Cancer and HIV/AIDS Research Literatures

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Abstract: Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. This article introduces recent research reports as references in the cancer and HIV/AIDS related studies.
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1. Introduction

Cancer is the general name for a group of more than 100 diseases. Although there are many kinds of cancer, all cancers start because abnormal cells grow out of control. Untreated cancers can cause serious illness and death. The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

The following introduces recent reports as references in the related studies.

Adamson, P. C., M. J. Huchko, et al. "Acceptability and Accuracy of Cervical Cancer Screening Using a Self-Collected Tampon for HPV Messenger-RNA Testing among HIV-Infected Women in South Africa." PLoS One. 2015 Sep 2;10(9):e0137299. doi: 10.1371/journal.pone.0137299. eCollection 2015.

BACKGROUND: HIV increases women's risk for high-risk human papillomavirus (hrHPV) infection and invasive cervical cancer. South Africa has a high HIV prevalence but low cervical cancer screening coverage. Self-collection of cervical specimens and hrHPV testing, including hrHPV messenger-RNA (mRNA) testing, are methods aimed at increasing screening rates. However, data are limited on the acceptability and accuracy of tampon-based self-collection for hrHPV mRNA testing in HIV-infected women. METHODS: We recruited 325 HIV-infected women seeking care at a government HIV clinic in Pretoria, South Africa. A clinician performed a pelvic examination and obtained an endocervical specimen. Study participants performed self-collection using a tampon. Both clinician- and self-collected specimens were tested for hrHPV mRNA. Acceptability of both collection methods was assessed, the prevalence of hrHPV mRNA in our study population was estimated, test positivity of the two collection methods were compared, and test agreement was assessed by calculating the kappa-statistic, sensitivity, and specificity. RESULTS: Over 90% of women reported no difficulties self-collecting specimens and 82% were willing to perform the tampon-collection at home. Based on clinician-collection specimens, the prevalence of hrHPV mRNA in our study population was 36.7% (95% CI: 31.4%-42.0%). There was no difference in test positivity between clinician-collection, 36.7%, and tampon-collection, 43.5% (p-value = 0.08). Using clinician-collection as the reference test, the sensitivity and specificity for hrHPV mRNA of tampon-collection were 77.4% (95% CI: 69.8-85.0%) and 77.8% (95% CI: 71.9-83.6%), respectively. CONCLUSIONS: Tampon-based self-collection is acceptable to women and has similar hrHPV mRNA positivity rates as clinician-collection, but has reduced sensitivity and specificity compared to clinician-collection. The hrHPV mRNA prevalence in our study population is high, but similar to other high-risk populations, and highlights the need for improved cervical cancer screening. Further research into the optimal use of tampon-based collection as a cervical cancer screening tool is warranted.

Akarolo-Anthony, S. N., L. D. Maso, et al. "Cancer burden among HIV-positive persons in Nigeria: preliminary findings from the Nigerian AIDS-cancer match study." Infect Agent Cancer. 2014 Mar 5;9(1):1. doi: 10.1186/1750-9378-9-1.

BACKGROUND: Although Nigeria has a large HIV epidemic, the impact of HIV on cancer in Nigerians is unknown. METHODS: We conducted a

registry linkage study using a probabilistic matching algorithm among a cohort of HIV positive persons registered at health facilities where the Institute of Human Virology Nigeria (IHVN) provides HIV prevention and treatment services. Their data was linked to data from 2009 to 2012 in the Abuja Cancer Registry. Match compatible files with first name, last name, sex, date of birth and unique HIV cohort identification numbers were provided by each registry and used for the linkage analysis. We describe demographic characteristics of the HIV clients and compute Standardized Incidence Ratios (SIRs) to evaluate the association of various cancers with HIV infection. RESULTS: Between 2005 and 2012, 17,826 persons living with HIV (PLWA) were registered at IHVN. Their median age (Interquartile range (IQR)) was 33 (27-40) years; 41% (7246/17826) were men and 59% (10580/17826) were women. From 2009 to 2012, 2,029 clients with invasive cancers were registered at the Abuja Cancer Registry. The median age (IQR) of the cancer clients was 45 (35-68) years. Among PLWA, 39 cancer cases were identified, 69% (27/39) were incident cancers and 31% (12/39) were prevalent cancers. The SIR (95% CI) for the AIDS Defining Cancers were 5.7 (4.1, 7.2) and 2.0 (0.4, 3.5), for Kaposi Sarcoma and Cervical Cancer respectively. CONCLUSION: The risk of Kaposi Sarcoma but not Cervical Cancer or Non-Hodgkin's Lymphoma, was significantly increased among HIV positive persons, compared to the general population in Nigeria.

Althoff, K. N., K. A. McGinnis, et al. "Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults." Clin Infect Dis. 2015 Feb 15;60(4):627-38. doi: 10.1093/cid/ciu869. Epub 2014 Oct 30.

BACKGROUND: Although it has been shown that human immunodeficiency virus (HIV)-infected adults are at greater risk for aging-associated events, it remains unclear as to whether these events happen at similar, or younger ages, in HIV-infected compared with uninfected adults. The objective of this study was to compare the median age at, and risk of, incident diagnosis of 3 age-associated diseases in HIV-infected and demographically similar uninfected adults. METHODS: The study was nested in the clinical prospective Veterans Aging Cohort Study of HIV-infected and demographically matched uninfected veterans, from 1 April 2003 to 31 December 2010. The outcomes were validated diagnoses of myocardial infarction (MI), end-stage renal disease (ESRD), and non-AIDS-defining cancer (NADC). Differences in mean age at, and risk of, diagnosis by HIV status were estimated using multivariate linear regression models and Cox proportional hazards models, respectively. RESULTS: A total of 98 687 (31% HIV-infected and 69% uninfected) adults contributed >450 000 person-years and 689 MI, 1135 ESRD, and 4179 NADC incident diagnoses. Mean age at MI (adjusted mean difference, -0.11; 95% confidence interval [CI], -.59 to .37 years) and NADC (adjusted mean difference, -0.10 [95% CI, -.30 to .10] years) did not differ by HIV status. HIV-infected adults were diagnosed with ESRD at an average age of 5.5 months younger than uninfected adults (adjusted mean difference, -0.46 [95% CI, -.86 to -.07] years). HIV-infected adults had a greater risk of all 3 outcomes compared with uninfected adults after accounting for important confounders. CONCLUSIONS: HIV-infected adults had a higher risk of these age-associated events, but they occurred at similar ages than those without HIV.

Anderson, J., M. Wysong, et al. "Evaluation of Cervical Cancer Screening Programs in Cote d'Ivoire, Guyana, and Tanzania: Effect of HIV Status." PLoS One. 2015 Sep 25;10(9):e0139242. doi: 10.1371/journal.pone.0139242. eCollection 2015.

BACKGROUND: HIV infection increases a woman's risk for cervical cancer, and cervical cancer incidence and mortality rates are higher in countries with high HIV prevalence and limited resources for screening. Visual inspection with acetic acid (VIA) allows screening and treatment of cervical lesions in a single-visit approach (SVA), but data on its performance in HIV-infected women are limited. This study's objective was to examine cervical cancer screening using VIA/SVA in programs serving HIV-infected women. METHODS: A VIA/SVA program with cryotherapy for VIA-positive lesions was implemented in Cote d'Ivoire, Guyana, and Tanzania from 2009 to 2012. The effect of HIV status on VIA positivity and on presence of cryotherapy-eligible lesions was examined using a cross-sectional study design, with Chi-square tests for comparisons and constructed multivariate logistic regression models. A P-value of < 0.05 was significant. FINDINGS: VIA was performed on 34,921 women, 10% (3,580) were VIA positive; 2,508 (85%) eligible women received cryotherapy during the same visit; only 234 (52%) of those who postponed returned for treatment; 622 (17%) VIA-positive women had lesions too large to be treated with cryotherapy and were referred for excisional treatment. In multivariate analysis-controlling for HIV status, location of the screening clinic, facility location, facility type, and country-compared to HIV-uninfected/unknown women, HIV-infected women had higher odds of being VIA positive (OR 1.95, 95% CI 1.76, 2.16, P<0.0001) and of having large lesions requiring referral (OR 1.93, 95% CI 1.49, 2.51, P< 0.0001). Minor treatment complications

occurred in 19 of 3,032 (0.63%) women; none required further intervention. CONCLUSIONS: This study found that compared to HIV-uninfected/unknown women, HIV-infected women had nearly twice the odds of being VIA-positive and to require referral for large lesions. SVA was safe and resulted in significant reductions in loss to follow-up. There is increased need for excisional treatment in countries with high HIV prevalence.

Antoniou, T., N. Jembere, et al. "A population-based study of the extent of colorectal cancer screening in men with HIV." BMC Health Serv Res. 2015 Feb 1;15:51. doi: 10.1186/s12913-015-0711-9.

BACKGROUND: Because of the increased life-expectancy of persons with HIV, the need for age-appropriate colorectal cancer screening among these patients will increase. We examined rates of colorectal cancer screening among HIV-infected men aged 50 to 65 years. METHODS: We used Ontario's administrative databases to identify all men between the ages of 50 and 65 years who were alive on April 1, 2007, and identified HIV-infected men using a validated case-finding algorithm. We excluded men with a history of colorectal cancer, anal cancer, inflammatory bowel disease and any colorectal investigation in the preceding five-years, and used multivariable regression to compare rates of colorectal cancer screening between men with and without HIV during five years of follow-up. RESULTS: We identified 743,801 men between the ages of 50 and 65 years, of whom 1,432 (0.19%) were HIV-infected. The proportions of men with and without HIV who underwent any screening during the 5-year follow up period were 49.1% (95% CI 46.5% to 51.7%) and 41.4% (95% CI 41.3% to 41.5%), respectively. Compared with HIV-negative men, men with HIV had lower rates of fecal occult blood testing [adjusted rate ratio (aRR) 0.74; 95% confidence interval (CI) 0.63 to 0.87] and barium-enema radiography (aRR 0.66; 95% CI 0.39 to 1.12), but higher rates of colonoscopy (aRR 1.24; 95% CI 1.13 to 1.37), flexible sigmoidoscopy (aRR 1.72; 95% CI 1.28 to 2.30) and rigid sigmoidoscopy (aRR 2.98; 95% CI 2.26 to 3.93). CONCLUSION: As with the general population of men aged 50 to 65 years, less than half of the population of men with HIV received colorectal cancer screening. Strategies are required to improve uptake of this intervention.

Badke, G. L., G. B. de Aguiar, et al. "Cerebral Metastasis from Breast Cancer in a Male Patient with HIV." Case Rep Neurol Med. 2015;2015:482839. doi: 10.1155/2015/482839. Epub 2015 Jan 28.

Context. Breast cancer (BC) in men is a rare condition, corresponding to 1% of all neoplasms in this gender. Some studies show that up to 93% of BC cases in men are advanced disease. If its occurrence constitutes an uncommon fact, the appearance of a metastasis to the central nervous system (CNS) is extremely rare. The objective of the present study is to present the case of a male patient, bearer of HIV infection, who presented with BC and later metastasis to the CNS. We also include a brief review of the literature. Case Report. We describe a case of a male patient, 59 years old, with HIV infection and a history of BC treated 4 years earlier, which progressed into headache and vertigo. Neuroimaging exams showed lesions suggestive of cerebral metastasis and a stereotaxic biopsy confirmed BC metastasis. Conclusion. Breast cancer in men with metastasis to the CNS is a rare condition and similar reports were not found in the available databases. It should be pointed out that even though rare, it should be considered among the differential diagnoses for SNC metastases in men, although HIV infection favors the appearance of some types of cancer.

Bansil, P., J. Lim, et al. "Performance of Cervical Cancer Screening Techniques in HIV-Infected Women in Uganda." J Low Genit Tract Dis. 2015 Jul;19(3):215-9. doi: 10.1097/LGT.0000000000000090.

OBJECTIVE: Women infected with human immunodeficiency virus (HIV) have a higher risk of HPV infections and developing cervical cancer, thus screening them is imperative. This study was aimed to evaluate and compare the performance of 3 cervical cancer screening options among HIV-infected women in Uganda. MATERIALS AND METHODS: Data from 2,337 Ugandan women who reported their HIV status were obtained from a population-based cervical cancer screening study. Women were offered 3 screening tests: vaginal and cervical careHPV and visual inspection with acetic acid (VIA), and the results were evaluated by HIV status. RESULTS: The prevalence of HIV infection was 16.5%. Women infected with HIV had a higher prevalence of cervical intraepithelial neoplasia grade 2+ (CIN2+) than uninfected women (12.9% vs 1.7%; $p < .001$). The sensitivity for cervical careHPV among the HIV-infected women was 94.3% compared to 81.3% among the uninfected women. Whereas the sensitivity for vaginal careHPV was also higher among the HIV-infected women, the sensitivity of VIA was higher among the uninfected women. The mean vaginal and cervical careHPV signal strength was higher in the HIV-infected women than in the uninfected women ($p < .001$). CONCLUSIONS: CareHPV is very sensitive for detecting CIN2+ in HIV-infected women, even using a vaginal sample. The sensitivity of careHPV in HIV-infected women is higher than in HIV-uninfected

women. However, additional research is needed to determine the best option for screening and triage of HPV-positive women that can be implemented in low-resource settings, especially among HIV- and HPV-positive women.

Barnes, E., C. Saxon, et al. "Cancer prevalence in a metropolitan HIV clinic." J Int AIDS Soc. 2014 Nov 2;17(4 Suppl 3):19651. doi: 10.7448/IAS.17.4.19651. eCollection 2014.

