HIV and Cancer Risk in Context of High ART Coverage in Botswana

Scott Dryden-Peterson,[1,2,3] Neo Tapela, [1,2,4] Isaac Nkele,[1] Oaitse John,[1] Gita Suneja,[5] Surbhi Grover,[6] Memory Bvochora-Nsingo,[7]
Malebogo Pusoentsi,[4] Joseph Makhema,[1] Mompati Mmalane,[1] Mukendi Kayembe,[4] Shahin Lockman[1,2,3]

[1]Botswana Harvard AIDS Inst., Gaborone; [2]Brigham and Women's Hosp, Boston; [3]Harvard T.H. Chan Sch. of Pub. Health, Boston; [4]Botswana Ministry of Health, Gaborone; [5]Duke University, Durham, NC, [6]University of Pennsylvania, Philadelphia, PA, [7]Gaborone Private Hospital, Gaborone;

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Background:

Antiretroviral therapy (ART) has reduced incidence of Kaposi sarcoma (KS) and several types of lymphoma, however impact of ART on risk of development other cancers is less certain.

- Early ART in START trial (Borges *et al*. CID 2016) led to large reductions in risk of KS and non-Hodgkin lymphoma, but no apparent affect on risk of other malignancies (including HPV-associated cancers)
- Expansion of ART in Botswana (2003-2008) (Dryden-Peterson *et al.* PLoS One 2016) was associated with increased incidence of HPV-associated cancers

Community surveys (2013-2015) indicated that Botswana nearly achieved the UNAIDS 90-90-90 targets (Gaolathe *et al.* Lancet HIV 2016)

Objective:

We sought to estimate the excess risk for leading cancers among people living with HIV in Botswana in the setting of high ART coverage.

Methods:

Ongoing Thabatse Cancer Cohort

- Prospective enrollment of consenting patients presenting for specialized oncology care at the four principal treatment centers in Botswana: Princess Marina Hospital (Oct 2010 to Feb 2018), Gaborone Private Hospital (Nov 2012 to Feb 2018), Nyangabgwe Referral Hospital (Jan 2015 to Feb 2018), Bokamoso Private Hospital (Apr 2016 to Feb 2018)
- Cancer diagnoses abstracted from clinical and pathology records, patients HIV tested if not known positive

Analytic approach

- Utilized population from public Botswana AIDS Incidence Survey (2013) to determine age- and sex-specific estimates of HIV prevalence
- Following finding no substantive differences in time to treatment or cancer stage, we assumed that conditional on age, sex and cancer type, patients with and without HIV had equal likelihood of enrollment
- We used indirect standardization to estimate age- and sex-standardized incidence ratios (SIR) for leading cancer types and for all cancers combined, and to estimate proportion of cancers attributable to HIV (PAF)

Results:

- 3007 patients enrolled, 108 (3.6%) excluded due to uncertain HIV status

Table 1: Participant characteristics.

	HIV Status	
	HIV-Infected (N = 1642)	HIV-Uninfected (N = 1265)
Age, years, median (IQR)	44.1 (37.8,51.4)	59.4 (48.3,69.5)
Male Sex, no. (%)	509 (31%)	404 (32%)
Primary school education only, no. (%)	717 (44%)	793 (63%)
Personal income >$50/month, no. (%)	862 (53%)	747 (59%)
Electricity in home, no. (%)	1058 (65%)	931 (74%)
Household with indoor toilet, no. (%)	528 (32%)	523 (42%)
Rural residence, no. (%)	1295 (79%)	1065 (85%)
Ever smoked, no. (%)	435 (27%)	287 (23%)
Current alcohol use, no. (%)	168 (10%)	104 (8%)
Histology or cytology diagnosis, no. (%)	1388 (89%)	1142 (98%)
Cancer stage		
- I, no. (%)	189 (15%)	96 (10%)
- II, no. (%)	521 (41%)	246 (26%)
- III, no. (%)	330 (26%)	335 (35%)
- IV, no. (%)	232 (18%)	274 (29%)
On ART at time cancer diagnosis, no. (%)	1291 (83%)	—
Years of ART prior to cancer, median (IQR)	4.96 (4.4, 8.9)	—
Current ART regimen		
- TDF/FTC/EFV, no. (%)	600 (39%)	—
- ZDV/3TC/EFV, no. (%)	392 (25%)	—
- PI, no. (%)	70 (5%)	—
- TDF/FTC/DTG, no. (%)	50 (3%)	—
- Other or Unknown, no. (%)	179 (12%)	—
- None, no. (%)	261 (17%)	—
CD4 count (per cells/μL), median (IQR)	339.0 (209, 515)	—
Recent HIV viral load		
- >1000 copies, no. (%)	65 (4%)	—
- <1000 copies, no. (%)	1009 (61%)	—
- not available, no. (%)	568 (35%)	—

