



# Will the hard-won gains in the battle against HIV be lost on the battleground of HPV?

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The inception of HIV treatment programmes in sub-Saharan Africa (SSA) was marked by many challenges. It was clear that large numbers of people were going to require treatment and the question was, how were public health services going to deliver in the face of seemingly insurmountable obstacles? There were limited resources in both the human and health financing sectors, denialism on the part of politicians, and paralysing stigma for those living with HIV. Nevertheless, the battle began! Botswana was the first country in Africa to establish a national HIV treatment programme in 2002, with other countries rapidly following suit and by 2008, over 5 million people in the sub-continent had access to antiretroviral treatment (ART).

## Historical challenges of HIV programmes

Challenges became evident as HIV treatment programme roll-outs continued - centralised treatment centres were difficult to access for people residing in distant communities; diagnostic tests were expensive; ART regimens were toxic and often associated with stigmatising side effects; there was limited access to laboratory monitoring for biochemical and metabolic side effects and HIV viral loads. Two decades later, a unified approach by health care communities, people living with HIV (PLWH), governments, non-governmental organisations and civil society has changed the playing field!

## Success of HIV treatment programmes

67% of the 38.4 million of the global population living with HIV live in SSA, over 80% access ART<sup>1</sup> and HIV viral suppression rates are reported to be between 73% to 95%.<sup>2</sup> The roll-out of the test and treat strategy has resulted in widespread access to HIV services across populations. The standard HIV treatment is now a single tablet regimen, with a markedly improved side effects profile, annual HIV viral load monitoring is within the reach of most programmes and long-acting injectable ART is on the horizon.

The life expectancy for PLWH in the region is approaching that of the general population and elimination agendas for mother to child transmission are being achieved. The critical issue being discussed in public health programmes is now HIV prevention. For HIV elimination targets to be reached, public health programmes must be intentional and focused on prevention strategies. We are winning the battle against HIV!

## Emerging challenges

The maturation of the HIV epidemic together with successful HIV treatment programmes translates into people growing

old with HIV. The increased life expectancy of PLWH results in an increase of ageing associated, non-communicable diseases (NCDs) which include cardiovascular, bone, metabolic, neurodegenerative disorders and cancer.<sup>3</sup> Many HIV treatment programmes are ill equipped to screen for, diagnose and manage these NCDs. How important is it for HIV clinicians to address these issues? The answer to this depends on the understanding of the magnitude of the problem.

## Cancer in PLWH

We will now turn our attention to cancer in PLWH. On a global scale, cancer is the second leading cause of death after cardiovascular disease. In SSA there were an estimated 801,392 new cancer cases and 520,158 cancer deaths in 2020.<sup>5</sup> In PLWH, the incidence of cancer is higher than in the general population and is reported to be increasing. In a South African modelling study, Finestone et al showed an increased forecast incidence of cancer in PLWH when compared to the general population.<sup>4</sup> The South African HIV Cancer Match Study included over 5 million PLWH, and describe 29,580 incident cancer diagnoses, with exponential increases in both men and women over 40 years of age. These cancers may be broadly categorised into infection-related and infection-unrelated. The global burden of infection-related cancers was 15.4%, and in SSA it was over 30%. This makes infections one of the leading causes of cancer in the region.<sup>6</sup>

Infectious agents are modifiable causes of cancer and 11 infectious pathogens have been classified as group 1 carcinogens by the International Agency for Research in Cancer (IARC). The 4 most important are a bacterium, *Helicobacter pylori*, and 3 viruses – human papillomavirus (HPV), hepatitis B and hepatitis C.<sup>7</sup> These 4 agents, also known as oncogenic pathogens, are responsible for 90% of infection-related cancers worldwide.<sup>6</sup>