INTRODUCTION: Morbidity and mortality rates from AIDs defining cancers have fallen significantly since the introduction of highly active antiretroviral therapy (HAART). Patients are now living longer with HIV and are at a greater risk of other HIV- and non-HIV related malignancies. We report what we believe to be the first UK cancer prevalence study in the modern HAART era. METHODS: A retrospective review of electronic clinic letters was performed for all patients currently receiving, and those who had died whilst receiving, their HIV care at our centre. Demographics of patients with pre-cancerous changes, an active or previous cancer were recorded. RESULTS: There were 438 active patients (369 male, 69 female) and 18 deceased patients (12 male, 6 female) in April 2014. Thirty-six out of four hundred fifty-six (8%) cancer diagnoses were found overall. Thirty-one out of four hundred thirty-eight (7%) diagnoses in active patients and 5/18 (28%) in deceased patients. More than half of those diagnosed with cancer were aged 50 or over (17/31 [55%]). In active patients 17/31 (55%) were AIDs defining cancers, with the most common type of cancer diagnosis overall being Kaposi's sarcoma (12/31 [39%]). There were 5/31 (16%) cases of non-Hodgkin's lymphoma. The most common non-AIDs defining cancer was basal cell carcinoma of which there were 5/31 (16%) cases, followed by squamous cell carcinoma (3/31 [10%]) and testicular cancer (3/31 [10%]). Other cancers included colorectal (2/31 [6%]) and prostate cancer (1/31 [3%]). In all five deceased patients, cancer was the cause of death. There were four acute presentations with an aggressive glioma, Burkitt's lymphoma, an undiagnosed primary lung malignancy and a late diagnosed cervical cancer. The fifth patient died following the recurrence of a transitional cell cancer of the bladder after an initial diagnosis of seven years earlier. Eighteen out of sixty-nine (26%) of females were found to have at least mild dyskariosis on cervical screening. Anal intraepithelial neoplasia was diagnosed in 4/438 (1%) of patients. CONCLUSIONS: Non-AIDS defining malignancies account for almost half of the cancers in our cohort. This number may rise further as patients live longer with HIV. Good communication between oncologists and HIV physicians is paramount to manage the complex interactions of HIV and cancer, increase HIV testing in cancer services and address cancer risk factors in existing HIV patients.

Bateman, A. C., K. Katundu, et al. "The burden of cervical pre-cancer and cancer in HIV positive women in Zambia: a modeling study." BMC Cancer. 2015 Jul 24;15:541. doi: 10.1186/s12885-015-1558-5.

BACKGROUND: HIV infection is associated with a higher incidence of precancerous cervical lesions and their progression to invasive cervical cancer (ICC). Zambia is a global epicenter of HIV and ICC, yet the overall burden of cervical pre-cancer [cervical intraepithelial neoplasia 3 (CIN3)] and ICC among its HIV positive adult female population is unknown. The objective of this study was to determine the burden of cervical disease among HIV positive women in Zambia by estimating the number with CIN3 and ICC. METHODS: We conducted a cross-sectional study among 309 HIV positive women attending screening in Lusaka (Zambia's most populated province) to measure the cervical disease burden by visual inspection with acetic acid enhanced by digital cervicography (DC), cytology, and histology. We then used estimates of the prevalence of CIN3 and ICC from the cross-sectional study and Spectrum model-based estimates for HIV infection among Zambian women to estimate the burden of CIN3 and ICC among HIV positive women nationally. RESULTS: Over half (52 %) of the study participants screened positive by DC, while 45 % had cytologic evidence of high grade squamous intraepithelial lesions (SIL) or worse. Histopathologic evaluation revealed that 20 % of women had evidence of CIN2 or worse, 11 % had CIN3 or worse, and 2 % had ICC. Using the Spectrum model, we therefore estimate that 34,051 HIV positive women in Zambia have CIN3 and 7,297 have ICC. CONCLUSIONS: The DC, cytology, and histology results revealed a large cervical disease burden in this previously unscreened HIV positive population. This very large burden indicates that continued scale-up of cervical cancer screening and treatment is urgently needed.

Bertisch, B., S. Franceschi, et al. "Risk factors for anal cancer in persons infected with HIV: a nested case-control study in the Swiss HIV Cohort Study." Am J Epidemiol. 2013 Sep 15;178(6):877-84. doi: 10.1093/aje/kwt153. Epub 2013 Jul 30.

Although persons infected with human immunodeficiency virus (HIV), particularly men who have sex with men, are at excess risk for anal cancer, it has been difficult to disentangle the influences of anal exposure to human papillomavirus (HPV) infection, immunodeficiency, and combined antiretroviral therapy. A case-control study that included 59 anal

cancer cases and 295 individually matched controls was nested in the Swiss HIV Cohort Study (1988-2011). In a subset of 41 cases and 114 controls, HPV antibodies were tested. A majority of anal cancer cases (73%) were men who have sex with men. Current smoking was significantly associated with anal cancer (odds ratio (OR) = 2.59, 95% confidence interval (CI): 1.25, 5.34), as were antibodies against L1 (OR = 4.52, 95% CI: 2.00, 10.20) and E6 (OR = infinity, 95% CI: 4.64, infinity) of HPV16, as well as low CD4+ cell counts, whether measured at nadir (OR per 100-cell/muL decrease = 1.53, 95% CI: 1.18, 2.00) or at cancer diagnosis (OR per 100-cell/muL decrease = 1.24, 95% CI: 1.08, 1.42). However, the influence of CD4+ cell counts appeared to be strongest 6-7 years prior to anal cancer diagnosis (OR for <200 vs. >/=500 cells/muL = 14.0, 95% CI: 3.85, 50.9). Smoking cessation and avoidance of even moderate levels of immunosuppression appear to be important in reducing long-term anal cancer risks.

Borges, A. H., J. D. Lundgren, et al. "Thrombocytopenia is associated with an increased risk of cancer during treated HIV disease." AIDS. 2014 Nov 13;28(17):2565-71. doi: 10.1097/QAD.0000000000000433.

OBJECTIVE: To assess the relationship between platelet counts and risk of AIDS and non-AIDS-defining events. DESIGN: Prospective cohort. METHODS: EuroSIDA patients with at least one platelet count were followed from baseline (first platelet >/= 1 January 2005) until last visit or death. Multivariate Poisson regression was used to assess the relationship between current platelet counts and the incidence of non-AIDS-defining (pancreatitis, end-stage liver/renal disease, cancer, cardiovascular disease) and AIDS-defining events. RESULTS: There were 62 898 person-years of follow-up (PYFU) among 12 279 patients, including 1168 non-AIDS-defining events [crude incidence 18.6/1000 PYFU, 95% confidence interval (CI) 17.5-19.6] and 735 AIDS-defining events (crude incidence 11.7/1000 PYFU, 95% CI 10.8-12.5). Patients with thrombocytopenia (platelet count </=100 x 10/l) had a slightly increased incidence of AIDS-defining events [adjusted incidence rate ratio (aIRR) 1.42, 95% CI 1.07-1.86], when compared to those with platelet counts 101-200 x 10/l, whereas the incidence of non-AIDS-defining events was more than two-fold higher (aIRR 2.66, 95% CI 2.17-3.26). Among non-AIDS-defining events, the adjusted incidence of cancer (aIRR 2.20, 95% CI 1.61-3.01), but not cardiovascular disease (aIRR 0.66, 95% CI 0.32-1.34), was significantly higher in patients with thrombocytopenia. The association between thrombocytopenia and cancer remained unaltered in sensitivity analyses requiring repeated platelet counts to confirm thrombocytopenia and lagging platelets by 1 year prior to clinical events. CONCLUSION: Patients with thrombocytopenia had increased incidence of AIDS-defining and non-AIDS-defining events, but the association with the latter, in particular cancer, was stronger. Future studies should investigate whether the pathophysiological processes underlying thrombocytopenia are associated with the development of cancer during treated HIV disease.

Cachay, E., W. Agmas, et al. "Five-year cumulative incidence of invasive anal cancer among HIV-infected patients according to baseline anal cytology results: an inception cohort analysis." HIV Med. 2015 Mar;16(3):191-5. doi: 10.1111/hiv.12190. Epub 2014 Sep 6.

OBJECTIVES: The aim of the study was to estimate the cumulative incidence of, and rates of progression to, invasive anal cancer (IAC) according to baseline anal cytology screening category in an unselected HIV clinical care cohort in the antiretroviral era. METHODS: A retrospective cohort analysis of HIV-infected patients under care at the University of California at San Diego Owen Clinic was carried out. Patients were eligible for this analysis if they had at least two anal cytohistological results available for longitudinal analysis. Kaplan-Meier analysis was used to estimate the cumulative incidence of IAC over time according to baseline cytology category [less than high-grade intraepithelial lesion (HSIL) versus HSIL]. Cox regression analysis was used to adjust for the following covariates: antiretroviral use, level of HIV viraemia, smoking status and infrared photocoagulation (IRC) ablation therapy. RESULTS: Between 2000 and 2012, we followed 2804 HIV-infected patients for a median of 4 years under a clinic protocol requiring baseline anal cytology screening. Incident IAC was diagnosed in 23 patients. Patients with a baseline HSIL anal cytology had an estimated 5-year probability of progression to IAC of 1.7% and an estimated annual progression risk of 1 in 263. None of the examined covariates was significantly associated with IAC incidence when examined in separate unadjusted Cox models. CONCLUSIONS: HIV-infected patients with a baseline HSIL anal cytology had a 5-year cumulative incidence of IAC of 1.65%, with an upper 95% confidence bound of 4.5%. This population-based study provides quantitative risk estimates that may be used for counselling patients regarding management options for abnormal cytology results.

Castilho, J. L., P. M. Luz, et al. "HIV and cancer: a comparative retrospective study of Brazilian and U.S. clinical cohorts." Infect Agent Cancer. 2015 Feb

2;10:4. doi: 10.1186/1750-9378-10-4. eCollection 2015.

BACKGROUND: With successful antiretroviral therapy, non-communicable diseases, including malignancies, are increasingly contributing to morbidity and mortality among HIV-infected persons. The epidemiology of AIDS-defining cancers (ADCs) and non-AIDS-defining cancers (NADCs) in HIV-infected populations in Brazil has not been well described. It is not known if cancer trends in HIV-infected populations in Brazil are similar to those of other countries where antiretroviral therapy is also widely available. METHODS: We performed a retrospective analysis of clinical cohorts at Instituto Nacional de Infectologia Evandro Chagas (INI) in Rio de Janeiro and Vanderbilt Comprehensive Care Clinic (VCCC) in Nashville from 1998 to 2010. We used Poisson regression and standardized incidence ratios (SIRs) to examine incidence trends. Clinical and demographic predictors of ADCs and NADCs were examined using Cox proportional hazards models. RESULTS: This study included 2,925 patients at INI and 3,927 patients at VCCC. There were 57 ADCs at INI (65% Kaposi sarcoma), 47 at VCCC (40% Kaposi sarcoma), 45 NADCs at INI, and 82 at VCCC. From 1998 to 2004, incidence of ADCs remained statistically unchanged at both sites. From 2005 to 2010, ADC incidence decreased in both cohorts (INI incidence rate ratio per year = 0.74, $p < 0.01$; VCCC = 0.75, $p < 0.01$). Overall Kaposi sarcoma incidence was greater at INI than VCCC (3.0 vs. 1.2 cases per 1,000 person-years, $p < 0.01$). Incidence of NADCs remained constant throughout the study period (overall INI incidence 3.6 per 1,000 person-years and VCCC incidence 5.3 per 1,000 person-years). Compared to general populations, overall risk of NADCs was increased at both sites (INI SIR = 1.4 [95% CI 1.1-1.9] and VCCC SIR = 1.3 [1.0-1.7]). After non-melanoma skin cancers, the most frequent NADCs were anal cancer at INI (n = 7) and lung cancer at VCCC (n = 11). In multivariate models, risk of ADC was associated with male sex and immunosuppression. Risk of NADC was associated with increased age. CONCLUSIONS: In both cohorts, ADCs have decreased over time, though incidence of KS was higher at INI than VCCC. Rates of NADCs remained constant over time at both sites.

Chawki, S., G. Ploussard, et al. "Bladder cancer in HIV-infected adults: an emerging concern?" J Int AIDS Soc. 2014 Nov 2;17(4 Suppl 3):19647. doi: 10.7448/IAS.17.4.19647. eCollection 2014.

INTRODUCTION: As HIV-infected patients get older more non-AIDS-related malignancies are to be seen. Cancer now represents almost one third of all causes of deaths among HIV-infected patients (1). Albeit bladder cancer is one of the most common malignancy worldwide (2), only 13 cases of bladder cancer in HIV-infected patients have been reported in the literature so far (3). MATERIALS AND METHODS: We conducted a monocentric study in our hospital. We selected all patients who were previously admitted (from 1998 to 2013) in our hospital with diagnoses of HIV and bladder cancer. The objective was to assess the prevalence and characteristics of bladder cancers in HIV-infected patients in our hospital. RESULTS: Based on our administrative HIV database (6353 patients), we found 15 patients (0.2%) with a bladder cancer. Patients' characteristics are presented in Table 1. Patients were mostly men and heavy smokers. Their median nadir CD4 cell count was below 200 and most had a diagnosis of AIDS. A median time of 14 years was observed in those patients, between the diagnosis of HIV-infection and the occurrence of bladder cancer, although in patients much younger (median age 56) than those developing bladder cancer without HIV infection (71.1 years) (4). Haematuria was the most frequent diagnosis circumstance in HIV-infected patients who had relatively preserved immune function on highly active antiretroviral therapy (HAART). Histopathology showed relatively advanced cancers at diagnosis with a high percentage of non transitional cell carcinoma (TCC) tumor and of TCC with squamous differentiation, suggesting a potential role for human papilloma virus (HPV) co-infection. Death rate was high in this population. CONCLUSIONS: Bladder cancers in HIV-infected patients remain rare but occur in relatively young HIV-infected patients with a low CD4 nadir, presenting with haematuria, most of them being smokers, and have aggressive pathological features that are associated with severe outcomes.

Coghill, A. E., M. S. Shiels, et al. "Elevated Cancer-Specific Mortality Among HIV-Infected Patients in the United States." J Clin Oncol. 2015 Jul 20;33(21):2376-83. doi: 10.1200/JCO.2014.59.5967. Epub 2015 Jun 15.

PURPOSE: Despite advances in the treatment of HIV, HIV-infected people remain at increased risk for many cancers, and the number of non-AIDS-defining cancers is increasing with the aging of the HIV-infected population. No prior study has comprehensively evaluated the effect of HIV on cancer-specific mortality. PATIENTS AND METHODS: We identified cases of 14 common cancers occurring from 1996 to 2010 in six US states participating in a linkage of cancer and HIV/AIDS registries. We used Cox regression to examine the association between patient HIV status and death resulting from the presenting cancer (ascertained from death certificates), adjusting for age, sex,

race/ethnicity, year of cancer diagnosis, and cancer stage. We included 1,816,461 patients with cancer, 6,459 (0.36%) of whom were HIV infected. RESULTS: Cancer-specific mortality was significantly elevated in HIV-infected compared with HIV-uninfected patients for many cancers: colorectum (adjusted hazard ratio [HR], 1.49; 95% CI, 1.21 to 1.84), pancreas (HR, 1.71; 95% CI, 1.35 to 2.18), larynx (HR, 1.62; 95% CI, 1.06 to 2.47), lung (HR, 1.28; 95% CI, 1.17 to 1.39), melanoma (HR, 1.72; 95% CI, 1.09 to 2.70), breast (HR, 2.61; 95% CI, 2.06 to 3.31), and prostate (HR, 1.57; 95% CI, 1.02 to 2.41). HIV was not associated with increased cancer-specific mortality for anal cancer, Hodgkin lymphoma, or diffuse large B-cell lymphoma. After further adjustment for cancer treatment, HIV remained associated with elevated cancer-specific mortality for common non-AIDS-defining cancers: colorectum (HR, 1.40; 95% CI, 1.09 to 1.80), lung (HR, 1.28; 95% CI, 1.14 to 1.44), melanoma (HR, 1.93; 95% CI, 1.14 to 3.27), and breast (HR, 2.64; 95% CI, 1.86 to 3.73). CONCLUSION: HIV-infected patients with cancer experienced higher cancer-specific mortality than HIV-uninfected patients, independent of cancer stage or receipt of cancer treatment. The elevation in cancer-specific mortality among HIV-infected patients may be attributable to unmeasured stage or treatment differences as well as a direct relationship between immunosuppression and tumor progression.

