **Conclusions:** Over 350 patients have been identified as having anal abnormalities. Routine anal pap screening is easily performed in an HMO setting utilizing clinic support staff. High grade lesions were present in 67% and correlated with pap smear but not CD4 nadir. Routine anal pap smears in PLWH followed by HRA w/bx and trx HGAIN should be standard of care for PLWH.

20. Prediction of high-grade anal intraepithelial neoplasia using DNA methylation measurements – preliminary data

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Abstract. Background: New and better methods are needed to improve diagnosis of high-grade anal neoplasia, for prevention of anal cancer. **Methods:** A total of 43 normal, 46 low-grade, 54 high-grade and 5 cancer biopsies were utilised for this study. Using annotated H&E samples, areas of interest were dissected and DNA extracted from formalin-fixed specimens. HPV typing was carried out by pyrosequencing a ~150bp fragment of the L1 major capsid protein using GP6+ as a sequencing primer. DNA methylation was measured for human gene EPB41L3 and four HPV targets (HPV16, HPV18, HPV31 and HPV33). A methylation score, S5, composed of a combination of the methylation levels of all the targets was calculated. The classification ability of the S5 score was evaluated by receiver operating characteristics (ROC) and area under the ROC curve (AUC). **Results:** The S5 score was significantly different between the four groups ($P < 0.0001$). The ROC curve comparing <AIN2 to AIN2+ cases (excluding cancers) had an AUC of 0.7871 (95% CI 0.7081 to 0.8662) with a P -value of < 0.0001 . For 90% sensitivity, the specificity was 38%. The majority of normal biopsies (86%) were not infected by any HPV type. With low-grade AIN, 48% of the biopsy samples contained high-risk HPV types, while 33% contained low-risk HPV types. With high-grade AIN, 84% of the samples contained high-risk HPV types and 8% had low-risk HPV types only. **Conclusions:** DNA methylation shows promise as a biomarker in the detection of high-grade anal neoplasia.

21. Anal Aptima testing alone and with anal cytology for detection of anal high-grade squamous intraepithelial lesions

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Abstract. Background: Better methods are needed to identify patients at the highest risk of HSIL to maximize efficiency of referral for high resolution anoscopy. This study was designed to determine if Aptima HPV testing improves identification of patients at risk of biopsy-proven anal HSIL when cytology shows ASC-US or LSIL, and to compare Aptima with HPV L1 DNA PCR. **Methods:** 656 HIV-positive and 287 HIV-negative patients attending the UCSF Anal Neoplasia Clinic had an anal swab for Thinprep anal cytology and HPV L1 DNA PCR, a second anal swab into Thinprep media for Aptima HPV testing, and high resolution anoscopy with biopsy. Aptima-positive specimens were reflex-tested with Aptima HPV16 and 18/45. **Results:** 309 (33%) patients were diagnosed with HSIL. 425 (45%) patients were Aptima-positive, including 131 (14%) for HPV16 and 73 (8%) for HPV18/45. There was excellent agreement between Aptima and L1 PCR for HPV 16 ($\kappa = 0.80$ (0.74, 0.86) and 18/45 ($\kappa = 0.82$ (0.74, 0.90)). Absolute risk of biopsy-proven HSIL among patients with ASC-US or LSIL on cytology was 17.5% and was 1.6 fold higher (95%CI 1.4–1.9) if they were Aptima HPV-positive and 2.4-fold higher (95% CI 1.8–3.2) if they were Aptima HPV16-positive, compared with ASC-US or LSIL on cytology alone. The absolute risk of HSIL among Aptima HPV16-positive patients with ASC-US/LSIL on cytology was also 2.9-fold (95%CI 2.0–4.3) higher than among Aptima HPV16-negative patients (41.8% versus 14.5%). **Conclusions:** Aptima works well in anal Thinprep specimens. Addition of Aptima testing to ASC-US/LSIL cytology specimens improves identification of patients with HSIL.

