HPV Vaccination among People Living with HIV

Dr. Betty Njoroge, MBChB, MPH

Center for Clinical Research (CCR), KEMRI

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Background

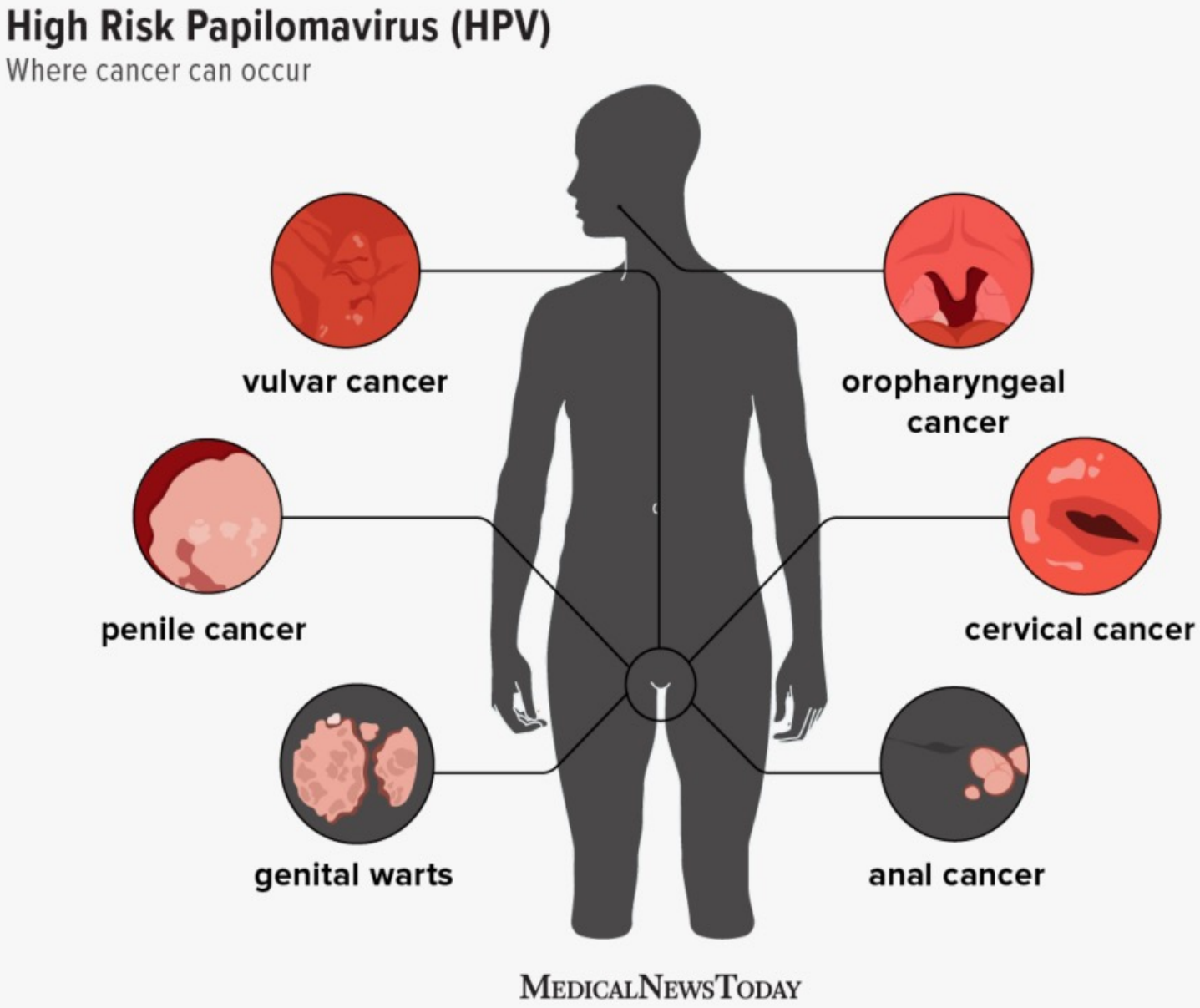
- The human papillomavirus (HPV) is a highly contagious and prevalent virus that is primarily sexually transmitted
- More than 200 types of HPV exist and are categorized as low-risk and high-risk HPV.
- Low-risk types do not cause cancer and are treatable.
- High-risk (HR) oncogenic HPV types causes six types of cancer
- Persons with HIV are at increased risk of HPV infection, HPV disease, and HPV-related cancers compared to HIV negative persons.
- Women living with HIV have higher HPV prevalence and cervical cancer incidence than HIV-negative women, partly due to HIV's modifying effect on HPV pathogenesis