D'Souza, G., T. E. Carey, et al. "Epidemiology of head and neck squamous cell cancer among HIV-infected patients." J Acquir Immune Defic Syndr. 2014 Apr 15;65(5):603-10. doi: 10.1097/QAI.0000000000000083.

BACKGROUND: HIV-infected individuals have a higher incidence of head and neck cancer (HNC). METHODS: Case series of 94 HIV-infected HNC patients (HIV-HNC) at 6 tertiary care referral centers in the US between 1991 and 2011. Clinical and risk factor data were abstracted from the medical record. Risk factors for survival were analyzed using Cox proportional hazard models. Human papillomavirus (HPV) and p16 testing was performed in 46 tumors. Findings were compared with Surveillance Epidemiology and End Results HNC (US-HNC) data. RESULTS: This study represents the largest HIV-HNC series reported to date. HIV-HNC cases were more likely than US-HNC to be male (91% vs. 68%), younger (median age, 50 vs. 62 years), nonwhite (49% vs. 18%), and current smokers (61% vs. 18%). Median HIV-HNC survival was not appreciably lower than US-HNC survival (63 vs. 61 months). At diagnosis, most cases were currently on highly active antiretroviral therapy (77%) but had detectable HIV viremia (99%), and median CD4 was 300 cells per microliter (interquartile range = 167-500). HPV was detected in 30% of HIV-HNC and 64% of HIV-oropharyngeal cases. Median survival was significantly lower among those with CD4 counts </=200 than >200 cells per microliter at diagnosis (16.1 vs. 72.8 months, P < 0.001). In multivariate analysis, poorer survival was associated with CD4 <100 cells per microliter [adjusted hazard ratio (aHR) = 3.09, 95% confidence interval (CI): 1.15 to 8.30], larynx/hypopharynx site (aHR = 3.54, 95% CI: 1.34 to 9.35), and current tobacco use (aHR = 2.54, 95% CI: 0.96 to 6.76). CONCLUSIONS: Risk factors for the development of HNC in patients with HIV infection are similar to the general population, including both HPV-related and tobacco/alcohol-related HNC.

Duncan, K. C., K. J. Chan, et al. "HAART slows progression to anal cancer in HIV-infected MSM." AIDS. 2015 Jan 28;29(3):305-11. doi: 10.1097/QAD.0000000000000537.

OBJECTIVE: Antiretrovirals do not prevent anal intraepithelial neoplasia. However, the influence of antiretrovirals in the natural history of invasive anal cancer is less clear. The objective is to investigate the impact of antiretrovirals in the time to the development of anal cancer in HIV-positive MSM. DESIGN: A retrospective analysis of cases of anal cancer in a cohort of HIV-positive MSM receiving antiretrovirals between 1988 and 2008. METHODS: Time from first CD4 cell count or HIV RNA viral load test to anal cancer diagnosis was analysed using Cox regression and Kaplan-Meier curves. Anal cancer cases treated in the era prior to HAART (<1996) were compared with those treated later (1996-2008). RESULTS: Anal cancer cases (n = 37) were compared with a cohort of 1654 HIV-positive MSM on antiretrovirals. Antiretrovirals were started in the pre-HAART era by 70% of cancer cases, and median CD4 cell count nadir was 70 cells/mul (10-130). Time to development of anal cancer was shorter for cases treated during the pre-HAART era [adjusted hazard ratio (AHR) 3.04, 95% confidence interval (95% CI) 1.48-6.24, P = 0.002], with a CD4 cell count nadir less than 100 cells/mul (AHR 2.21, 95% CI 1.06-4.62, P = 0.035) and longer duration of CD4 cell count less than 100 cells/mul (AHR 1.33, 95% CI 1.11-1.58, P = 0.002). CONCLUSION: Results show that severe immunosuppression and starting therapy pre-HAART are associated with an increased risk of anal cancer. HIV-positive MSM initiating antiretrovirals during the HAART era (1996-2008) had a longer time to the development of anal cancer than those treated pre-HAART. Our results suggest that early use of HAART may delay progression to anal cancer.

Engels, E. A. and M. M. Madeleine "Invited commentary: Biological and clinical insights from epidemiologic research into HIV, HPV, and anal cancer." Am J Epidemiol. 2013 Sep 15;178(6):885-7. doi: 10.1093/aje/kwt149. Epub 2013 Jul 30.

Anal cancer is common among people infected with human immunodeficiency virus (HIV). This cancer is caused by human papillomavirus, and immunosuppression likely contributes to its development. In this issue of the Journal, Bertisch et al. (Am J Epidemiol. 2013;178(6):877-884) present the results of a case-control study of anal cancer among HIV-infected people in Switzerland. They demonstrate that anal cancer risk is increased in association with a low CD4+ cell count (a clinical measurement of immune status). In particular, HIV-induced immunosuppression was most severe among cases approximately 6-7 years prior to the diagnosis of anal cancer. A plausible biological interpretation is that immunosuppression is important at an early stage of the development of anal cancer, but that the neoplastic process becomes irreversible over time with persistent human papillomavirus infection and genetic damage. With current efforts to provide earlier combination antiretroviral therapy to HIV-infected people, anal cancer incidence may start to decline. Bertisch et al. also demonstrate a strong association between serum antibodies against the human papillomavirus type 16 protein E6 and anal cancer risk, highlighting the role of this viral oncoprotein in carcinogenesis. Additional biomarkers could help refine clinical approaches to anal cancer screening and prevention for the HIV-infected population.

Flynn, J. K. and P. R. Gorry "Stem memory T cells (TSCM)-their role in cancer and HIV immunotherapies." Clin Transl Immunology. 2014 Jul 18;3(7):e20. doi: 10.1038/cti.2014.16. eCollection 2014 Jul.

Stem memory T cells (TSCM) have been described in mice, non-human primates and in humans, constituting approximately 2-4% of the total CD4(+) and CD8(+) T-cell population in the periphery. TSCM represent the earliest and long-lasting developmental stage of memory T cells, displaying stem cell-like properties, and exhibiting a gene profile between naive and central memory T cells. Their self-renewal capacity and long-term survival has sparked interest in the cancer and human immunodeficiency virus (HIV) fields. How and when the formation of TSCM occurs during the immune response to pathogens and the therapeutic potential of these cells are currently being investigated. This review will explore the potential role of TSCM to be used as, or targeted by, immunotherapies and vaccines for treatment of cancer and HIV.

Fraunholz, I. B., A. Haberl, et al. "Long-term effects of chemoradiotherapy for anal cancer in patients with HIV infection: oncological outcomes, immunological status, and the clinical course of the HIV disease." Dis Colon Rectum. 2014 Apr;57(4):423-31. doi: 10.1097/DCR.0000000000000057.

BACKGROUND: Despite the increasing evidence for chemoradiotherapy as standard treatment for anal cancer in patients with HIV infection, there is still some uncertainty regarding increased toxicity and adverse effects on the immune status. OBJECTIVE: We report the clinical outcome of 5-fluorouracil/mitomycin C-based concurrent chemoradiotherapy for anal carcinoma in patients with HIV infection with an emphasis on the long-term course of CD4 counts and the HIV-related morbidity during follow-up. DESIGN AND SETTINGS: A retrospective single-institution chart review was performed. PATIENTS: Between 1997 and 2012, 36 HIV-positive patients were treated with standard chemoradiotherapy (median tumor dose, 54 (range, 50.4-60.4) Gy at 1.8 Gy/fraction; 5-fluorouracil, 800-1000 mg/m(2), days 1-4 or 1-5; mitomycin C, 10 mg/m(2), day 1, in the first and fifth week). MAIN OUTCOME MEASURES: A retrospective analysis was performed with respect to tumor response, local control, cancer and overall survival, and toxicity. Immunological parameters, including pre- and posttreatment CD4 counts, viral load, and HIV-specific morbidity were recorded during follow-up. RESULTS: Chemoradiotherapy could be completed in all patients. Acute grade 3 toxicities occurred in 17/36 patients (47%). Complete response was achieved in 31 patients (86%). Five-year local control, colostomy-free, cancer-specific, and overall survival were 72%, 87%, 77%, and 74%. The median pretreatment CD4 count significantly decreased from 367 cells/muL to 139 cells/muL, 3 to 7 weeks after completion of chemoradiotherapy ($p < 0.001$). Four patients (11%) experienced opportunistic illnesses during the follow-up (median, 66; range, 10-164 months). LIMITATIONS: This study is limited by its retrospective design and its small sample size. CONCLUSIONS: Our data confirm again that, in the highly active antiretroviral therapy era, anal cancer can be treated in HIV-positive patients with standard chemoradiotherapy, with a clinical outcome similar to their HIV-negative counterparts. The chemoradiotherapy-related decline of the CD4 counts, which remain decreased up to 6 years after chemoradiotherapy, was not associated with increased HIV-related clinical morbidity.

Getinet, M., B. Gelaw, et al. "Prevalence and predictors of Pap smear cervical epithelial cell

abnormality among HIV-positive and negative women attending gynecological examination in cervical cancer screening center at Debre Markos referral hospital, East Gojjam, Northwest Ethiopia." BMC Clin Pathol. 2015 Sep 23;15:16. doi: 10.1186/s12907-015-0016-2. eCollection 2015.

BACKGROUND: Cervical cancer is the leading cause of cancer related death among women in developing countries. Cervical cancer is preceded by cervical surface epithelial cell abnormalities (ECA) which can be detected by Pap smear test. Simultaneous human papillomavirus and human immunodeficiency virus (HIV) infection increases cervical cancer. Data on the prevalence and predictors of ECA among women in Ethiopia is limited. Hence, we aimed to determine the prevalence and associated factors of ECA among women. METHODS: A comparative cross-sectional study was conducted among HIV+ and HIV- women attending gynecological examination in cervical cancer screening center at the Debre Markos referral hospital. The study subjects were stratified by HIV status and systematic random sampling method was used to recruit study participants. Cervical smears were collected for Pap smear examination. Logistic regression analysis was employed to examine the possible risk factors of cervical ECA. RESULTS: A total of 197 HIV+ and 194 HIV- women were enrolled in the study. The overall prevalence of cervical ECA was 14.1 % of which the prevalence of atypical squamous cells undetermined significance (ASCUS), low grade squamous intraepithelial lesion (SIL), high grade SIL, squamous cell carcinoma and ASC, cannot exclude high grade SIL (ASCH) were 5.1, 3.8, 4.1 and 1.0 %, 0.0 % respectively. Significantly higher prevalence of ECA (17.8 %) was observed among HIV+ women (COR 1.9, 95 % CI: 1.1 - 3.4, p = 0.036) as compared to HIV-women (10.3 %). Multiple sexual partnership (AOR 3.2, 95 % CI: 1.1 - 10.0, p = 0.04), early ages of first sexual contact (<15 years) (AOR 5.2, 95 % CI: 1.5 - 17.9, p = 0.009), parity greater than three (AOR 10.9, 95 % CI: 4.2 - 16.8, p < 0.001) and long term oral contraceptive pills (OCP) use (AOR 11.9, 95 % CI: 2.1 - 16.7, p = 0.02) were significant predictors of prevalence of ECA. CONCLUSIONS: Cervical ECA is a major problem among HIV-infected women. Lower CD4+ T-cell counts of below 350 cells/mul, HIV infection, multiple sexual partnership, early age at first sexual contact, parity greater than three and long term OCP use were significant predictors of prevalence of ECA. Strengthening screening program in HIV+ women should be considered.

Goedert, J. J., L. C. Swenson, et al. "Risk of breast cancer with CXCR4-using HIV defined by V3 loop sequencing." J Acquir Immune Defic Syndr. 2015 Jan 1;68(1):30-5. doi: 10.1097/QAI.0000000000000400.

OBJECTIVE: Evaluate the risk of female breast cancer associated with HIV-CXCR4 (X4) tropism as determined by various genotypic measures. METHODS: A breast cancer case-control study, with pairwise comparisons of tropism determination methods, was conducted. From the Women's Interagency HIV Study repository, one stored plasma specimen was selected from 25 HIV-infected cases near the breast cancer diagnosis date and 75 HIV-infected control women matched for age and calendar date. HIV-gp120 V3 sequences were derived by Sanger population sequencing (PS) and 454-pyro deep sequencing (DS). Sequencing-based HIV-X4 tropism was defined using the geno2pheno algorithm, with both high-stringency DS [false-positive rate (3.5) and 2% X4 cutoff], and lower stringency DS (false-positive rate, 5.75 and 15% X4 cutoff). Concordance of tropism results by PS, DS, and previously performed phenotyping was assessed with kappa (kappa) statistics. Case-control comparisons used exact P values and conditional logistic regression. RESULTS: In 74 women (19 cases, 55 controls) with complete results, prevalence of HIV-X4 by PS was 5% in cases vs 29% in controls (P = 0.06; odds ratio, 0.14; confidence interval: 0.003 to 1.03). Smaller case-control prevalence differences were found with high-stringency DS (21% vs 36%, P = 0.32), lower stringency DS (16% vs 35%, P = 0.18), and phenotyping (11% vs 31%, P = 0.10). HIV-X4 tropism concordance was best between PS and lower stringency DS (93%, kappa = 0.83). Other pairwise concordances were 82%-92% (kappa = 0.56-0.81). Concordance was similar among cases and controls. CONCLUSIONS: HIV-X4 defined by population sequencing (PS) had good agreement with lower stringency DS and was significantly associated with lower odds of breast cancer.

Gomez, A., A. J. Montero, et al. "Clinical outcomes in breast cancer patients with HIV/AIDS: a retrospective study." Breast Cancer Res Treat. 2015 Feb;149(3):781-8. doi: 10.1007/s10549-015-3275-9. Epub 2015 Feb 7.

