Prevention and treatment of Cervical Cancer for Women Living with HIV

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IAS Webinar: February 18, 2026

Objectives

1)Understand the burden of disease of cervical cancer in WLWH well-treated with antiretroviral therapy (ART)

2) Discuss the role of secondary prevention with screening and triage pathways in cervical cancer screening and its role in the setting of HIV

3) Discuss innovative therapeutics for precancer and HPV persistence

4) Discuss the role of screening and treatment of precancer and its relevance to WHO elimination strategy and Rwanda’s Mission 2027

Background

- Cervical cancer is 1st or 2nd leading cause of cancer deaths among women in most LMICs
- HPV infection with ~14 high risk types is responsible for nearly all cervical cancer, with precancer and then cancer developing over many years of *persistent* infection
- HPV types 16 and 18 cause ~70% of cervical cancers, most women clear the HPV infection
- Primary prevention: HPV vaccines prevent nearly all infection with the targeted types; originally provided as 3 doses, now with most countries using one dose
- Secondary prevention: HPV infection and precancers can be detected and treated prior to the development of cancer

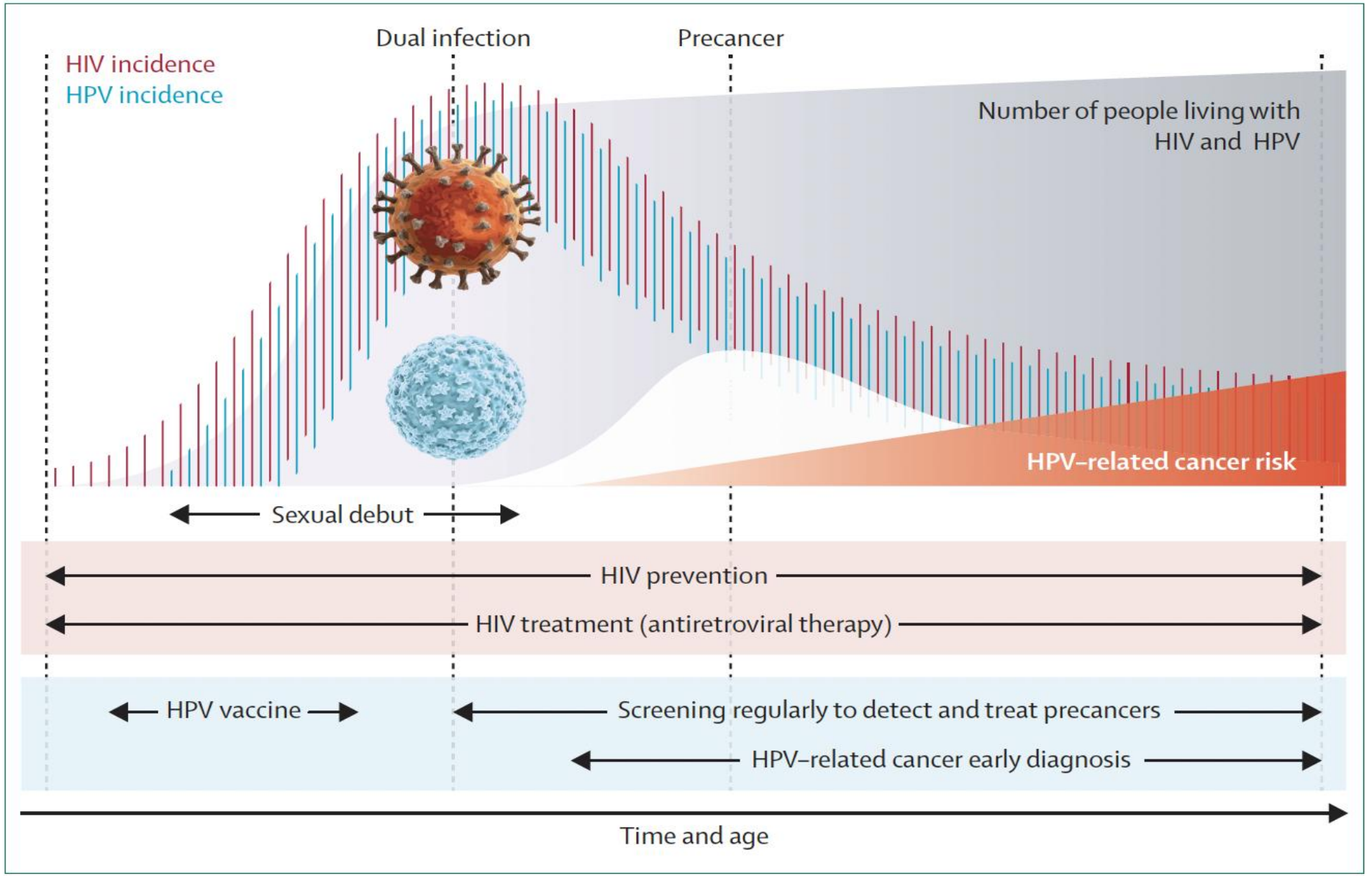
Global strategy to eliminate cervical cancer