22. Changes in incidence of anal intraepithelial neoplasia III (AINIII) and invasive anal cancer in San Francisco vs. Los Angeles counties, 1998–2012

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Abstract. Background: Increasing incidence of AINIII can serve as a marker for locations where anal cancer screening and treatment programs have been established. This study compared counties in California with high vs. low AINIII incidence rates to determine if increased detection of AINIII correlated with decreasing incidence of anal squamous cell cancer (SCCA). **Methods:** SCCA incidence rates were obtained from the California Cancer Registry for the diagnosis years 1998-2012. California HIV/AIDS registry data was used to determine the prevalence of HIV+ Men who have Sex with Men (MSM). **Results:** San Francisco County (SF) had the highest incidence rates of AINIII and the highest prevalence of MSM HIV/AIDS. Los Angeles County (LA) had the second highest prevalence of MSM HIV/AIDS in CA but a much lower incidence of AINIII. After 2001 the incidence of AIN III in males increased from 2.8 to 27.0 in SF vs. from 0.3 to 1.7 in LA (per 100 000pt*yr). In SF after 2001 the rate of increase of incidence of localized and advanced SCCA decreased (localized from 0.17 to -0.02, advanced from 0.12 to 0.022 cases/ptyr²). In LA the incidence rate of localized and advanced SCCA continued to increase after 2001 (localized from 0.014 to 0.017, advanced from 0.011 to 0.024 cases/ptyr²) **Conclusions:** In SF the rate of increase in incidence of SCCA slowed beginning in 2001, coincident with increasing incidence of AINIII. In LA where a much smaller increase in AINIII detection occurred, no slowing in the rate of increase of incidence of SCCA was seen.

23. A phase 1/2 evaluation of ADXS11-001 *Lm*-LLO immunotherapy, mitomycin, 5-fluorouracil (5-FU) and IMRT for anal cancer

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This study was financially supported by Advaxis Inc. and the Farrah Fawcett Foundation.

Abstract. Background: Human papillomavirus (HPV) DNA is present in the majority of anal cancer. ADXS11-001 *Lm*-LLO immunotherapy is a live attenuated *Listeria monocytogenes* (*Lm*) bioengineered to secrete a HPV-16-E7 fusion protein targeting HPV transformed cells. The *Lm* vector is phagocytosed by antigen presenting cells where it cross presents, stimulating MHC class 1 and 2 pathways resulting in specific T-cell immunity to tumors. We performed this study to determine the feasibility of administering ADXS11-001 with standard chemoradiation (CRT) and its impact on progression free survival (PFS) in the treatment of locally advanced anal cancer. **Methods:** A Phase 2 study for patients with anal squamous cell cancer, any TN1-2 or T2 (>4 cm) any N by endoscopic exam or MRI, without evidence of metastases. Patients received standard 54 Gy IMRT with 2 cycles of mitomycin and 5-FU. ADXS11-001, 1x10⁹ colony forming units IV, was given x 1 dose before CRT then x 3 additional monthly doses after CRT. **Results:** The study enrolled the first patient in April 2013. Thus far we have enrolled and treated 10 patients (median age 60.5 years, range 37–71) including 6 patients with pelvic adenopathy. Grade 3 toxicities related to ADXS11-001: 1 patient with back pain and chills/rigors, 1 patient with chills/rigors, and 1 patient with hypokalemia. All toxicities were within 24 h of dosing. The first seven patients who completed treatment have no evidence of progression. **Conclusions:** This preliminary data demonstrates tolerability of ADXS11-001 when administered with standard chemoRT. Preliminary efficacy appears promising in locally advanced anal cancer.