The purpose of the study is to describe what is the presentation of breast cancer in women with HIV, their tolerance to therapy, the most common complications of treatment and their outcomes. Retrospective chart review of patients with HIV diagnosed with breast cancer between January 1, 1989 and December 31, 2013 at the University of Miami/Jackson Memorial Hospital (UM/JMH) 47 females and 1 male were included in the analysis. The median age of diagnosis was 46 years (IQR 41-52) and 64% of the women were premenopausal. Median

CD4(+) count was 330 cells/microL (IQR 131-589 cells/microL). 41% had AIDS at time of diagnosis. 94% of patients presented with locoregional disease and 6% with late stage breast cancer. 52% had ER(+) tumors. 6% had HER-2/neu tumor expression and 21 % had triple negative disease. The 5 year PFS was 50% (95% CI 34-64%), the 5 year OS was 44% (95% CI 29-58%), and the Breast cancer-specific survival was 57% (95% CI 40-70%). Death was attributed to breast cancer in 22 patients, AIDS progression in 6 patients, other medical condition in 1, and for 4, the cause was unknown. Serious adverse events were documented in 46% of patients treated with chemotherapy. Targeted therapy was well tolerated. Patients with HIV/AIDS and breast cancer pose a major challenge for oncologists. Surgery, radiation, and endocrine therapy are well tolerated. Standard dose chemotherapy can have life-threatening side effects which can be managed with growth factor support and antimicrobial prophylaxis. All cancer therapy can be given while continuing with antiviral therapy at full dose.

Gopal, S., C. J. Achenbach, et al. "Moving forward in HIV-associated cancer." J Clin Oncol. 2014 Mar 20;32(9):876-80. doi: 10.1200/JCO.2013.53.1376. Epub 2014 Feb 18.

Guidry, J. A., E. Lubetkin, et al. "Promoting cancer prevention and control in community-based HIV/AIDS service organizations: are they ready?" AIDS Educ Prev. 2014 Feb;26(1):43-55. doi: 10.1521/aeap.2014.26.1.43.

Community-based organizations (CBOs) serving persons living with HIV or AIDS face the challenge of an aging population with more chronic diseases. This study assessed cancer programming needs of AIDS service organizations (ASOs) in New York, New Jersey, and Connecticut by conducting a community needs assessment. Sixty (58%) of 103 organizations completed the survey. ASOs conduct activities most related to early steps along the cancer care continuum, but they also express great interest in expanding cancer-focused programming into new areas. ASOs have resources or capacities in assisting HIV+ clients with mental health or substance abuse problems, but there exists a need for funding in undertaking or expanding cancer-focused programs. ASOs are receptive to collaborating with researchers on disseminating cancer prevention and control knowledge in their settings. Community-academic research partnerships enable resonant training and technical assistance methods to be explored that will enhance the abilities of ASOs to bring cancer-related programming to their clients.

Hadjiandreou, M. M. and G. D. Mitsis "Taking a break from chemotherapy to fight drug-resistance: The cases of cancer and HIV/AIDS." Conf Proc IEEE Eng Med Biol Soc. 2013;2013:197-200. doi: 10.1109/EMBC.2013.6609471.

In this work, we present how optimized treatment interruptions during chemotherapy may be used to control drug-resistance, a major challenge for clinicians worldwide. Specifically, we examine resistance in cancer and HIV/AIDS. For each disease, we use mathematical models alongside real data to represent the respective complex biological phenomena and optimal control algorithms to design optimized treatment schedules aiming at controlling disease progression and patient death. In both diseases, it is shown that the key to controlling resistance is the optimal management of the frequency and magnitude of treatment interruptions as a way to facilitate the interplay between the competitive resistant/sensitive strains.

Hanisch, R. A., S. L. Cherne, et al. "Human papillomavirus type 16 viral load in relation to HIV infection, cervical neoplasia and cancer in Senegal." Cancer Epidemiol. 2014 Aug;38(4):369-75. doi: 10.1016/j.canep.2014.04.005. Epub 2014 May 19.

BACKGROUND: The importance of human papillomavirus (HPV) viral load in the pathogenesis of cervical cancer among HIV-infected and HIV-uninfected women has not yet been established. METHODS: In this cross-sectional study, HPV-16 viral loads were measured using previously-collected and frozen cervical swab samples from 498 HPV-16 positive Senegalese women (368 HIV-seronegative, 126 HIV-1 and/or HIV-2 seropositive). The real-time polymerase chain reaction assay was used to quantify HPV-16 E7 copy number normalized by human cellular DNA (beta-actin), and viral loads were log10 transformed. Associations between HPV-16 viral load, degree of cervical abnormality, and HIV status were assessed using multinomial and linear regression methods. RESULTS: Compared to women with normal cytology, the likelihood of CIN1 (ORa: 1.21, 95% CI 0.93-1.57), CIN2-3 (ORa: 2.38, 95% CI 1.72-3.29) and cancer (ORa: 2.12, 95% CI 1.52-2.96) was found to increase for each 1-unit log10 increase in HPV-16 viral load. Compared to HIV-negative women, HIV-positive women had higher average HPV-16 viral load values (betaa: 0.39, 95% CI 0.03-0.75), even after accounting for degree of cervical abnormality. CONCLUSION: In our study of women including those with cancer, HPV-16 viral load was associated with a higher likelihood of cervical abnormalities. However, substantial overlaps across categories of disease severity existed. Higher viral load among HIV-infected individuals may indicate

that HIV infection influences HPV viral replication factors.

Harding, R., L. Selman, et al. "Wellbeing among sub-Saharan African patients with advanced HIV and/or cancer: an international multicentred comparison study of two outcome measures." Health Qual Life Outcomes. 2014 May 31;12:80. doi: 10.1186/1477-7525-12-80.

BACKGROUND: Despite the high mortality rates of HIV and cancer in sub-Saharan Africa, there are few outcome tools and no comparative data across conditions. This study aimed to measure multidimensional wellbeing among advanced HIV and/or cancer patients in three African countries, and determine the relationship between two validated outcome measures. METHODS: Cross-sectional self-reported data from palliative care populations in Kenya, Uganda and South Africa using FACIT-G+Pal and POS measures. RESULTS: Among 461 participants across all countries, subscale "social and family wellbeing" had highest (best) score. Significant country effect showed lower (worse) scores for Uganda on 3 FACIT G subscales: Physical, Social + family, and functional. In multiple regression, country and functional status accounted for 21% variance in FACIT-Pal. Worsening functional status was associated with poorer POS score. Kenyans had worse POS score, followed by Uganda and South Africa. Matrix of correlational coefficients revealed moderate correlation between the POS and FACIT-Pal core scale (0.60), the FACIT-G and POS (0.64), and FACIT-G + Pal with POS (0.66). CONCLUSIONS: The data reveal best status for family and social wellbeing, which may reflect the sample being from less individualistic societies. The tools appear to measure different constructs of wellbeing in palliative care, and reveal different levels of wellbeing between countries. Those with poorest physical function require greatest palliative and supportive care, and this does not appear to differ according to diagnosis.

Hessol, N. A., O. Martinez-Maza, et al. "Lung cancer incidence and survival among HIV-infected and uninfected women and men." AIDS. 2015 Jun 19;29(10):1183-93. doi: 10.1097/QAD.0000000000000690.

OBJECTIVES: To determine the lung cancer incidence and survival time among HIV-infected and uninfected women and men. DESIGN: Two longitudinal studies of HIV infection in the United States. METHODS: Data from 2549 women in the Women's Interagency HIV Study (WIHS) and 4274 men in the Multicenter AIDS Cohort Study (MACS), all with a history of cigarette smoking, were analyzed. Lung cancer incidence rates and incidence rate ratios were calculated using Poisson regression analyses. Survival time was assessed using Kaplan-Meier and Cox proportional-hazard analyses. RESULTS: Thirty-seven women and 23 men developed lung cancer (46 HIV-infected and 14 HIV-uninfected) during study follow-up. In multivariable analyses, the factors that were found to be independently associated with a higher lung cancer incidence rate ratios were older age, less education, 10 or more pack-years of smoking, and a prior diagnosis of AIDS pneumonia (vs. HIV-uninfected women). In an adjusted Cox model that allowed different hazard functions for each cohort, a history of injection drug use was associated with shorter survival, and a lung cancer diagnosis after 2001 was associated with longer survival. In an adjusted Cox model restricted to HIV-infected participants, nadir CD4 lymphocyte cell count less than 200 was associated with shorter survival time. CONCLUSIONS: Our data suggest that pulmonary damage and inflammation associated with HIV infection may be causative for the increased risk of lung cancer. Encouraging and assisting younger HIV-infected smokers to quit and to sustain cessation of smoking is imperative to reduce the lung cancer burden in this population.

Hleyhel, M., A. Belot, et al. "Trends in survival after cancer diagnosis among HIV-infected individuals between 1992 and 2009. Results from the FHDH-ANRS CO4 cohort." Int J Cancer. 2015 Nov 15;137(10):2443-53. doi: 10.1002/ijc.29603. Epub 2015 Jun 2.

Although the decline in cancer mortality rates with the advent of combination antiretroviral therapy (cART) in HIV-infected individuals can be mostly explained by a decrease in cancers incidence, we looked here if improved survival after cancer diagnosis could also contribute to this decline. Survival trends were analyzed for most frequent cancers in the HIV-infected population followed in the French Hospital Database on HIV: 979 and 2,760 cases of visceral and non-visceral Kaposi's sarcoma (KS), 2,339 and 461 cases of non-Hodgkin lymphoma (NHL) and Hodgkin's lymphoma (HL), 446 lung, 312 liver and 257 anal cancers. Five-year Kaplan-Meier survival rates were estimated for four periods: 1992-1996, 1997-2000, 2001-2004 and 2005-2009. Cox proportional hazard models were used to compare survival across the periods, after adjustment for confounding factors. For 2001-2004, survival was compared to the general population after standardization on age and sex. Between the pre-cART (1992-1996) and early-cART (1997-2000) periods, survival improved after KS, NHL, HL and anal cancer and remained stable after lung and liver cancers. During the cART era, 5-year survival improved after

visceral and non-visceral KS, NHL, HL and liver cancer, being 83, 92, 65, 87 and 19% in 2005-2009, respectively, and remained stable after lung and anal cancers, being 16 and 65%, respectively. Compared with the general population, survival in HIV-infected individuals in 2001-2004 was poorer for hematological malignancies and similar for solid tumors. For hematological malignancies, survival continues to improve after 2004, suggesting that the gap between the HIV-infected and general populations will close in the future.

Hoffmann, C., F. Kohrs, et al. "HIV-associated lung cancer: survival in an unselected cohort." Scand J Infect Dis. 2013 Oct;45(10):766-72. doi: 10.3109/00365548.2013.810813. Epub 2013 Jul 23.

BACKGROUND: Lung cancer is one of the most common non-AIDS-defining malignancies in HIV-infected patients. However, data on clinical outcome and prognostic factors are scarce. METHODS: This was a national German multicentre, retrospective cohort analysis of all cases of lung cancer seen in HIV-infected individuals from 2000 through 2010. Survival was analyzed with respect to the use of antiretroviral therapy (ART), specific lung cancer therapies, and other potential prognostic factors. RESULTS: A total of 72 patients (mean age 55.5 y, CD4 T-cells 383/mul) were evaluated in this analysis. At time of lung cancer diagnosis, 86% were on ART. Of these, 79% had undetectable HIV-1 RNA (< 50 copies/ml) for a mean duration of 4.0 y. All but 1 patient were current or former heavy smokers (mean 42 package y). The median estimated overall survival was 1.08 y, with a 2-y overall survival of 24%. The prognosis did not improve during the observation time. A limited lung cancer stage of I-IIIA was associated with better overall survival when compared with the advanced stages IIIb/IV (p = 0.0003). Other factors predictive of improved overall survival were better performance status, CD4 T-cells > 200/mul, and a non-intravenous drug use transmission risk for HIV. CONCLUSIONS: Currently, most cases of lung cancer occur in the setting of limited immune deficiency and a long-lasting viral suppression. As in HIV-negative cases, the clinical stage of lung cancer is highly predictive of survival, and long-term overall survival can only be achieved at the limited stages. The still high mortality underscores the importance of smoking cessation strategies in HIV-infected patients.

Huchko, M. J., J. Sneden, et al. "A comparison of two visual inspection methods for cervical cancer screening among HIV-infected women in Kenya." Bull World Health Organ. 2014 Mar 1;92(3):195-203. doi: 10.2471/BLT.13.122051. Epub 2014 Jan 15.

OBJECTIVE: To determine the optimal strategy for cervical cancer screening in women with human immunodeficiency virus (HIV) infection by comparing two strategies: visual inspection of the cervix with acetic acid (VIA) and VIA followed immediately by visual inspection with Lugol's iodine (VIA/VILI) in women with a positive VIA result. METHODS: Data from a cervical cancer screening programme embedded in two HIV clinic sites in western Kenya were evaluated. Women at a central site underwent VIA, while women at a peripheral site underwent VIA/VILI. All women positive for cervical intraepithelial neoplasia grade 2 or worse (CIN 2+) on VIA and/or VILI had a confirmatory colposcopy, with a biopsy if necessary. Overall test positivity, positive predictive value (PPV) and the CIN 2+ detection rate were calculated for the two screening methods, with biopsy being the gold standard. FINDINGS: Between October 2007 and October 2010, 2338 women were screened with VIA and 1124 with VIA/VILI. In the VIA group, 26.4% of the women tested positive for CIN 2+; in the VIA/VILI group, 21.7% tested positive (P < 0.01). Histologically confirmed CIN 2+ was detected in 8.9% and 7.8% (P = 0.27) of women in the VIA and VIA/VILI groups, respectively. The PPV of VIA for biopsy-confirmed CIN 2+ in a single round of screening was 35.2%, compared with 38.2% for VIA/VILI (P = 0.41). CONCLUSION: The absence of any differences between VIA and VIA/VILI in detection rates or PPV for CIN 2+ suggests that VIA, an easy testing procedure, can be used alone as a cervical cancer screening strategy in low-income settings.

Ivy, W., 3rd, S. R. Nesheim, et al. "Cancer Among Children With Perinatal Exposure to HIV and Antiretroviral Medications-New Jersey, 1995-2010." J Acquir Immune Defic Syndr. 2015 Sep 1;70(1):62-6. doi: 10.1097/QAI.0000000000000695.