## HPV-attributable cancer

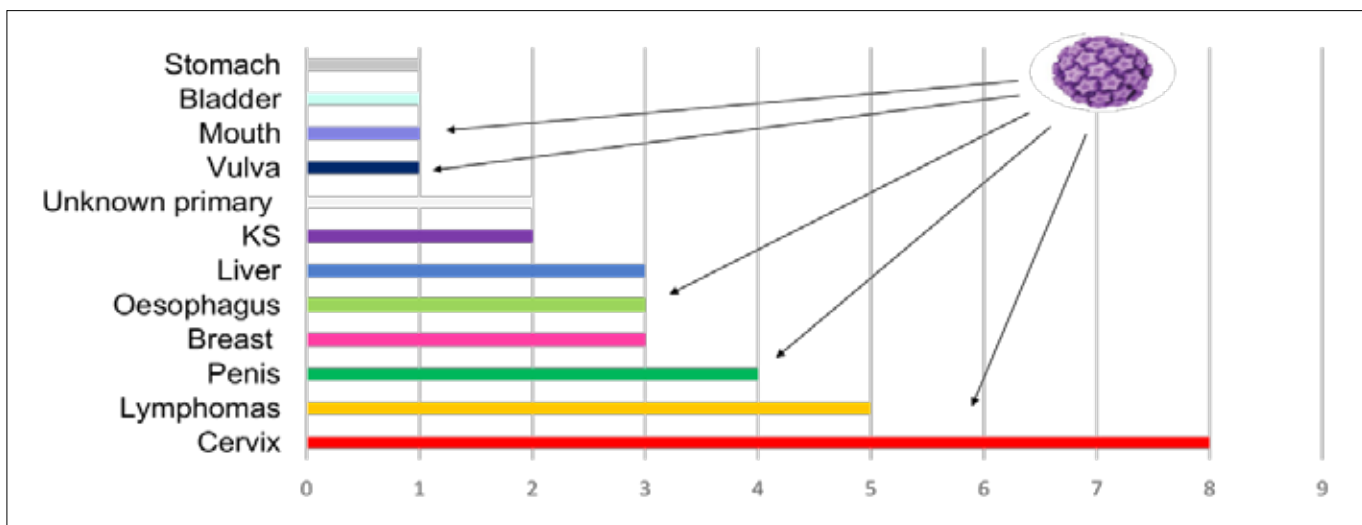
The most important oncogenic pathogen in SSA is HPV, with estimated prevalence rates in women of approximately 24%. In women living with HIV (WLWH) the reported rates are higher reaching 80% in Zambia and 90% in Uganda. The age standard incidence rate (ASIR) of HPV-attributable cancers is 19.3 cases per 100,000 person years giving the region the highest ASIR of HPV-attributable cancer of all global regions, with an estimated 120,000 cases in 2018.<sup>9</sup> HPV is the oncogenic pathogen in over 90% of cervical and anal cancers,

70% of vulvar and vaginal cancers, 60% of penile cancers, and between 60 and 70% of oropharyngeal cancers.<sup>6</sup> HPV-attributable cancers are found in both men and women, but women are disproportionately affected, with cervical cancer (CC) the best characterised. The SSA region has the highest burden of CC globally with an ASIR of 31.0 per 100,000 women and remains the leading cause of cancer and cancer-related deaths in women in the region, and it is important to note that WLWH are 5 times more likely to develop CC than their uninfected peers.<sup>8</sup>

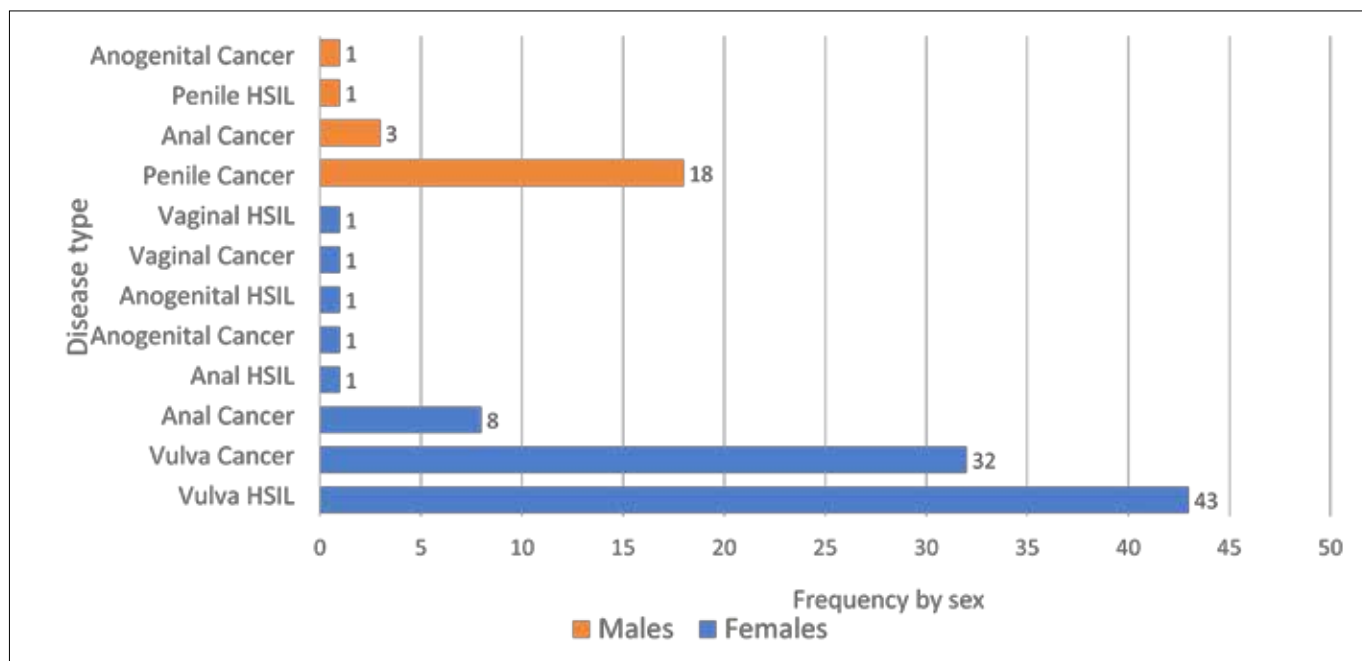
Other HPV-attributable cancers are increasing, and numbers vary by country. The variation may well be due to diagnostic challenges and limited reporting by cancer registries in some countries. Data from a cohort of PLWH in Zimbabwe show that 50% of all cancer-related deaths in 2022 were due to HPV-attributable cancers,<sup>10</sup> see **Figure 1**.