24. Psychological effects of anal screening programme using qualitative methods: To explore the perceptions and experiences of patients and clinicians in anal cytology screening and High Resolution Anoscopy

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Abstract. Background: The British HIV association produced guidelines in the United Kingdom in 2008 on sexual and reproductive health of people living with HIV infection to advice on anal cancer in HIV infection. They advocated that all major centres should develop local guidelines for anal screening (BHIVA, 2008). This study is designed to produce evidence which could help inform a number of criteria as identified in the UK National Screening Committee (UK NSC) in particular research will help inform criterion 15 (UKNSC 2012: 12). The overall aim of this study was to draw from clinical expertise, and patients' perceptions and experiences to help inform clinical practice for anal screening in sexual health clinics in the UK to include tests and diagnostic procedures only and not treatment. There is limited research conducted on the psychological impact of anal screening. **Methods:** A qualitative study was conducted where clinicians from sexual health clinics in the UK undertaking anal cytology screening and high resolution anoscopy, and patients living with HIV who have undergone anal cytology and high resolution anoscopy from the researchers employing NHS Trust were recruited. **Results:** Preliminary findings indicate that patients and clinicians identified that cancer is a worry; the actual procedure is uncomfortable; associated with pain, is acceptable but tolerability was variable. Information available on AIN or anal screening is very limited in the UK and that there are associated psychological effects like anxiety, fear, and embarrassment. **Conclusions:** Lessons from this study should advise the UKNSC on the psychological impact of future screening

25. Anal dysplasia in a mixed cohort of HIV positive patients in London

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Abstract. Background: Cytological surveillance offered to all patients attending an HIV outpatient clinic. **Methods:** Standard LBC repeated annually. Those with Low grade abnormality or higher were offered High Resolution Anoscopy. **Results:** The clinic cohort as of December 2014 comprises 145 MSM, 159 heterosexual men, 234 women. Uptake of cytology was 98.5% in MSM, 52% in Heterosexual men and 50% in women. The most abnormal cytology on repeat testing was mild dyskaryosis 21% in MSM, 4% in Heterosexual males and 2% in females. Moderate/severe dyskaryosis was found in 7%, 1% and 1% respectively. HRA was performed in 41 MSM, 3 men and 3 Women. The most abnormal histology in MSM was AIN 1 in 23% and AIN 2/3 in 14%. 21% of MSM had anal warts at initial screening. Of this group cytological findings were: mild dyskaryosis in 9%, and moderate/severe dyskaryosis in 9%. For those without anal warts the findings were 16% and 4% respectively. No heterosexual man had anal warts. **Conclusions:** We found only low rates of AIN in HIV positive women and heterosexual men, in contrast to previous reports from France.

26. Anal papillary immature metaplasia – the LSIL which mimics HSIL

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Abstract. Background: Papillary immature metaplasia (PIM) has been well-described in the cervix, as a form of low-grade intraepithelial lesion (LSIL), which can cause diagnostic confusion with high-grade intraepithelial lesion (HSIL), both cytologically and histologically. However, PIM has not previously been specifically described in the anal canal. **Methods:** In the Study of the Prevention of Anal Cancer (SPANAC), a natural history study of human papillomavirus (HPV) infection and related lesions of the anal canal in homosexual men, we identified examples of PIM in high-resolution anoscopy-guided biopsies. Clinical, morphological and molecular features are described. **Results:** Of 482 men recruited to end 2014, 11 examples of PIM were identified in biopsies from 9 men (4 HIV positive), aged 40–61 years. Each PIM lesion had characteristic histological features of slender papillae covered by a multilayer of immature squamous cells. Variable degrees of nuclear atypia were present and the differential diagnosis included HSIL in 4 cases. Immunostaining for p16 was negative in each PIM lesion, thus excluding HSIL. In each biopsy, there was adjacent or admixed typical exophytic LSIL. Histologic HSIL was found in the same octant of the anal canal in 1 case and in a different octant in 5. HPV typing on 9 tissue samples following laser capture microdissection revealed the PIM-associated genotype to be HPV 6 in 5 cases and HPV 11 in 4. **Conclusions:** Like its cervical counterpart, anal PIM is a form of LSIL, associated with low-risk HPV types. Increased awareness of this entity may prevent misdiagnosis as HSIL.