BACKGROUND: Concerns remain regarding the cancer risk associated with perinatal antiretroviral (ARV) exposure among infants. No excessive cancer risk has been found in short-term studies. METHODS: Children born to HIV-infected women (HIV-exposed) in New Jersey from 1995 to 2008 were identified through the Enhanced HIV/AIDS Reporting System and cross-referenced with data from the New Jersey State Cancer Registry to identify new cases of cancer among children who were perinatally exposed to ARV. Matching of individuals in the Enhanced HIV/AIDS Reporting System to the New Jersey State Cancer Registry was conducted based on name, birth date, Social Security number, residential address, and sex using AutoMatch. Age- and sex-standardized incidence ratio (SIR) and exact 95% confidence

intervals (CIs) were calculated using New Jersey (1979-2005) and US (1999-2009) cancer rates. RESULTS: Among 3087 children (29,099 person-years; median follow-up: 9.8 years), 4 were diagnosed with cancer. Cancer incidence among HIV-exposed children who were not exposed to ARV prophylaxis (22.5 per 100,000 person-years) did not differ significantly from the incidence among children who were exposed to any perinatal ARV prophylaxis (14.3 per 100,000 person-years). Furthermore, the number of cases observed among individuals exposed to ARV did not differ significantly from cases expected based on state (SIR = 1.21; 95% CI: 0.25 to 3.54) and national (SIR = 1.27; 95% CI: 0.26 to 3.70) reference rates. CONCLUSIONS: Our findings are reassuring that current use of ARV for perinatal HIV prophylaxis does not increase cancer risk. We found no evidence to alter the current federal guidelines of 2014 that recommend ARV prophylaxis of HIV-exposed infants.

Jaquet, A., M. Odutola, et al. "Cancer and HIV infection in referral hospitals from four West African countries." Cancer Epidemiol. 2015 Sep 12. pii: S1877-7821(15)00182-4. doi: 10.1016/j.canep.2015.09.002.

The consequences of the HIV epidemic on cancer epidemiology are sparsely documented in Africa. We aimed to estimate the association between HIV infection and selected types of cancers among patients hospitalized for cancer in four West African countries. A case-referent study was conducted in referral hospitals of Benin, Cote d'Ivoire, Nigeria and Togo. Each participating clinical ward included all adult patients seeking care with a confirmed diagnosis of cancer. All patients were systematically screened for HIV infection. HIV prevalence of AIDS-defining and some non-AIDS defining cancers (Hodgkin lymphoma, leukemia, liver, lung, skin, pharynx, larynx, oral cavity and anogenital cancers) were compared to a referent group of cancers reported in the literature as not associated with HIV. Odds ratios adjusted on age, gender and lifetime number of sexual partners (aOR) and their 95% confidence intervals (CI) were estimated. Among the 1644 cancer patients enrolled, 184 (11.2%) were identified as HIV-infected. The HIV prevalence in the referent group (n=792) was 4.4% [CI 3.0-5.8]. HIV infection was associated with Kaposi sarcoma (aOR 34.6 [CI: 17.3-69.0]), non-Hodgkin lymphoma (aOR 3.6 [CI 1.9-6.8]), cervical cancer (aOR 4.3 [CI 2.2-8.3]), anogenital cancer (aOR 17.7 [CI 6.9-45.2]) and squamous cell skin carcinoma (aOR 5.2 [CI 2.0-14.4]). A strong association is now reported between HIV infection and Human Papillomavirus (HPV)-related cancers including cervical cancer and anogenital cancer. As these cancers are amenable to prevention strategies, screening of HPV-related cancers among HIV-infected persons is of paramount importance in this African context.

Kapambwe, S., V. V. Sahasrabuddhe, et al. "Implementation and Operational Research: Age Distribution and Determinants of Invasive Cervical Cancer in a "Screen-and-Treat" Program Integrated With HIV/AIDS Care in Zambia." J Acquir Immune Defic Syndr. 2015 Sep 1;70(1):e20-6. doi: 10.1097/QAI.0000000000000685.

BACKGROUND: Cervical cancer screening efforts linked to HIV/AIDS care programs are being expanded across sub-Saharan Africa. Evidence on the age distribution and determinants of invasive cervical cancer (ICC) cases detected in such programs is limited. METHODS: We analyzed program operations data from the Cervical Cancer Prevention Program in Zambia, the largest public sector programs of its kind in sub-Saharan Africa. We examined age distribution patterns by HIV serostatus of histologically confirmed ICC cases and used multivariable logistic regression to evaluate independent risk factors for ICC among younger (</=35 years) and older (>35 years) women. RESULTS: Between January 2006 and April 2010, of 48,626 women undergoing screening, 571 (1.2%) were diagnosed with ICC, including 262 (46%) HIV seropositive (median age: 35 years), 131 (23%) HIV seronegative (median age: 40 years), and 178 (31%) of unknown HIV serostatus (median age: 38 years). Among younger (</=35 years) women, being HIV seropositive was associated with a 4-fold higher risk of ICC [adjusted odds ratio = 4.1 (95% confidence interval: 2.8, 5.9)] than being HIV seronegative. The risk of ICC increased with increasing age among HIV-seronegative women and women with unknown HIV serostatus, but among HIV-seropositive women, the risk peaked around age 35 and nonsignificantly declined with increasing ages. Other factors related to ICC included being married (vs. being unmarried/widowed) in both younger and older women, and with having 2+ (vs. </=1) lifetime sexual partners among younger women. CONCLUSIONS: HIV infection seems to have increased the risk of cervical cancer among younger women in Zambia, pointing to the urgent need for expanding targeted screening interventions.

Kenya, S., O. Carrasquillo, et al. "Human Papilloma Virus and Cervical Cancer Education Needs among HIV-Positive Haitian Women in Miami." Womens Health Issues. 2015 May-Jun;25(3):262-6. doi: 10.1016/j.whi.2014.12.007. Epub 2015 Apr 9.

BACKGROUND: Haitian immigrant women, the largest growing Black ethnic group in Miami, experience the highest rates of cervical cancer and

account for one of the largest populations diagnosed with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) in South Florida. Using community-based participatory research methods, we conducted a pilot study to examine human papilloma virus (HPV)/cervical cancer knowledge and identify intervention preferences among HIV positive Haitian women. METHODS: Community health workers conducted three focus groups with 21 HIV-positive Haitian women. All sessions were conducted in Haitian Kreyol, digitally recorded, and subsequently interpreted and transcribed into English. The first focus group assessed HPV/cervical cancer knowledge, the second session explored HPV/cervical cancer considerations specific to HIV-positive women, and the third focus group discussed HPV/cervical cancer screening and intervention preferences. Data analysis was guided by a grounded theory approach. FINDINGS: Our sample had limited HPV/cervical cancer knowledge. Misconceptions about screening, transmission, and treatment were common. Participants felt that stigma by providers impacted negatively the care they received and that stigma by the community diminished social support. Strong support for culturally tailored interventions to improve HPV/cervical cancer knowledge was expressed. Although no participants had participated in research previously, all were willing to participate in future trials. CONCLUSIONS: There is critical need for culturally relevant interventions to improve HPV/cervical cancer knowledge among HIV-positive Haitian women.

Kohler, R. E., J. Tang, et al. "High rates of cervical cancer among HIV-infected women at a referral hospital in Malawi." Int J STD AIDS. 2015 Jun 30. pii: 0956462415592999.

OBJECTIVE: Cervical cancer is the most common cancer among women in Malawi. National guidelines recommend screening women aged 30-45 years every five years; however, no specific recommendations exist for women with HIV. We aimed to assess the frequency of high-grade dysplasia (CIN 2 or CIN3) and cervical cancer among women in central Malawi and to examine associations with CIN2+ (CIN2/3 or cancer). METHODS: We extracted cervical pap smear, biopsy, loop electrosurgical excision procedure and uterine specimen reports from a hospital pathology database from November 2012 to November 2013. We used logistic regression to estimate associations with CIN2+. RESULTS: We reviewed specimens from 824 women; we excluded 194 with unknown HIV status, leaving 630 in the analytic sample. Twelve percent had high-grade dysplasia and 109 women (17%) had cancer. Twenty-five percent of high-grade dysplasia cases and 35% of cancers occurred among women outside recommended screening ages. The odds of having CIN2+ were 6.55 times (95% CI 4.44-9.67) greater for HIV+ women. CONCLUSIONS: High-grade dysplasia and cervical cancer are very common among Malawian women, especially HIV+ women. HIV infection was strongly associated with CIN2+. Expanding screening to women not covered by current guidelines could avert a substantial proportion of cervical cancer cases in Malawi.

Korir, A., N. Mauti, et al. "Developing clinical strength-of-evidence approach to define HIV-associated malignancies for cancer registration in Kenya." PLoS One. 2014 Jan 23;9(1):e85881. doi: 10.1371/journal.pone.0085881. eCollection 2014.

BACKGROUND: Sub-Saharan Africa cancer registries are beset by an increasing cancer burden further exacerbated by the AIDS epidemic where there are limited capabilities for cancer-AIDS match co-registration. We undertook a pilot study based on a "strength-of-evidence" approach using clinical data that is abstracted at the time of cancer registration for purposes of linking cancer diagnosis to AIDS diagnosis. METHODS/FINDINGS: The standard Nairobi Cancer Registry form was modified for registrars to abstract the following clinical data from medical records regarding HIV infection/AIDS in a hierarchal approach at time of cancer registration from highest-to-lowest strength-of-evidence: 1) documentation of positive HIV serology; 2) antiretroviral drug prescription; 3) CD4+ lymphocyte count; and 4) WHO HIV clinical stage or immune suppression syndrome (ISS), which is Kenyan terminology for AIDS. Between August 1 and October 31, 2011 a total of 1,200 cancer cases were registered. Of these, 171 cases (14.3%) met clinical strength-of-evidence criteria for association with HIV infection/AIDS; 69% (118 cases were tumor types with known HIV association - Kaposi's sarcoma, cervical cancer, non-Hodgkin's and Hodgkin's lymphoma, and conjunctiva carcinoma) and 31% (53) were consistent with non-AIDS defining cancers. Verifiable positive HIV serology was identified in 47 (27%) cases for an absolute seroprevalence rate of 4% among the cancer registered cases with an upper boundary of 14% among those meeting at least one of strength-of-evidence criteria. CONCLUSIONS/SIGNIFICANCE: This pilot demonstration of a hierarchal, clinical strength-of-evidence approach for cancer-AIDS registration in Kenya establishes feasibility, is readily adaptable, pragmatic, and does not require additional resources for critically under staffed cancer registries. Cancer is an emerging public health challenge, and African nations need to develop well designed population-

based studies in order to better define the impact and spectrum of malignant disease in the backdrop of HIV infection.

Kumakech, E., S. Andersson, et al. "Integration of HIV and cervical cancer screening perceptions and preferences of communities in Uganda." BMC Womens Health. 2015;15:23. doi: 10.1186/s12905-015-0183-4. Epub 2015 Mar 11.

BACKGROUND: Despite the fact that HIV-positive women carry an increased risk of developing cervical cancer (CC) in comparison with HIV-negative women, HIV and CC screening programs in many developing countries have remained unintegrated. The objective of this study is to explore perceptions and preferences of community members in Uganda, including women, men, and village health teams, regarding the integration of HIV and CC screening services in a single-visit approach. METHODS: This qualitative study was conducted in three districts in Uganda. Data were collected through focus group discussions with women and village health teams, and individual interviews with men. Respondents were purposely selected from among those linked to three CC clinics in the three districts. The content analysis method was used to analyze the data. RESULTS: Three themes emerged from the data, namely appreciating the benefits of integration, worrying about the challenges of integration, and preferences for integration. The women endorsed the benefits. However, there were worries that integration would prolong the waiting time at the health facility and induce tiredness in both the healthcare providers and the women. There were also fears of being found positive for both HIV and CC and the consequences such as stress, self-isolation, and social conflicts. Participants, particularly the women, considered the challenges of screening integration to be manageable by, for example, taking a day off work to visit the hospital, delegating house chores to other family members, or taking a packed lunch on visiting the hospital. CONCLUSIONS: The community members in Uganda perceive the benefits of HIV and CC screening integration to outweigh the challenges, and expect that the challenges can be minimized or managed by the women. Therefore, when considering HIV and CC screening integration, it is important to not only recognize the benefits but also take into consideration the perceived challenges and preferences of community members.

Kumakech, E., S. Andersson, et al. "Integration of HIV and cervical cancer screening perceptions of healthcare providers and policy makers in Uganda." BMC Public Health. 2014 Aug 7;14:810. doi: 10.1186/1471-2458-14-810.

BACKGROUND: HIV-positive women have an increased risk of developing cervical cancer (CC) compared to the HIV-negative women. Despite this, HIV and CC screening programs in many developing countries have remained disintegrated. Therefore, the objective of the study was to explore perceptions of healthcare providers (HCP) and policy makers (PM) about integration of HIV and CC screening services in Uganda. METHODS: This was a qualitative study conducted among 16 participants comprising of 12 healthcare providers and 4 policy makers in Uganda. Data were collected through individual interviews. Participants were purposively selected from different level of health facilities with clinics for HIV and CC screening services. Content analysis method was used to analyze the data. RESULTS: Three themes emerged from the data, namely appreciating benefits of integration, worrying about the limited health system capacity and potential consequences of integration and feeling optimistic about integration under improved health system conditions. The benefits embraced the women - particularly the HIV-positive women- but also men, healthcare providers and the health system or the government. There were worries that HIV stigma and shortage of healthcare workers would affect the effective delivery of the integrated program. CONCLUSION: Integration of HIV and CC screening can offer manifold benefits to all stakeholders in the health system, more so to the women. However, its feasibility in developing countries such as Uganda will most likely be hampered by weak and inefficient health systems. Therefore, when considering HIV and CC screening integration, it is important not to only recognize the benefits but also take into account resources requirements for addressing the existing weaknesses and inefficiencies in the health systems such as limited infrastructure, insufficient drugs and supplies, inadequate and poorly motivated healthcare workers.

Legarth, R., L. H. Omland, et al. "Association Between Educational Level and Risk of Cancer in HIV-infected Individuals and the Background Population: Population-based Cohort Study 1995-2011." J Infect Dis. 2015 Apr 22. pii: jiv247.