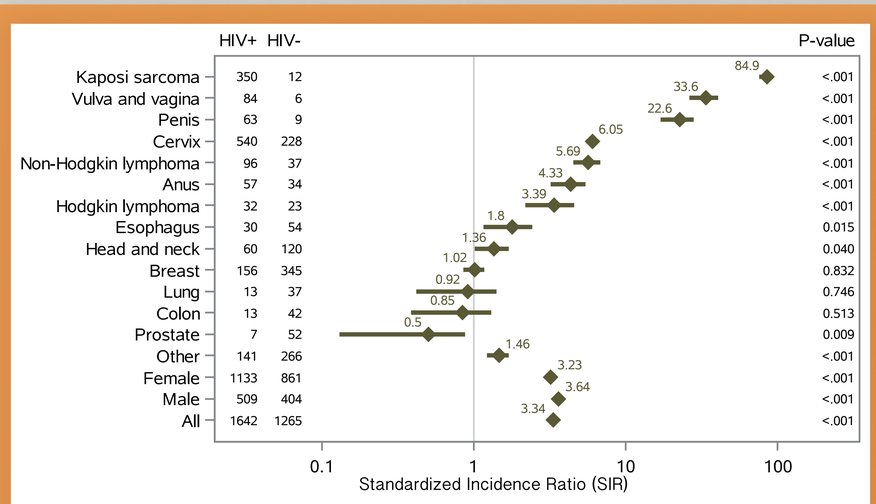


Figure 1: Age- and sex-standardized incidence ratios for leading cancer types in Botswana, HIV-infected compared with HIV-uninfected adults.
Cancer types with fewer than 50 cases were combined in Other.

Population fraction attributable to HIV: 39.5% (95% CI 37-42)

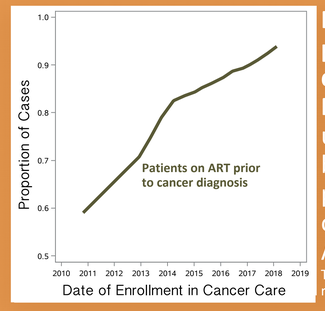


Figure 2: ART use prior to cancer diagnosis among PLWH. Since universal ART became Botswana policy in 2016, 91% of patients received ART prior to cancer.
Trend estimated using local regression (LOESS).

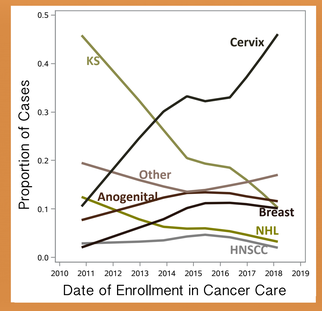


Figure 3: Longitudinal distribution of cancer types among PLWH.
Trends estimated using local regression (LOESS). Anogenital group includes penile, anal, vaginal, and vulvar squamous cell carcinomas. KS indicates Kaposi sarcoma, and HNSCC indicates squamous cell carcinoma of the pharynx, hypopharynx, oropharynx, tongue, and oral cavity.

Limitations:

- Despite standardizing on age and sex, residual confounding possible (e.g. smoking)
- Currently unable to provide separate estimates for risk by duration of ART or CD4 strata which would inform long term trends
- Cancers treated primarily with surgery alone (e.g. conjunctival, limited stage colon or other solid malignancies) are under-represented
- Majority of cases developed in PLWH with CD4<350 prior to ART initiation, so may not represent burden with earlier ART initiation

Conclusions:

- High ART utilization has led to substantial change in distribution of cancers
- Among PLWH, over 90% of cancers arise among people receiving long-term ART
- Despite high ART coverage, HIV infection is dominant risk for development of cancer with 40% of cancers attributable to HIV

Botswana Harvard AIDS Institute Partnership for HIV Research and Education · Brigham and Women's Hospital · Harvard T.H. Chan School of Public Health · Botsogo Botswana Oncology Global Outreach

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For more information contact:
Scott Dryden-Peterson, MD MSc
sldrydenpeterson@bwh.harvard.edu
François-Xavier Bagnoud 306
651 Huntington Avenue
Boston, MA 02115