27. Nationwide assessment of HPV types in cancers, including anal cancer, in the U.S: implications for current HPV 16/18 and new 9-valent vaccines

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Abstract. Background: This study sought to determine the pre-vaccine type-specific prevalence of human papillomavirus (HPV)-associated cancers in the United States (US) to evaluate the potential impact of the HPV types in the current and the candidate 9-valent HPV vaccines. **Methods:** The Centers for Disease Control and Prevention partnered with seven US population-based cancer registries to obtain archival tissue for cancers diagnosed from 1993-2005. HPV testing was performed on 2,670 cases that were fairly representative of all participating cancer registry cases by age and gender. Demographic and clinical data were evaluated by anatomic site and HPV status. Current US cancer registry data and the detection of HPV types were used to estimate the number of cancers potentially preventable through vaccination. **Results:** HPV DNA was detected in 91% of cervical, 91% of anal, 75% of vaginal, 70% of oropharyngeal, 69% of vulvar, 63% of penile, 32% of oral cavity, and 21% of laryngeal cancers. A vaccine targeting HPV 16/18 potentially prevents the majority of invasive cervical (66%), anal (79%), oropharyngeal (60%), and vaginal (55%) cancers, as well as many penile (48%), vulvar (49%) cancers: 24,800 cases annually. A candidate 9-valent vaccine also targeting HPV 31/33/45/52/58 may prevent an additional 4%-18% of cancers: 4,000 cases annually. For most cancers, younger age at diagnosis was associated with higher HPV16/18 prevalence. With the exception of oropharyngeal cancers, HPV 16/18 prevalence was similar across racial/ethnic groups **Conclusions:** In the US, current vaccines will reduce most HPV-associated cancers; a smaller but significant additional reduction would be contributed by the new 9-valent vaccine.

28. Topical Cidofovir to treat high-grade anal intraepithelial neoplasia in HIV infected patients (CIDAN12-GESIDA 7412 Study)

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Abstract. Background: Anal intraepithelial neoplasia (AIN) incidence is increased in HIV-infected patients specially in men who have sex with men. There have been few prospective trials evaluating new therapeutic options for AIN. **Methods:** Pilot clinical trial to estimate the efficacy of topical cidofovir in the treatment of high-grade AIN, confirmed with high resolution anoscopy (HRA) and

biopsy in 15 HIV-infected men who have sex with men. Patients received intranal cidofovir 1% cream 3 nights per week during 4 weeks. A new HRA with biopsy was performed in all patients after completion of treatment at 8 and 20 weeks. Complete response (CR) was defined as clinical and histological remission, and partial response (PR) as the evolution to low-grade AIN or the reduction of at least 50% of the area of AIN. The primary endpoint of the study was CR at 8 weeks post treatment. **Results:** Baseline characteristics: median (IQR) age 36 years (28.75–43.25), median (IQR) CD4+ count 508.5 cells/mm³ (358–629.75) and viral load <50 copies/ml in 93.75%. At 8 weeks, 10/15 patients (66%) achieved CR. At 20 weeks 7 of the 10 (70%) patient remained in CR, but 20% had a recurrence. 3 patients with high-grade AIN at 8 weeks improved at week 20 (1 low-grade AIN (PR) and 2 CR). A reduction in the number of HPV-viral genotypes was observed, from 5.2 to 2.73 at 8 weeks ($P=0.002$). No systemic adverse effects were observed. 81.25% had local adverse effects (pruritus, burning, pain), but no patient withdrew from the study. **Conclusions:** Topical cidofovir 1% could be a therapeutic alternative in HIV-infected patients with high-grade AIN.

29. Perineal hygiene behaviors and other predictors of anal neoplasia in women with a history of HPV-mediated gynecological neoplasia: results of the Tasmanian Women's Anal and Gynecological Neoplasia Study