BACKGROUND: Human immunodeficiency virus (HIV)-infected individuals have increased risk of cancer. To our knowledge, no previous study has examined the impact of socioeconomic position on risk and prognosis of cancer in HIV infection. METHODS: Population-based cohort-study, including HIV-infected individuals diagnosed (without intravenous drug abuse or hepatitis C infection) (n = 3205), and a background population cohort matched by age, gender, and country of birth (n = 22 435) were analyzed. Educational level (low or high) and cancer

events were identified in Danish national registers. Cumulative incidences, incidence rate ratios (IRRs), and survival using Kaplan-Meier methods were estimated. RESULTS: Low educational level was associated with increased risk of cancer among HIV-infected individuals compared to population controls: all (adjusted-IRRs: 1.4 [95% confidence interval {CI}, 1.1-1.7] vs 1.1 [95% CI, .9-1.2]), tobacco- and alcohol-related (2.1 [95% CI, 1.3-3.4] vs 1.3 [95% CI, 1.1-1.6]), and other (1.7 [95% CI, 1.1-2.8] vs 0.9 [95% CI, .7-1.0]). Educational level was not associated with infection-related or ill-defined cancers. One-year-survival was not associated with educational level, but HIV-infected individuals with low educational level had lower 5-year-survival following infection-related and ill-defined cancers. CONCLUSIONS: Education is associated with risk and prognosis of some cancers in HIV infection, and diverges from what is observed in the background population.

Leslie, H. H., D. A. Karasek, et al. "Cervical cancer precursors and hormonal contraceptive use in HIV-positive women: application of a causal model and semi-parametric estimation methods." PLoS One. 2014 Jun 30;9(6):e101090. doi: 10.1371/journal.pone.0101090. eCollection 2014.

OBJECTIVE: To demonstrate the application of causal inference methods to observational data in the obstetrics and gynecology field, particularly causal modeling and semi-parametric estimation. BACKGROUND: Human immunodeficiency virus (HIV)-positive women are at increased risk for cervical cancer and its treatable precursors. Determining whether potential risk factors such as hormonal contraception are true causes is critical for informing public health strategies as longevity increases among HIV-positive women in developing countries. METHODS: We developed a causal model of the factors related to combined oral contraceptive (COC) use and cervical intraepithelial neoplasia 2 or greater (CIN2+) and modified the model to fit the observed data, drawn from women in a cervical cancer screening program at HIV clinics in Kenya. Assumptions required for substantiation of a causal relationship were assessed. We estimated the population-level association using semi-parametric methods: g-computation, inverse probability of treatment weighting, and targeted maximum likelihood estimation. RESULTS: We identified 2 plausible causal paths from COC use to CIN2+: via HPV infection and via increased disease progression. Study data enabled estimation of the latter only with strong assumptions of no unmeasured confounding. Of 2,519 women under 50 screened per protocol, 219 (8.7%) were diagnosed with CIN2+. Marginal modeling suggested a 2.9% (95% confidence interval 0.1%, 6.9%) increase in prevalence of CIN2+ if all women under 50 were exposed to COC; the significance of this association was sensitive to method of estimation and exposure misclassification. CONCLUSION: Use of causal modeling enabled clear representation of the causal relationship of interest and the assumptions required to estimate that relationship from the observed data. Semi-parametric estimation methods provided flexibility and reduced reliance on correct model form. Although selected results suggest an increased prevalence of CIN2+ associated with COC, evidence is insufficient to conclude causality. Priority areas for future studies to better satisfy causal criteria are identified.

Marcus, J. L., C. R. Chao, et al. "Prostate cancer incidence and prostate-specific antigen testing among HIV-positive and HIV-negative men." J Acquir Immune Defic Syndr. 2014 Aug 15;66(5):495-502. doi: 10.1097/QAI.0000000000000202.

BACKGROUND: We investigated whether the reported lower incidence of prostate cancer in HIV-positive men is a result of confounding factors or reduced screening. METHODS: We conducted a cohort study of 17,424 HIV-positive and 182,799 HIV-negative men enrolled in Kaiser Permanente (KP). Subjects were followed from the first KP enrollment after January 01, 1996 for KP Northern California (KPNC) and January 01, 2000 for KP Southern California until the earliest of prostate cancer diagnosis, loss to follow-up, or December 31, 2007. Poisson regression was used to compare cancer rates by HIV status adjusting for age, race, smoking, alcohol/drug abuse, overweight/obesity, and diabetes. For the KPNC subset, we analyzed additional available data by HIV status on testosterone deficiency, and on prostate-specific antigen (PSA) tests as a proxy for cancer screening. RESULTS: The prostate cancer incidence rate was 102/100,000 person-years in HIV-positive men (n = 74 cases) and 131/100,000 person-years in HIV-negative men (n = 1195 cases), with an adjusted rate ratio of 0.73 (95% confidence interval: 0.57 to 0.92; P = 0.008). The reduced risk among HIV-positive men was greater for higher-stage cancers, which are less likely to be biased by screening differences than lower-stage cancers. In the KPNC subset, more HIV-positive (90.8%) than HIV-negative men (86.2%) received a PSA test by age 55 (P < 0.001). Decreased risk for HIV-positive men remained when examined only among those with a previous PSA test, and with adjustment for testosterone deficiency (rate ratio = 0.55; 95% confidence interval: 0.39 to 0.80; P = 0.001). CONCLUSIONS: Prostate cancer incidence rates are lower in HIV-positive compared with HIV-negative

men, which is not explained by screening differences or the risk factors evaluated.

Maree, J. E. and K. A. Moitse "Exploration of knowledge of cervical cancer and cervical cancer screening amongst HIV-positive women." Curationis. 2014 Oct 10;37(1):1-7. doi: 10.4102/curationis.v37i1.1209.

BACKGROUND: Although preventable, cervical cancer, an AIDS-related disease, is the second most common cancer amongst South African women and the most common cancer amongst black women. OBJECTIVE: The objective of the study was to determine what women being treated for HIV and AIDS at a specific healthcare centre in Johannesburg knew about cervical cancer and cervical screening. METHOD: A survey design was used, with data gathered by means of a self-administered questionnaire. Convenience sampling selected 315 women to participate (n = 315). Descriptive statistics were used to analyse the data and chi-square testing found associations between categorical variables. RESULTS: The majority of respondents (78.7%; n = 248) indicated that they had heard of cervical cancer and 62.9% (n = 198) knew about the Pap smear, with nurses and doctors being the primary source of information. Of the women who knew about the Pap smear, less than one-third had had a smear done, the main reason being fear of the procedure. CONCLUSION: The study provided evidence that women attending the specific HIV clinic were more knowledgeable about cervical cancer and screening than those of unknown HIV status involved in previous studies. Knowledge was still at a low level, especially when their exceptionally high risk was taken into account. Once again it was found that having knowledge did not necessarily mean having had a Pap smear, which remains a huge challenge in the prevention of cervical cancer.

Meyer, J. E., V. J. Panico, et al. "HIV positivity but not HPV/p16 status is associated with higher recurrence rate in anal cancer." J Gastrointest Cancer. 2013 Dec;44(4):450-5. doi: 10.1007/s12029-013-9543-1.

AIM: Human papillomavirus (HPV) is a pathogenic factor of squamous cell carcinoma in various mucosal locations, including anal carcinoma (ACA). It is also known that patients positive for HIV are at high risk of ACA. The goal of this study was to examine clinical outcome in ACA in relation to HPV/p16 positivity, histologic tumor differentiation, and HIV status. Patients with oropharyngeal cancers that are positive for HPV and show overexpression of p16 as well as having non-keratinizing/basaloid histology have been reported to have better outcomes following chemoradiation (CRT). However, such relationships in ACA remain unknown. METHODS: Forty-two patients with SCC of the anus treated with CRT between 1997 and 2009 were identified. The tumors were subclassified as either non-keratinizing (including basaloid) or keratinizing categories. HPV testing was performed using SPF10-PCR, and all cases were immunostained for p16. RESULTS: There were 23 men and 19 women; 43% of men and 11% of women were HIV-positive (p = 0.04). Fifty-five percent of patients had local disease (stages I and II) and 41% were stages III and IV, with 4% stage unknown. All tumors were positive for high-oncogenic risk HPVs, and all were positive with p16 immunostain. Sixty-four percent of tumors were non-keratinizing/basaloid and 36 % were keratinizing. The keratinizing tumors were more common in HIV-positive patients (67%), whereas non-keratinizing/basaloid tumors were more common in HIV-negative patients (77%) (p = 0.008)..

Mungo, C., C. R. Cohen, et al. "Prevalence, characteristics, and outcomes of HIV-positive women diagnosed with invasive cancer of the cervix in Kenya." Int J Gynaecol Obstet. 2013 Dec;123(3):231-5. doi: 10.1016/j.ijgo.2013.07.010. Epub 2013 Sep 10.

OBJECTIVE: To determine the prevalence of invasive cervical cancer (ICC) and assess access to, and outcomes of, treatment for ICC among HIV-infected women in Kisumu, Kenya. METHODS: We performed a retrospective chart review to identify women diagnosed with ICC between October 2007 and June 2012, and to examine the impact of a change in the referral protocol. Prior to June 2009, all women with ICC were referred to a regional hospital. After this date, women with stage IA1 disease were offered treatment with loop electrosurgical excision procedure (LEEP) in-clinic. RESULTS: Of 4308 women screened, 58 (1.3%) were diagnosed with ICC. The mean age at diagnosis was 34years (range, 22-50years). Fifty-four (93.1%) women had stage IA1 disease, of whom 36 (66.7%) underwent LEEP, 7 (12.9%) had a total abdominal hysterectomy, and 11 (20.4%) had unknown or no treatment. At 6, 12, and 24months after LEEP, 8.0% (2/25), 25.0% (6/24), and 41.2% (7/17) of women had a recurrence of cervical intraepithelial neoplasia 2 or worse, respectively. CONCLUSION: Most HIV-positive women diagnosed with ICC through screening had early-stage disease. The introduction of LEEP in-clinic increased access to treatment; however, recurrence was high, indicating the need for continued surveillance.

Murphy, A. B., R. Bhatia, et al. "Are HIV-infected men vulnerable to prostate cancer treatment disparities?" Cancer Epidemiol Biomarkers Prev. 2014

Oct;23(10):2009-18. doi: 10.1158/1055-9965.EPI-14-0614. Epub 2014 Jul 25.

BACKGROUND: HIV-infected (HIV(+)) men face cancer treatment disparities that impact outcome. Prostate cancer treatment and treatment appropriateness in HIV(+) men are unknown. METHODS: We used electronic chart review to conduct a retrospective cohort study of 43 HIV(+) cases with prostate cancer and 86 age- and race-matched HIV-uninfected (HIV(-)) controls with prostate cancer, ages 40 to 79 years, from 2001 to 2012. We defined treatment appropriateness using National Comprehensive Cancer Network guidelines and the Charlson comorbidity index (CCI) to estimate life expectancy. RESULTS: Median age was 59.5 years at prostate cancer diagnosis. Median CD4(+) T-cell count was 459.5 cells/mm(3), 95.3% received antiretroviral therapy, and 87.1% were virally suppressed. Radical prostatectomy was the primary treatment for 39.5% of HIV(+) and 71.0% of HIV(-) men (P = 0.004). Only 16.3% of HIV(+) versus 57.0% of HIV(-) men received open radical prostatectomy (P < 0.001). HIV(+) men received more radiotherapy (25.6% vs. 16.3%, P = 0.13). HIV was negatively associated with open radical prostatectomy (OR = 0.03, P = 0.007), adjusting for insurance and CCI. No men were undertreated. Fewer HIV(+) men received appropriate treatment (89.2% vs. 100%, P = 0.003), due to four overtreated HIV(+) men. Excluding AIDS from the CCI still resulted in fewer HIV(+) men receiving appropriate treatment (94.6% vs. 100%, P = 0.03). CONCLUSION: Prostate cancer in HIV(+) men is largely appropriately treated. Under- or overtreatment may occur from difficulties in life expectancy estimation. HIV(+) men may receive more radiotherapy and fewer radical prostatectomies, specifically open radical prostatectomies. IMPACT: Research on HIV/AIDS survival indices and etiologies and outcomes of this prostate cancer treatment disparity in HIV(+) men are needed.

Musumeci, F., S. Schenone, et al. "Hck inhibitors as potential therapeutic agents in cancer and HIV infection." Curr Med Chem. 2015;22(13):1540-64.

Hematopoietic cell kinase (Hck) is a member of the Src-family of non-receptor tyrosine kinases, which plays many roles in signalling pathways involved in the regulation of cell processes. Hck is expressed in cells of hematopoietic origin, specifically myelomonocytic cells and B lymphocytes. It participates in phagocytosis, adhesion, migration, regulation of protrusion formation on cell membrane, lysosome exocytosis, podosome formation and actin polymerization. More importantly from a medicinal chemistry point of view, high levels of Hck are involved in chronic myeloid leukemia and other hematologic tumors. Furthermore, Hck activity has been associated with virus infections including HIV-1. In particular, Hck is activated by the HIV-1 accessory protein Nef, a multifunctional HIV-1 protein that accelerates progression to AIDS and enhances the infectivity of progeny viruses. Nef binding to Hck leads to kinase activation which is important in AIDS pathogenesis. For these reasons, Hck represents a potentially good therapeutic target for the treatment of both specific cancers and HIV infection. This article summarizes Hck biological activities connected with malignancies and HIV infection, many of which have been only recently reported, and presents an overview of the compounds endowed with Hck inhibitory activity, especially focusing on the medicinal chemistry aspect.

Mwanahamuntu, M. H., V. V. Sahasrabuddhe, et al. "Utilization of cervical cancer screening services and trends in screening positivity rates in a 'screen-and-treat' program integrated with HIV/AIDS care in Zambia." PLoS One. 2013 Sep 18;8(9):e74607. doi: 10.1371/journal.pone.0074607. eCollection 2013.

BACKGROUND: In the absence of stand-alone infrastructures for delivering cervical cancer screening services, efforts are underway in sub-Saharan Africa to dovetail screening with ongoing vertical health initiatives like HIV/AIDS care programs. Yet, evidence demonstrating the utilization of cervical cancer prevention services in such integrated programs by women of the general population is lacking. METHODS: We analyzed program operations data from the Cervical Cancer Prevention Program in Zambia (CCPPZ), the largest public sector programs of its kind in sub-Saharan Africa. We evaluated patterns of utilization of screening services by HIV serostatus, examined contemporaneous trends in screening outcomes, and used multivariable modeling to identify factors associated with screening test positivity. RESULTS: Between January 2006 and April 2011, CCPPZ services were utilized by 56,247 women who underwent cervical cancer screening with visual inspection with acetic acid (VIA), aided by digital cervicography. The proportion of women accessing these services who were HIV-seropositive declined from 54% to 23% between 2006-2010, which coincided with increasing proportions of HIV-seronegative women (from 22% to 38%) and women whose HIV serostatus was unknown (from 24% to 39%) (all p-for trend<0.001). The rates of VIA screening positivity declined from 47% to 17% during the same period (p-for trend <0.001), and this decline was consistent across all HIV serostatus categories. After adjusting for demographic and sexual/reproductive factors, HIV-seropositive women

were more than twice as likely (Odds ratio 2.62, 95% CI 2.49, 2.76) to screen VIA-positive than HIV-seronegative women.