- WHO 2030 targets
  - 90% of girls fully vaccinated by age 15 years
  - 70% of women at risk screened **with high performance test** by 35 yo, again at 45 yo
  - 90% of women with cervical disease (precancer or cancer) followed up and treated

- Mathematical modeling suggests that meeting the targets by 2030 in low- and lower-middle-income countries will result in:
  - Median cervical cancer incidence rate will fall by 42% by 2045, and by 97% by 2120, averting more than 74 million new cases of cervical cancer;
  - Median cumulative number of cervical cancer deaths averted will be 300 000 by 2030, over 14 million by 2070, and over 62 million by 2120.

HPV and cervical cancer among WLWH

- WLWH have higher incidence, prevalence and persistence of HPV and related disease (precancers)
- WLWH *have 6-fold* higher burden of cervical cancer, even in ART era
- >80% of WLWH live in SSA, which has the heaviest burden of both HIV and cervical cancer, and currently limited capacity for screening and treatment programs
- Guidelines for screening WLWH recommend earlier and more frequent screening, requiring even more resources
- Risk of not achieving lower cervical cancer incidence, morbidity and mortality from a largely preventable disease
- Best approach to cervical cancer control for WLWH is *integration* into HIV care services -- a structure parallel to that for women not living with HIV



Prevention and control of HPV-related cancers in people living with HIV

Anneli Uusküla, Anna Tisler, Jack DeHovitz, Gad Murenzi, Philip E Castle, Gary Clifford**