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Abstract. Background: Almost two-thirds of anal cancers occur in HIV-negative women. We sought to evaluate behavioral and clinical predictors of abnormal anal cytology in those with previously treated HPV-mediated gynecological neoplasia under follow-up at the Royal Hobart Hospital, Tasmania, Australia. **Methods:** Eligible women were invited for anal cytology and a questionnaire comprising clinical and behavioral variables. Liquid-based cytology was conducted by the Royal Hobart Hospital Pathology Department. Potential predictors were evaluated by log-binomial and multinomial logistic regression. **Results:** Of 124 participants 63.7% had normal cytology; 9.7% had possible LSIL, 1.6% LSIL, 15.3% possible HSIL, and 9.7% HSIL. No-one had invasive cancer. Potent predictors of abnormal cytology were self-reported front-to-back (FTB) wiping after urination, defecation, or both. Post-defecation FTB wiping remained robust to mutual adjustment (aRR: 2.34; 95% CI: 0.99, 5.55; $P=0.05$). Wiping back-to-front (BTF) or each site separately showed no association. Other predictors were inflammatory bowel disease, current tobacco smoking, and childhood parental smoking. Strong but non-significant positive associations were previous pregnancy, tobacco-smoking partners, and regular wood-smoke exposure. Such associations concur with the literature, further validating the dataset. **Conclusions:** We show for the first time that FTB perineal wiping is a risk factor for anal neoplasia in women. A likely explanation is auto-inoculation of genital HPV into the peri-anus and anal canal. The particularly robust association for post-defecation FTB wiping may be explained by micro-abrasions from bowel movements facilitating HPV access to basal epithelium. Our results warrant further biological explanation and possible recommendation of specific perineal hygiene methods for women.

30. Low- or high-risk human papilloma virus genotype infections in intra-anal condylomatous lesions containing areas of anal intraepithelial neoplasia in HIV+ men-who-have-sex-with-men

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Abstract. Background: Most intra-anal condylomata are presumed non-dysplastic or low-grade AIN (LGAIN), caused by low-risk HPV genotypes. We earlier demonstrated that up to 20% of condylomata contain regions of high-grade AIN (HGAIN). We hypothesized these HGAIN regions are caused by high-risk HPV genotypes. **Methods:** 42 condylomatous papules from 42 HIV+ MSM were graded as non-dysplastic ($n=8$), LGAIN ($n=21$) or HGAIN ($n=13$). Whole tissue sections (WTS) were analyzed by SPF10 PCR/LiPA25 HPV genotyping system. In case of multiple HPV types, regions were selected by a pathologist and isolated by laser capture microdissection (LCM) for HPV genotyping. **Results:** 38/42 (91%) WTS tested positive for HPV. Of the HPV positive WTS, 23/38 (61%) contained a single HPV type and 15/38 (39%) contained multiple HPV types. In the latter, 77 regions

were isolated by LCM, of which 34 (44%) showed a single HPV type and 43 no HPV. Added up, 36/38 (95%) WTS showed a single HPV type in each lesional component studied. Low-risk (6,11) were presumed causative in 8/13 (62%) of HGAIN WTS, high-risk (16,33,52,58) HPV types were causative in 6/13 (46%) HGAIN WTS. One WTS contained 2 high-grade lesions caused by different hrHPV types. For LGAIN WTS, these rates were 15/21 (71%) versus 3/21 (14%). **Conclusions:** Individual dysplastic regions in condylomata are caused by single HPV genotypes. Low-risk HPV genotypes are presumed causative for most LGAIN and HGAIN regions. High-risk HPV genotypes are responsible for a minority of LGAIN lesions, but for a substantial proportion of HGAIN lesions.

31. Health-related quality of life and sexual functioning of HIV-positive men who have sex with men who are treated for anal intraepithelial neoplasia

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Abstract. Background: Screening for anal intraepithelial neoplasia (AIN) may have a negative impact on quality of life. Studies describing the negative effects of treatment of AIN on health-related quality of life (HRQL) and sexual functioning (SF) are limited. We evaluated the impact of three treatment options for AIN on HRQL and SF in HIV-positive men-who-have-sex-with-men (MSM). **Methods:** Patients enrolled in the Treatment of Anal Intraepithelial Neoplasia (TRAIN) trial, which compared electrocautery, topical fluorouracil and imiquimod for the treatment of AIN, were studied. HRQL and SF were assessed before, during and four weeks after treatment. HRQL was assessed using the EQ5D, SF was assessed using items derived from the international index of erectile function (IIEF) and the female sexual function index (FSFI) adapted for anal intercourse. **Results:** 131/148 patients (89%) completed at least one questionnaire. Patients in the imiquimod group were more likely to report pain/discomfort at week 8 than patients in the electrocautery group. Patients in the electrocautery group were more likely to report anxiety/depression and were less satisfied with their overall sex life at week 16 than patients in the imiquimod- and fluorouracil groups. Patients in the electrocautery group were more likely to report pain/discomfort and problems with usual activities at week 20 than patients in the fluorouracil group. **Conclusions:** All treatment options had a negative impact on certain aspects of HRQL. Electrocautery had significantly more negative effects on HRQL than imiquimod and fluorouracil and also had a negative effect on sexual functioning.