Odafe, S., K. Torpey, et al. "Integrating cervical cancer screening with HIV care in a district hospital in Abuja, Nigeria." Niger Med J. 2013 May;54(3):176-84. doi: 10.4103/0300-1652.114590.

BACKGROUND: Human immunodeficiency virus positive (HIV+) women have a higher risk of developing invasive cervical cancer compared with uninfected women. This study aims to document programmatic experience of integrating cervical cancer screening using Visual Inspection and Acetic Acid (VIA) into HIV care as well as to describe patients' characteristics associated with positive VIA findings amongst HIV+ women. MATERIALS AND METHODS: A cross-sectional study analysed routine service data collected at the antiretroviral therapy (ART) and cervical cancer screening services. Our program integrated screening for cervical cancer using VIA technique to HIV care and treatment services through a combination of stakeholder engagement, capacity building for health workers, creating a bi-directional referral between HIV and reproductive health (RH) services and provider initiated counselling and screening for cervical cancer. Information on patients' baseline and clinical characteristics were captured using an electronic medical records system and then exported to Statistical Package for the Social Sciences (SPSS). Logistic regression model was used to estimate factors that influence VIA results. RESULTS: A total of 834 HIV+ women were offered VIA screening between April 2010 and April 2011, and 805 (96.5%) accepted it. Complete data was available for 802 (96.2%) women. The mean age at screening and first sexual contact were 32.0 (SD 6.6) and 18.8 (SD 3.5) years, respectively. VIA was positive in 52 (6.5%) women while 199 (24.8%) had a sexually transmitted infection (STI). Of the 199 who had a STI, eight (4.0%) had genital ulcer syndrome, 30 (15.1%) had lower abdominal pain syndrome and 161 (80.9%) had vaginal discharge syndrome. Presence of lower abdominal pain syndrome was found to be a significant predictor of a positive VIA result (P = 0.001). Women with lower abdominal pain syndrome appeared to be more likely (OR 47.9, 95% CI: 4.8-480.4, P = 0.001) to have a positive VIA result.

Okuma, Y., N. Yanagisawa, et al. "Concomitant chemoradiotherapy and antiretroviral therapy for HIV-infected patients with locoregionally advanced non-small cell lung cancer: benefit and tolerability of treatment in 2 cases." Onkologie. 2013;36(10):586-90. doi: 10.1159/000355162. Epub 2013 Sep 17.

BACKGROUND: Human immunodeficiency virus (HIV)-infected patients are surviving longer since the advent of antiretroviral therapy. Therefore, more patients are developing non-AIDS-defining cancers which increasingly determine mortality. CASE REPORTS: Here we present 2 cases of locally advanced non-small cell lung cancer treated initially with concomitant chemoradiotherapy and antiretroviral therapy. Both patients were male, ages 69 and 66, with known HIV infection and immunologically stable on antiretroviral therapy. Presenting symptoms included superior sulcus tumor with left arm immobility and sensory disturbance in case 1 and right lower bronchus constriction in case 2. Symptoms were controlled by chemoradiotherapy. CONCLUSION: These cases illustrate that intensive anticancer therapy administered to the HIV-infected population can be tolerated even though these patients seem to be too fragile for both chemotherapy and radiotherapy, especially since the potential benefit remains uncertain. Recent improvements in chemoradiotherapy and supportive care have enhanced tolerance for such therapy.

Pertusati, F., K. Hinsinger, et al. "PMPA and PMEA prodrugs for the treatment of HIV infections and human papillomavirus (HPV) associated neoplasia and cancer." Eur J Med Chem. 2014 May 6;78:259-68. doi: 10.1016/j.ejmech.2014.03.051. Epub 2014 Mar 17.

The synthesis and in vitro biological evaluation of novel phosphonamidate and phosphonodiamidate prodrugs of adefovir and tenofovir are reported. The selected synthetic approach from free phosphonic acid via bis-trimethylsilyl ester intermediates affords (L)-alanine ester derivatives in 10-70% yields. When assessed for their anti-HIV activity, all the prodrugs showed submicromolar activity. Noteworthy, the most potent derivative in the adefovir series contained a 5,6,7,8-tetrahydronaphtyl group, herein reported for the first time as an aryl moiety in a ProTide. A pronounced cytostatic activity of the above prodrugs is also reported. Selected compounds were tested for their antiproliferative activity against HPV-transformed cells and they were found significantly more active in comparison to their parent compounds. In this study a slightly improved activity of the adefovir derivatives over those of tenofovir was also noticed. However, no specificity for naturally HPV-transformed cell lines was observed.

Pham, P., A. Landolph, et al. "A biochemical analysis linking APOBEC3A to disparate HIV-1 restriction and skin cancer." J Biol Chem. 2013 Oct 11;288(41):29294-304. doi: 10.1074/jbc.M113.504175. Epub 2013 Aug 26.

Human deoxycytidine deaminase APOBEC3A (Apo3A) acts as an HIV-1 restriction factor in cells of myeloid lineage yet functions separately as a potent mutator for genomic DNA. Apo3A activity and C motif deamination specificity exhibit a striking dependence on pH that reflects these two distinct biological processes. Upon infection of macrophages, HIV-1 induces the formation of autophagosomes, and requires autophagosomes for replication, whereas inhibiting lysosomal fusion indicative of late stage autophagy. Here we show that Apo3A has optimal activity and a strict 5'-YYCR motif specificity in the pH 5.8-6.1 range, characteristic of enclosed autophagosomal membrane compartments, and reflective of the mutation pattern of HIV-1. In contrast to the high activity and narrow specificity of Apo3A at acid pH, a 13-30-fold reduction in specific activity is accompanied by relaxed C deamination specificity at pH 7.4-8. Notably, Apo3A is also expressed in keratinocytes, and is up-regulated in skin lesions. At pH 7.9, we show that Apo3A generates transcription-dependent CC --> TT tandem mutations on the non-transcribed strand, a hallmark signature of skin cancer. The biochemical data taken in conjunction with the biological up-regulation of Apo3A in skin lesions suggests that enzyme-catalyzed deaminations at adjacent C sites followed by normal replication generating CC --> TT mutations provides an alternative molecular basis for the initiation events in skin cancer in contrast to well established pathways in which CC dimers formed in response to UV radiation either undergo nonenzymatic spontaneous deaminations or aberrant replication.

Pillai, V. C., R. A. Parise, et al. "Potential interactions between HIV drugs, ritonavir and efavirenz and anticancer drug, nilotinib--a study in primary cultures of human hepatocytes that is applicable to HIV patients with cancer." J Clin Pharmacol. 2014 Nov;54(11):1272-9. doi: 10.1002/jcph.333. Epub 2014 May 27.

Nilotinib is used to treat chronic myeloid leukemia (CML), and is metabolized by CYP3A. With a black-box warning for QT prolongation, which is exposure dependent, controlling for drug interactions is clinically relevant. Treatments of HIV patients with CML are with HAART drugs, ritonavir and efavirenz, may cause complex drug interactions through CYP3A inhibition or induction. We evaluated the interactions of ritonavir or efavirenz on nilotinib using human hepatocytes and compared these interactions with those of ketoconazole or rifampin, classical CYP3A inhibitor and inducer, respectively. Hepatocytes were treated with vehicle, ritonavir (10 muM), ketoconazole (10 muM), efavirenz (10 muM), or rifampin (10 muM) for 5 days. On day 5, nilotinib (3 muM) was coincubated for an additional 24-48 hours. The concentrations of nilotinib were quantitated in collected samples (combined lysate and medium) by LC-MS.

Polizzotto, M. N., G. Chen, et al. "Leveraging Cancer Therapeutics for the HIV Cure Agenda: Current Status and Future Directions." Drugs. 2015 Sep;75(13):1447-59. doi: 10.1007/s40265-015-0426-6.

Despite effective antiretroviral therapy (ART) and undetectable HIV RNA in the plasma, latent replication-competent HIV persists indefinitely in long-lived cells. Cessation of ART results in rebound of HIV from these persistent reservoirs. While this was thought to be an insurmountable obstacle to viral eradication, recent cases suggest otherwise. To date one patient has been "cured" of HIV and several others have been able to interrupt ART without viral rebound for prolonged periods. These events have sparked renewed interest in developing strategies that will allow eradication of HIV in infected individuals. We review the current knowledge of HIV latency and the viral reservoir, describe the potential utility of emerging cancer therapeutics in HIV cure research with an emphasis on pathways implicated in reservoir persistence, and outline opportunities and challenges in the context of the current clinical trial and regulatory environment.

Ports, K. A., F. Haffejee, et al. "Integrating cervical cancer prevention initiatives with HIV care in resource-constrained settings: A formative study in Durban, South Africa." Glob Public Health. 2015 Feb 5:1-14.

Cervical cancer screening rates remain suboptimal among women in South Africa (SA), where cervical cancer prevalence is high. The rollout of HIV-related services across SA may provide a means to deliver cervical cancer screening to populations with limited access to health care systems. In this mixed methods study, psychosocial factors influencing cervical cancer prevention and perceptions of the provision of Pap smears in HIV care settings were examined. Structured interviews were conducted with women (n = 67) from a municipal housing estate in Durban, SA. Key informants (n = 12) also participated in semi-structured interviews. Findings revealed that participants had low cervical cancer knowledge, but desired more information. Relevant themes included the normalisation of HIV and beliefs that cervical cancer might be worse than HIV. A comprehensive community clinic was desired by most, even if HIV-positive patients were treated there. This study provides important insight into integrating cervical cancer screening with HIV clinics, which may

increase cancer screening among South African women.

Raffetti, E., L. Albini, et al. "Cancer incidence and mortality for all causes in HIV-infected patients over a quarter century: a multicentre cohort study." BMC Public Health. 2015 Mar 12;15:235. doi: 10.1186/s12889-015-1565-0.

BACKGROUND: We aimed to assess cancer incidence and mortality for all-causes and factors related to risk of death in an Italian cohort of HIV infected unselected patients as compared to the general population. METHODS: We conducted a retrospective (1986-2012) cohort study on 16 268 HIV infected patients enrolled in the MASTER cohort. The standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) were computed using cancer incidence rates of Italian Cancer Registries and official national data for overall mortality. The risk factors for death from all causes were assessed using Poisson regression models. RESULTS: 1,195 cancer cases were diagnosed from 1986 to 2012: 700 AIDS-defining-cancers (ADCs) and 495 non-AIDS-defining-cancers (NADCs). ADC incidence was much higher than the Italian population (SIR = 30.8, 95% confidence interval 27.9-34.0) whereas NADC incidence was similar to the general population (SIR = 0.9, 95% CI 0.8-1.1).

Raffetti, E., F. Donato, et al. "The predictive role of NLR and PLR for solid non-AIDS defining cancer incidence in HIV-infected subjects: a MASTER cohort study." Infect Agent Cancer. 2015 Oct 5;10:34. doi: 10.1186/s13027-015-0032-y. eCollection 2015.

BACKGROUND: The neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), two low cost, routinely available inflammatory indices, have been found to be associated with risk of death in patients with solid cancer, in both general population and HIV-positive subjects. However, no study investigated the role of NLR and PLR as predictive of cancer incidence so far. METHODS: The aim of our study was to assess the association of PLR and NLR with risk of developing solid non-AIDS defining cancer (NADC) in HIV-infected subjects. We conducted a multicenter Italian cohort study from 2000 to 2012 including HIV-infected subjects naive at antiretroviral treatment at enrollment. The associations of NLR and PLR with NADC incidence were evaluated by univariate and multivariate analyses using both time independent and time dependent Cox proportional hazard models. RESULTS: Thirteen thousand five hundred fifty-nine patients (73.3 % males) with a mean age of 36.0 years (SD 10.0) were included. The median (inter-quartile range) of NLR and PLR at baseline were 1.47 (1.03-2.17) and 109.9 (79.6-155.3), respectively. During a median follow-up of 3.9 years, 337 subjects had a first diagnosis of solid NADC. The crude and age- and gender-standardized incidence rates were 3.57 and 3.91 per 1000 person-years, respectively. No statistically significant association was found between NLR and PLR and NADC incidence, using multivariate models, including also time-dependent Cox models with a cubic-spline for NLR and PLR. CONCLUSION: This study does not sustain the hypothesis that NRL and PLR may be useful for predicting the risk of cancer in HIV positive subjects.

Robbins, H. A., M. S. Shiels, et al. "Epidemiologic contributions to recent cancer trends among HIV-infected people in the United States." AIDS. 2014 Mar 27;28(6):881-90. doi: 10.1097/QAD.0000000000000163.

OBJECTIVE: HIV-infected people have elevated risk for some cancers. Changing incidence of these cancers over time may reflect changes in three factors: HIV population demographic structure (e.g. age distribution), general population (background) cancer rates, and HIV-associated relative risks. We assessed the contributions of these factors to time trends for 10 cancers during 1996-2010. DESIGN: Population-based registry linkage study. METHODS: We applied Poisson models to data from the U.S. HIV/AIDS Cancer Match Study to estimate annual percentage changes (APCs) in incidence rates of AIDS-defining cancers [ADCs: Kaposi sarcoma, non-Hodgkin lymphoma (NHL), and cervical cancer] and seven non-AIDS-defining cancers (NADCs). We evaluated HIV-infected cancer trends with and without adjustment for demographics, trends in background rates, and trends in standardized incidence ratios (SIRs, to capture relative risk). RESULTS: Cancer rates among HIV-infected people rose over time for anal (APC 3.8%), liver (8.5%), and prostate (9.8%) cancers, but declined for Kaposi sarcoma (1996-2000: -29.3%; 2000-2010: -7.8%), NHL (1996-2003: -15.7%; 2003-2010: -5.5%), cervical cancer (-11.1%), Hodgkin lymphoma (-4.0%), and lung cancer (-2.8%). Breast and colorectal cancer incidence did not change over time. Based on comparison to adjusted models, changing demographics contributed to trends for Kaposi sarcoma and breast, colorectal, liver, lung, and prostate cancers (all $P < 0.01$). Trends in background rates were notable for liver (APC 5.6%) and lung (-3.2%) cancers.