Cancer due to infection with HPV is largely preventable by vaccination and the World Health Organisation (WHO) has set ambitious targets to fully vaccinate 90% of girls before 15 years of age. Many SSA countries are falling behind and the recent COVID-19 pandemic retarded progress on many fronts. In Zimbabwe, the national HPV vaccination campaign was launched in 2018, and data reports 67% coverage for the first dose and 40% for the last dose.<sup>12</sup> Other countries have been slower in the introduction of HPV vaccination campaigns and work is required to identify the bottlenecks and address them.

Most countries in SSA have operationalised secondary prevention programmes for cervical cancer using visual inspection methods which can detect early disease and, where delivered in a ‘see-and-treat’ approach, may arrest disease progression. However, as the data supports, coverage



**Figure 1. Mortality by Cancer Diagnosis in a Zimbabwean Cohort of PLWH in 2022. 50% of all cancer deaths caused by HPV-attributable cancers** Data from the same cohort report the diagnosis of other HPV-attributable cancers<sup>11</sup>, see **Figure 2**.



**Figure 2. HPV-associated cancers – Looking beyond the cervix: experiences from a Zimbabwean cohort of people living with HIV.** HSIL: high grade squamous intraepithelial neoplasia (pre-cancer). Anogenital: defined as involving more than 1 anatomical site.

and uptake of these interventions is sub-optimal, and many women still present at an advanced stage of disease. Cancer treatment outcomes in PLWH with early stage are good, but treatment with surgical interventions and chemoradiation is expensive and inaccessible for most women in SSA.

### Conclusion and Recommendations

The increasing burden of infection-related cancer in PLWH demands urgent attention from HIV clinicians. These are largely preventable conditions and HIV programmes must consider how effective screening programmes can be introduced as part of routine care.

HPV-attributable cancers are diseases of public health concern and require the urgent attention of all the stakeholders in HIV programming - PLWH, health care professionals, civil society, and governments. The following is a list of strategic actions that require urgent implementation:

- Address the knowledge gaps around HPV and the infection-related cancers at all levels – grassroots communities, health care work force, health systems, policy makers in ministries of health.
- Create the demand for cancer screening and diagnostic services by information dissemination and debunking the myths surrounding infection-related cancer.
- Increased advocacy for the widespread roll out of HPV vaccination to girls and boys, no one should be left behind!
- The use of vaccine mop up campaigns for individuals who were missed in routine vaccination programmes. This strategy has been used for polio, measles, and other infectious diseases.
- The introduction of the WHO-recommended high performance screening test, HPV DNA, as the primary screening test for CC.
- Ensuring that a thorough annual physical examination is done for PLWH as part of routine care, thereby facilitating the detection of early, potentially curable disease.

HPV-attributable cancers are threatening the success of HIV treatment programmes in SSA, and the health care sector

can no longer remain silent! We have strategies that we can employ against this enemy. We can win the war and assist in securing the future for PLWH in our continent, in our lifetime!

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