32. The role of epidermal growth factor receptor over-expression in HPV-associated anal cell transformation

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Abstract. Background: Infection with high-risk human papillomaviruses can lead to the over-expression of the epidermal growth factor receptor (EGFR) and its active phosphorylated form (EGFR-P). Over-expression of EGFR/EGFR-P in some HPV-positive tumors correlates with a poor prognosis. While EGFR expression may increase with AIN lesion grade, less is known about the role of EGFR over-expression in anal cancer progression and invasion. **Methods:** We previously established an invasive HPV-16 positive cell line (AKC2) after transfecting the HPV-16 genome into normal HPV-negative primary anal cells (AK). We measured relative EGFR/EGFR-P expression levels in AK and AKC2 cultures by western blot, following stimulation with 10 ng/mL of EGF. We measured the EGF-R/EGFR-P expression and invasion levels of AKC2 cultures treated with 2 μ M of the EGFR tyrosine kinase inhibitor Iressa. In addition we investigated EGFR/EGFR-P expression levels in AKC2 cultures treated with 10 μ g/mL cidofovir, which we previously found to be effective in inhibiting AKC2 invasion. **Results:** We detected over a 10-fold increase in EGFR/EGFR-P expression in AKC2 cultures relative to AK parental cultures. We found that both Iressa and cidofovir could inhibit phosphorylation of EGFR in AKC2 cells by up to 20-fold and 2-fold respectively, relative to non-treated cultures. In addition we found that Iressa could inhibit AKC2 invasion down to basal levels. **Conclusions:** EGFR over-expression likely plays a key role in anal cell transformation and invasion and EGFR tyrosine kinase inhibitors should be considered for the treatment of anal cancers. Cidofovir could potentially serve as an alternative EGFR-P inhibitor and warrants further study.

33. Anal dysplasia screening and treatment in a southern HIV clinic: a descriptive analysis

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Abstract. **Background:** Human papilloma virus (HPV) in HIV-positive men-who-have-sex-with-men (MSM) has been associated with high-grade squamous intraepithelial lesions (HSIL) and rates of anal cancer exceeding that of cervical cancer in women prior to Papanicolaou screening. Few descriptive studies exploring the prevalence and predictors of abnormal anal pap smears (APS) and HSIL exist from populations in the southern United States. **Methods:** A retrospective chart review was performed on 356 HIV-positive patients from a NC-based HIV clinic who were 18 years or older and had received at least one APS. Demographic and clinical variables of interest were collected. Descriptive statistics were used for analysis. **Results:** 209 (60.1%) men were African American, and 116 (33.3%) were Caucasian with a median age of 42 (18-75). After the first APS, 28.1% (71/253) of patients did not have follow up anoscopy. Comparing patients with biopsy proven (BP) HSIL versus low-grade dysplasia (LSIL), patients were more likely to have LSIL if they were on ART ($P=0.02$) and had a higher CD4 count ($P=0.01$). Treatment success (TS) for both topical and infrared coagulation therapy (IRC) was 36.7% (18/49), 30.8% (4/13) for topical alone, and 38.9% (14/36) for IRC alone. **Conclusions:** Patients with a higher CD4 count and on ART were less likely to have anal HSIL. Smoking status, CD4 nadir, number of sexual partners, and race/ethnicity were not statistically associated with HSIL. Current treatment options in this population are imperfect at best, and further research is needed to refine screening and treatment of anal cancer.