Men & HPV Infection

- Globally, prevalence of HPV infection in men is higher than women but less persistent
- MSM living with HIV have the highest incidence of anal hrHPV, followed by MSM without HIV
- Oropharyngeal and anal cancers are more common among men than women

Disease	**Attributable HPV**
Anogenital warts	~ 100%
Anal cancer	71%
Oropharyngeal cancer	70%
Penis	45%

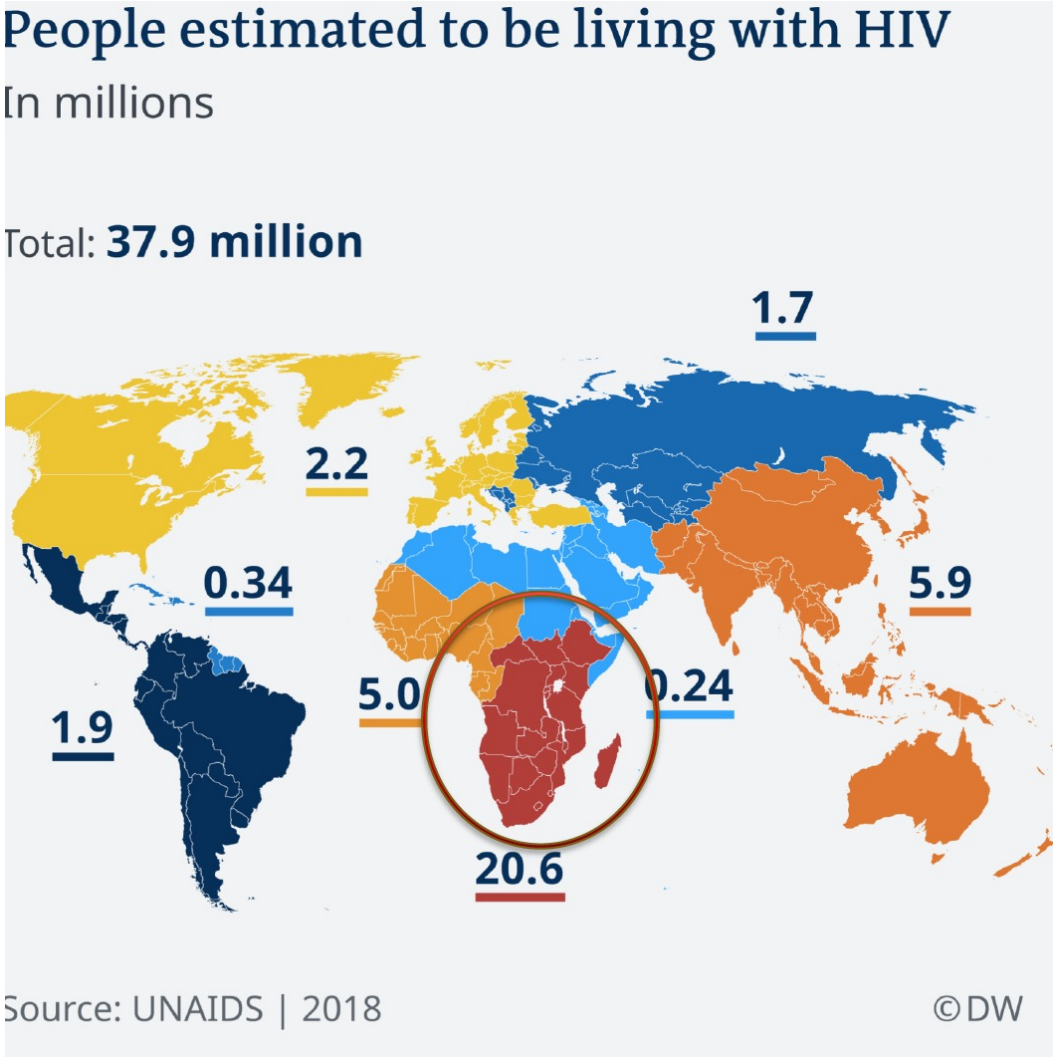
Wei F. Clifford GM. Clin Infect Dis 2023 ; Serrano B, L Bruni Obstet & Gyanec 2018; De Sanjose, Lancet Oncology