Sengayi, M., C. Babb, et al. "HIV testing and burden of HIV infection in black cancer patients in Johannesburg, South Africa: a cross-sectional study." BMC Cancer. 2015 Mar 18;15:144. doi: 10.1186/s12885-015-1171-7.

BACKGROUND: HIV infection is a known risk factor for cancer but little is known about HIV testing patterns and the burden of HIV infection in cancer patients. We did a cross-sectional analysis to identify predictors of prior HIV testing and to quantify the burden of HIV in black cancer patients in Johannesburg, South Africa. METHODS: The Johannesburg Cancer Case-control Study (JCCCS) recruits newly-diagnosed black cancer patients attending public referral hospitals for oncology and radiation therapy in Johannesburg . All adult cancer patients enrolled into the JCCCS from November 2004 to December 2009 and interviewed on previous HIV testing were included in the analysis. Patients were independently tested for HIV-1 using a single ELISA test . The prevalence of prior HIV testing, of HIV infection and of undiagnosed HIV infection was calculated. Multivariate logistic regression models were fitted to identify factors associated with prior HIV testing. RESULTS: A total of 5436 cancer patients were tested for HIV of whom 1833[33.7% (95% CI=32.5-35.0)] were HIV-positive. Three-quarters of patients (4092 patients) had ever been tested for HIV. The total prevalence of undiagnosed HIV infection was 11.5% (10.7-12.4) with 34% (32.0-36.3) of the 1833 patients who tested HIV-positive unaware of their infection. Men >49 years [OR 0.49(0.39-0.63)] and those residing in rural areas [OR 0.61(0.39-0.97)] were less likely to have been previously tested for HIV. Men with at least a secondary education [OR 1.79(1.11-2.90)] and those interviewed in recent years [OR 4.13(2.62 - 6.52)] were likely to have prior testing. Women >49 years [OR 0.33(0.27-0.41)] were less likely to have been previously tested for HIV. In women, having children <5 years [OR 2.59(2.04-3.29)], hormonal contraceptive use [OR 1.33(1.09-1.62)], having at least a secondary education [OR:2.08(1.45-2.97)] and recent year of interview [OR 6.04(4.45-8.2)] were independently associated with previous HIV testing. CONCLUSIONS: In a study of newly diagnosed black cancer patients in Johannesburg, over a third of HIV-positive patients were unaware of their HIV status. In South Africa black cancer patients should be targeted for opt-out HIV testing.

Shcherba, M., J. Shuter, et al. "Current questions in HIV-associated lung cancer." Curr Opin Oncol. 2013 Sep;25(5):511-7. doi: 10.1097/CCO.0b013e328363dfdb.

PURPOSE OF REVIEW: In this review, we explore current questions regarding risk factors contributing to frequent and early onset of lung cancer among populations with HIV infection, treatment, and outcomes of lung cancer in HIV-infected patients as well as challenges in a newly evolving era of lung cancer screening. RECENT FINDINGS: Lung cancer, seen in three-fold excess in HIV-infected populations, has become the most common non-AIDS defining malignancy in the highly active antiretroviral therapy era. HIV-associated lung cancer appears to be associated with young age at diagnosis, cigarette smoking, advanced stage at presentation, and a more aggressive clinical course. There is no unified explanation for these observations, and aside from traditional risk factors, HIV-related immunosuppression and biological differences might play a role. In addition to smoking cessation interventions, screening and early cancer detection in HIV-infected populations are of high clinical importance, although evidence supporting lung cancer screening in this particularly high-risk subset is currently lacking, as are prospective studies of lung cancer therapy.

Sichanh, C., F. Quet, et al. "Knowledge, awareness and attitudes about cervical cancer among women attending or not an HIV treatment center in Lao PDR." BMC Cancer. 2014 Mar 6;14:161. doi: 10.1186/1471-2407-14-161.

BACKGROUND: Cervical cancer is the first female cancer in Lao PDR, a low-income country with no national screening and prevention programs for this human papillomavirus (HPV) associated pathology. HIV-infected women have a higher risk of persistent oncogenic HPV infection.The purpose of this study was to determine the knowledge, awareness and attitudes about cervical cancer among Lao women attending or not an HIV treatment center, in order to understand if this attendance had offered an opportunity for information and prevention. METHODS: A cross-sectional case-control survey was conducted in three provinces of Lao PDR, Vientiane, Luang Prabang and Savannakhet. Cases were 320 women aged 25 to 65, living with HIV and followed in an HIV treatment center. Controls were 320 women matched for age and place of residence, not attending an HIV treatment center. RESULTS: Cases had a greater number of sexual partners and used condoms more often than controls. Only 36.6% of women had consulted a gynecologist (47.5% among cases and 25.6% among controls, $p < 0.001$) and 3.9% had benefited from at least one Pap smear screening (5.6% cases and 2.2% controls, $p = 0.02$). The average knowledge score was 3.5 on a 0 to 13 scale, significantly higher in cases than in controls ($p < 0.0001$). Despite having a lower education level and economic status, the women living with HIV had a better knowledge about cervical cancer and were more aware than the controls of the risk of developing such a cancer (35.9% vs. 8.4%, $p = 0.0001$). The main source of information was healthcare professionals.

The main reasons for not undergoing Pap smear were the absence of symptoms and the default of medical injunction for cases, the lack of information and ignorance of screening usefulness for controls. CONCLUSION: In Lao PDR, routine consultation in HIV treatment centers is not enough harnessed to inform women of their high risk of developing cervical cancer, and to perform screening testing and treatment of precancerous lesions. Implementing this cost-effective strategy could be the first step toward a national prevention program for cervical cancer.

Sigel, K., K. Crothers, et al. "Prognosis in HIV-infected patients with non-small cell lung cancer." Br J Cancer. 2013 Oct 1;109(7):1974-80. doi: 10.1038/bjc.2013.545. Epub 2013 Sep 10.

BACKGROUND: We conducted a population-based study to evaluate whether non-small cell lung cancer (NSCLC) prognosis was worse in HIV-infected compared with HIV-uninfected patients. METHODS: Using the Surveillance, Epidemiology and End Results (SEER) registry linked to Medicare claims, we identified 267 HIV-infected patients and 1428 similar controls with no evidence of HIV diagnosed with NSCLC between 1996 and 2007. We used conditional probability function (CPF) analyses to compare survival by HIV status accounting for an increased risk of non-lung cancer death (competing risks) in HIV-infected patients. We used multivariable CPF regression to evaluate lung cancer prognosis by HIV status adjusted for confounders. RESULTS: Stage at presentation and use of stage-appropriate lung cancer treatment did not differ by HIV status. Median survival was 6 months (95% confidence interval (CI): 5-8 months) among HIV-infected NSCLC patients compared with 20 months (95% CI: 17-23 months) in patients without evidence of HIV. Multivariable CPF regression showed that HIV was associated with a greater risk of lung cancer-specific death after controlling for confounders and competing risks. CONCLUSION: NSCLC patients with HIV have a poorer prognosis than patients without evidence of HIV. NSCLC may exhibit more aggressive behaviour in the setting of HIV.

Stefan, D. C. "Effect of HIV infection on the outcome of cancer therapy in children." Lancet Oncol. 2014 Nov;15(12):e562-7. doi: 10.1016/S1470-2045(14)70313-4. Epub 2014 Oct 26.

SUMMARY: Systematic studies comparing the outcomes of cancer treatment between children with and without HIV are scarce. The literature seems to suggest that, even with present therapeutic advances, prognosis is poor with HIV infection. The aim of this Review was to assess scientific publications from 1990 to present, addressing the difficulties associated with treatment of cancer in children with AIDS and the adaptive changes in therapy. Although much progress has been achieved, further research is needed about antiretroviral and cytotoxic drug interactions, the optimum use of supportive therapy including stem cells and bone marrow transplant, the timing of the initiation of highly active antiretroviral therapy, and the optimum use of protease inhibitors.

Suneja, G., M. Boyer, et al. "Cancer Treatment in Patients With HIV Infection and Non-AIDS-Defining Cancers: A Survey of US Oncologists." J Oncol Pract. 2015 May;11(3):e380-7. doi: 10.1200/JOP.2014.002709. Epub 2015 Apr 14.

PURPOSE: HIV-infected individuals with non-AIDS-defining cancers are less likely to receive cancer treatment compared with uninfected individuals. We sought to identify provider-level factors influencing the delivery of oncology care to HIV-infected patients. METHODS: A survey was mailed to 500 randomly selected US medical and radiation oncologists. The primary outcome was delivery of standard treatment, assessed by responses to three specialty-specific management questions. We used the chi(2) test to evaluate associations between delivery of standard treatment, provider demographics, and perceptions of HIV-infected individuals. Multivariable logistic regression identified associations using factor analysis to combine several correlated survey questions. RESULTS: Our response rate was 60%; 69% of respondents felt that available cancer management guidelines were insufficient for the care of HIV-infected patients with cancer; 45% never or rarely discussed their cancer management plan with an HIV specialist; 20% and 15% of providers were not comfortable discussing cancer treatment adverse effects and prognosis with their HIV-infected patients with cancer, respectively; 79% indicated that they would provide standard cancer treatment to HIV-infected patients. In multivariable analysis, physicians comfortable discussing adverse effects and prognosis were more likely to provide standard cancer treatment (adjusted odds ratio, 1.52; 95% CI, 1.12 to 2.07). Physicians with concerns about toxicity and efficacy of treatment were significantly less likely to provide standard cancer treatment (adjusted odds ratio, 0.67; 95% CI, 0.53 to 0.85). CONCLUSION: Provider-level factors are associated with delivery of nonstandard cancer treatment to HIV-infected patients. Policy change, provider education, and multidisciplinary collaboration are needed to improve access to cancer treatment.

Thorsteinsson, K., S. Ladelund, et al. "Incidence of cervical dysplasia and cervical cancer in women living

with HIV in Denmark: comparison with the general population." HIV Med. 2015 Jun 8. doi: 10.1111/hiv.12271.

OBJECTIVES: Women living with HIV (WLWH) are reportedly at increased risk of invasive cervical cancer (ICC). A recent publication found that WLWH in Denmark attend the national ICC screening programme less often than women in the general population. We aimed to estimate the incidence of cervical dysplasia and ICC in WLWH in Denmark compared with that in women in the general population. METHODS: We studied a nationwide cohort of WLWH and a cohort of 15 age-matched women per WLWH from the general population for the period 1999-2010. Pathology samples were obtained from The Danish Pathology Data Bank, which contains nationwide records of all pathology specimens. The cumulative incidence and hazard ratios (HRs) for time from inclusion to first cervical intraepithelial neoplasia (CIN)/ICC and time from first normal cervical cytology result to first CIN/ICC were estimated. Sensitivity analyses were performed to include prior screening outcome, screening intensity and treatment of CIN/ICC in the interpretation of results. RESULTS: We followed 1140 WLWH and 17 046 controls with no prior history of ICC or hysterectomy for 9491 and 156 865 person-years, respectively. Compared with controls, the overall incidences of CIN1 or worse (CIN1+), CIN2+ and CIN3+, but not ICC, were higher in WLWH and predicted by young age and a CD4 count < 200 cells/muL. In women with normal baseline cytology, incidences of CIN1+ and CIN2+ were higher in WLWH. However, when we compared subgroups of WLWH and controls where women in both groups were adherent to the national ICC screening programme and had a normal baseline cytology, incidences of CIN and ICC were comparable. CONCLUSIONS: Overall, WLWH developed more cervical disease than controls. Yet, in WLWH and controls adherent to the national ICC screening programme and with normal baseline cytology, incidences of CIN and ICC were comparable.

Torres, H. A. and V. Mulanovich "Management of HIV infection in patients with cancer receiving chemotherapy." Clin Infect Dis. 2014 Jul 1;59(1):106-14. doi: 10.1093/cid/ciu174. Epub 2014 Mar 18.

The optimal antiretroviral therapy (ART) regimen for human immunodeficiency virus (HIV)-infected patients with cancer remains unknown, as clinical trials are lacking and published data are insufficient to guide recommendations. When concomitant use of chemotherapy and ART is anticipated, overlap of toxic effects and drug-drug interactions between chemotherapy and ART may alter the optimal choice of ART. Prospective studies are urgently needed to further define the toxic effects of combined chemotherapy and ART in HIV-positive cancer patients. Such studies should aid the development of guidelines for treatment of this population. For now, clinicians should individualize decisions regarding treatment of HIV according to clinical and laboratory findings, cancer treatment plan (chemotherapy, radiotherapy, or surgery), liver or renal disease, potential adverse drug effects (eg, rash, gastrointestinal intolerance, bone marrow suppression), and patient preference. This review focuses on what infectious disease specialists need to know to select the most appropriate ART regimens for patients receiving chemotherapy.

Zohar, M. and B. Micha "Cancer Incidence in People Living with HIV/AIDS in Israel, 1981-2010." AIDS Res Hum Retroviruses. 2015 Sep;31(9):873-81. doi: 10.1089/AID.2015.0022. Epub 2015 Jun 15.

Antiretroviral therapy (ART) improved the survival of people living with HIV/AIDS (PLWHA) and decreased HIV-related morbidities. This study assesses the cancer incidence of all adult PLWHA in Israel by transmission routes before and after 1996. This cohort study was based on cross-matching the National HIV/AIDS and Cancer Registries of all HIV/AIDS and cancer cases reported from 1981 to 2010 with the National civil census. PLWHA were followed-up until cancer diagnosis, death, leaving Israel, or 2010, whichever occurred first. Cancer incidence was adjusted for age, and compared with the National incidence. Of all 5,154 PLWHA followed-up for 36,296 person-years, 362 (7.0%) developed cancer (997.4 cases per 100,000 person-years). Higher hazard ratios to develop cancer were demonstrated among older PLWHA, Jewish people, and intravenous drug users. Cancer incidence among PLWHA was higher in the pre-ART period than after 1997 (1,232.0 and 846.7 cases per 100,000 person-years, respectively). The incidence of AIDS-defining cancers was higher than non-AIDS-defining malignancies, and higher in the pre-ART than the post-ART period (777.0 and 467.2 cases per 100,000 person-years, respectively), while the incidence of non-AIDS-defining cancers showed the opposite trend (376.5 and 455.0 cases per 100,000 person-years, respectively). The incidence of AIDS-defining and non-AIDS-defining cancers declined between the pre-ART and the post-ART period by 2.0 to 3.4 times. PLWHA had higher rates of malignancies than the general population. In conclusion, cancer incidence among PLWHA was associated with age, and declined after ART introduction; yet it was higher than that of the general population. PLWHA may benefit from age-related cancer screening, increased

adherence to ART, and reduction of environmental oncogenes.

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