HPV can cause six types of cancer:

- **Cervical cancer**
- **Anal cancer**
- **Oropharyngeal cancer**
- **Penile cancer**
- **Vaginal cancer**
- **Vulvar cancer**

Geographic Overlap: HIV and cervical cancer incidence



Women living with HIV have

- ✓ Higher prevalence of high-risk-HPV (hr-HPV) coinfection
- ✓ Higher rates of HPV persistence
- ✓ Faster progression from hr HPV infection to intraepithelial lesion to invasive cancer

HPV Vaccines

HPV vaccines are highly effective and safe

- Human papillomavirus (HPV) vaccines are vaccines that prevent infection by certain types of human papillomavirus (HPV)
- There are four licensed vaccines against HPV:
  - Bivalent (2vHPV) - protects against HPV types 16 & 18
  - Quadrivalent (4vHPV) - protects against HPV types 6, 11, 16 & 18
  - 9-valent (9vHPV) - protects against HPV types HPV 6, 11, 16, 18, 31, 33, 45, 52, 58
- All HPV vaccines protect against at least HPV types 16 and 18, which cause the greatest risk of cervical cancer.

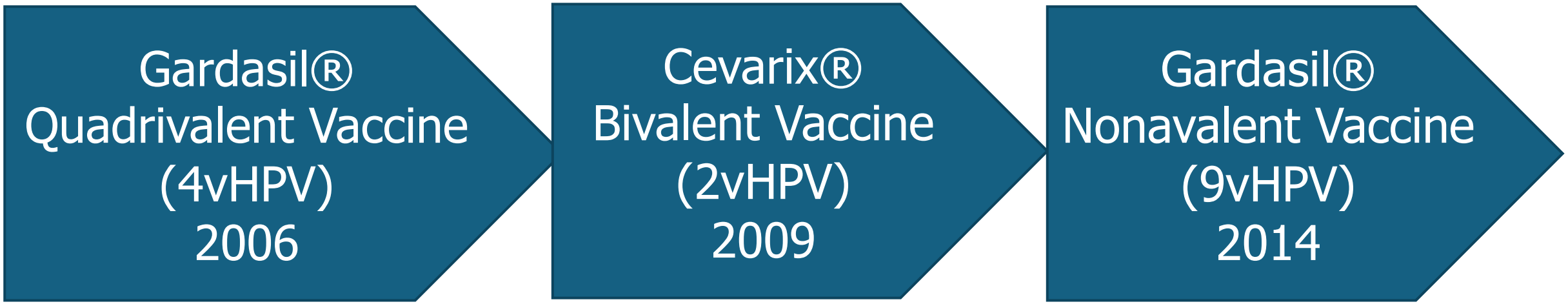
Schiller JT, Castlellsaque X, Garland S. Vaccine 2012, E.Jaora NEJM 2015, Harper D, *et al. Lancet* 2004; 364:1757–1765;, Harper D, *et al*. *Lancet* 2006; 367:1247–1255; GlaxoSmithKline Vaccine HPV-007 Study Group*. Lancet* 2009; 374:1975–1985

HPV Vaccines

- HPV vaccines offer protection against warts, penile or anal cancer, and prevent transmission to females.

- They additionally prevent some genital warts, with the quadrivalent and nonavalent vaccines that protect against HPV types HPV-6 and HPV-11 providing greater protection.

HPV Vaccines FDA Approval timelines



- Approval and use of HPV vaccines commences in 2006
- The vaccines have been in market and used for over 14 years
- And used in research settings for over 20 years

In 2018 the FDA expanded the approved use of the 9-valent vaccine to include women and men aged 27 through 45 years

HPV Vaccination among People Living with HIV

Immunogenicity & Safety

- **Safety:**
  - HPV vaccines have the same safety profile in PLWH as in the general population
  - Vaccination has no impact on CD4+ T cell count, HIV viral load, and HIV clinical stage

- **Immunogenicity:**
  - Robust immune response in PLWH ;
  - individuals living with HIV who are not immunosuppressed
    - Have lower immunogenic response to HPV vaccine
  - PLWIH have lower HPV antibody titers than those not living with HIV
    - But much higher than response from natural infection and demonstrated to be protective
  - Similar to the general population, titers peak one month and plateaus between 24 and 48 months post vaccination

[1]Staadegaard et al., 2022, [2]Denny et al., [3]2013; Levin et al., 2010; [4]Palefsky et al., 2021,[5]Kojic et al., 2014, [6]Mugo et al., 2018;

Efficacy

Limited data on HPV Vaccine efficacy among adult PLWH.

Evidence

- The rate of persistent infections **in PLWH is lower in vaccinated** than unvaccinated historical controls.
- Evidence of vaccine efficacy was found among MSM-LWH aged 16 to 26 years with no evidence of previous exposure to HPV vaccine-types at the time of vaccine initiation [2]

Inconclusive

- In contrast: the vaccine offered little to no protection against HPV among MSM-LWH older than 26 years

  ➔ a population with a high level of prior exposure to HPV vaccine-types

These data highlight the importance of vaccinating PLWH as early as possible to minimize the likelihood of prior HPV exposure, ideally before initiation of sexual activity.

[1]McClymont et al., 2019, [2]Palefsky et al., 2021a, [3]Hidalgo-Tenorio et al., 2021, [4]Wilkin et al., 2018, [5]Stelzle et al., 2021

HIV immune status and HPV vaccine response

- Effect of HIV on immune response mounted following HPV vaccination may depend on the degree to which HIV is controlled:
  - nadir CD4+
  - current CD4+ counts
  - HIV viral load.
- Rapid control of HIV infection by early and consistent ART improved preservation of immune function
- What we do not have data on is
  - Efficacy of lower HPV vaccine dose schedule (ex one dose)
  - Protection from HPV if individual acquires HIV after HPV vaccination
- The WHO recommends HPV vaccination for PWH aged 18–26 years,
  - vaccination rates among PLWIH remain low.

[1]Kazer et al., 2020

Guidelines for HPV Vaccination in PLWH

Organization	Doses	Age Range
WHO	At least 2 doses Ideally 3 doses	9 years and older
European AIDS clinical society	3 doses	9 – 26 years
ACIP	3 doses	9 – 40 years

2-dose schedule: 0, 6 months
3-dose vaccination schedule (0, 1–2 and 6 months)

Human papillomavirus vaccines: WHO position paper, December 2022
EACS Guidelines: 11th edition (October 2021) | EATG - human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices | MMWR (cdc.gov); European Centre for Disease Prevention and Control. Guidance on HPV vaccination in EU countries: focus on boys, people living with HIV and 9-valent HPV vaccine introduction, 2020. Stockholm: ECDC; 2020.

Summary

- Despite recommended HPV vaccination for PWH aged 18–26 years, vaccination rates among PWH remain low.
- Some countries vaccinate only 10-year-old girls due to limited vaccine supplies and funding
- There is need for to integrate HPV vaccination in HIV care and treatment programs
- Disease which is primarily caused by persistent infection with human papillomavirus (HPV) is potentially preventable with the completion of the HPV vaccine series.

Acknowledgments

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Thank You