Lancet HIV, 2025

Primary Prevention: HPV vaccination

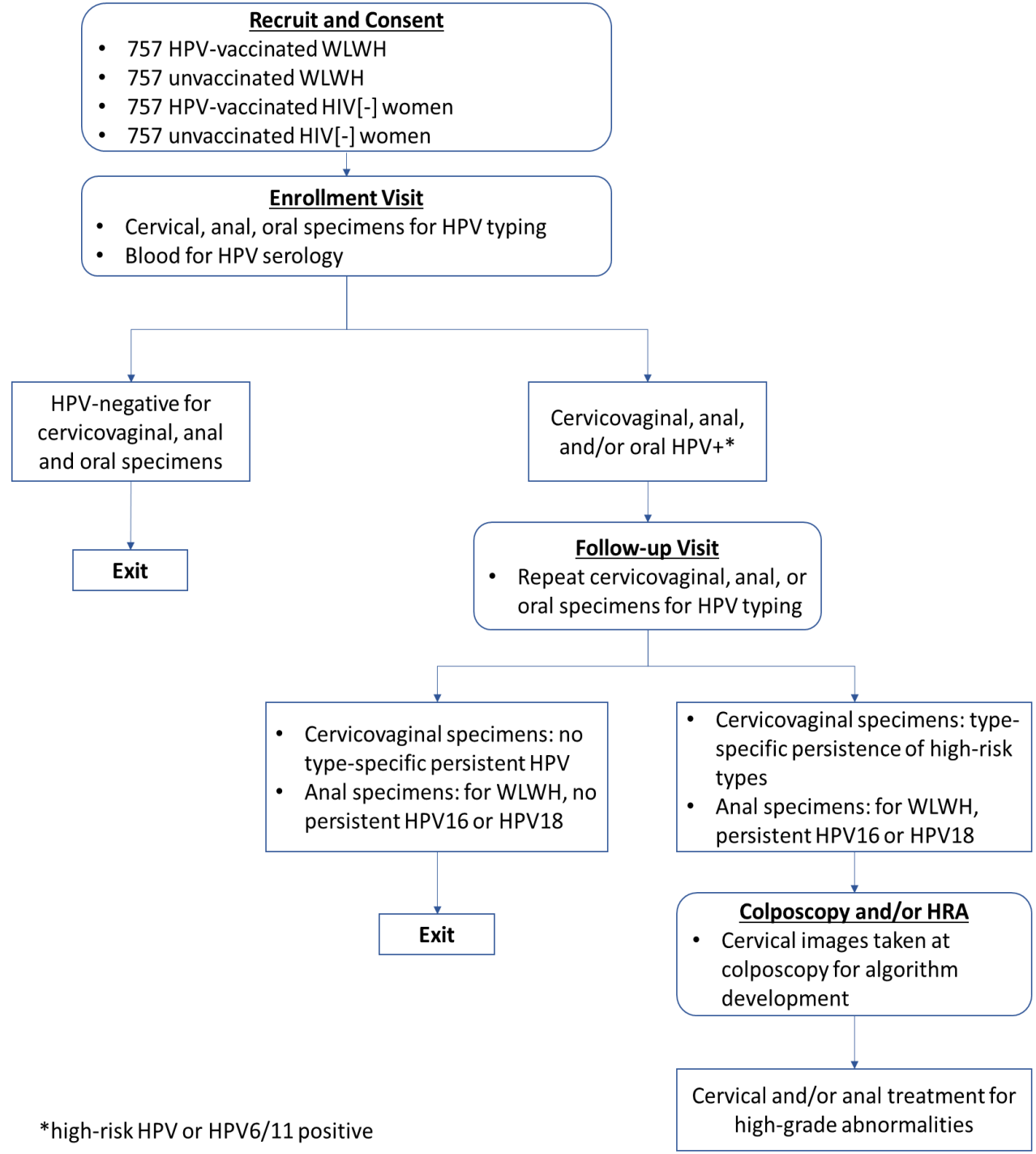
- First WHO target: 90% of girls vaccinated by age 15
- Best approach for cervical cancer prevention
- Vaccinating now protects **future** generations of women
- But women already infected with HPV (almost all unvaccinated adult women) need screening-i.e. secondary prevention

Open access Protocol

BMJ Open

Long-term human papillomavirus vaccination effectiveness and immunity in Rwandan women living with and without HIV: a study protocol

Gad Murenzi [1,2] Fabienne Shumbusho,[1,2] Natasha Hansen,[3] Athanase Munyaneza,[1,2] Julia C Gage,[3] Benjamin Muhoza,[1,2] Faustin Kanyabwisha,[1,2] Amanda Pierz,[4,5] Patrick Tuyisenge,[1,2] Kathryn Anastos [5,6] Philip E Castle [3,7]



Results - Vaccine Protection among WLWH

Cohort	N	Prevalence ratios (targeted vs. non-targeted/ non-cross-reactive)*	CI	Ratio of ratios	CI	P-value
WWH 1996+	497	0.183	(0.128-0.238)	0.664**	(0.404-0.923)	0.011
WWH <1996	242	0.276	(0.168-0.384)			
HIV- 1996+	596	0.118	(0.071-0.165)	0.644***	(0.452-0.837)	0.0003
HIV- <1996	193	0.060	(0.001-0.118)			
Total	1528					

*Targeted HPV types are 16 & 18. Non-targeted/non-cross HPV types include: 35, 39, 51, 52, 56, 58, 59, 68

** Ratio of vaccinated/unvaccinated within HIV+ women

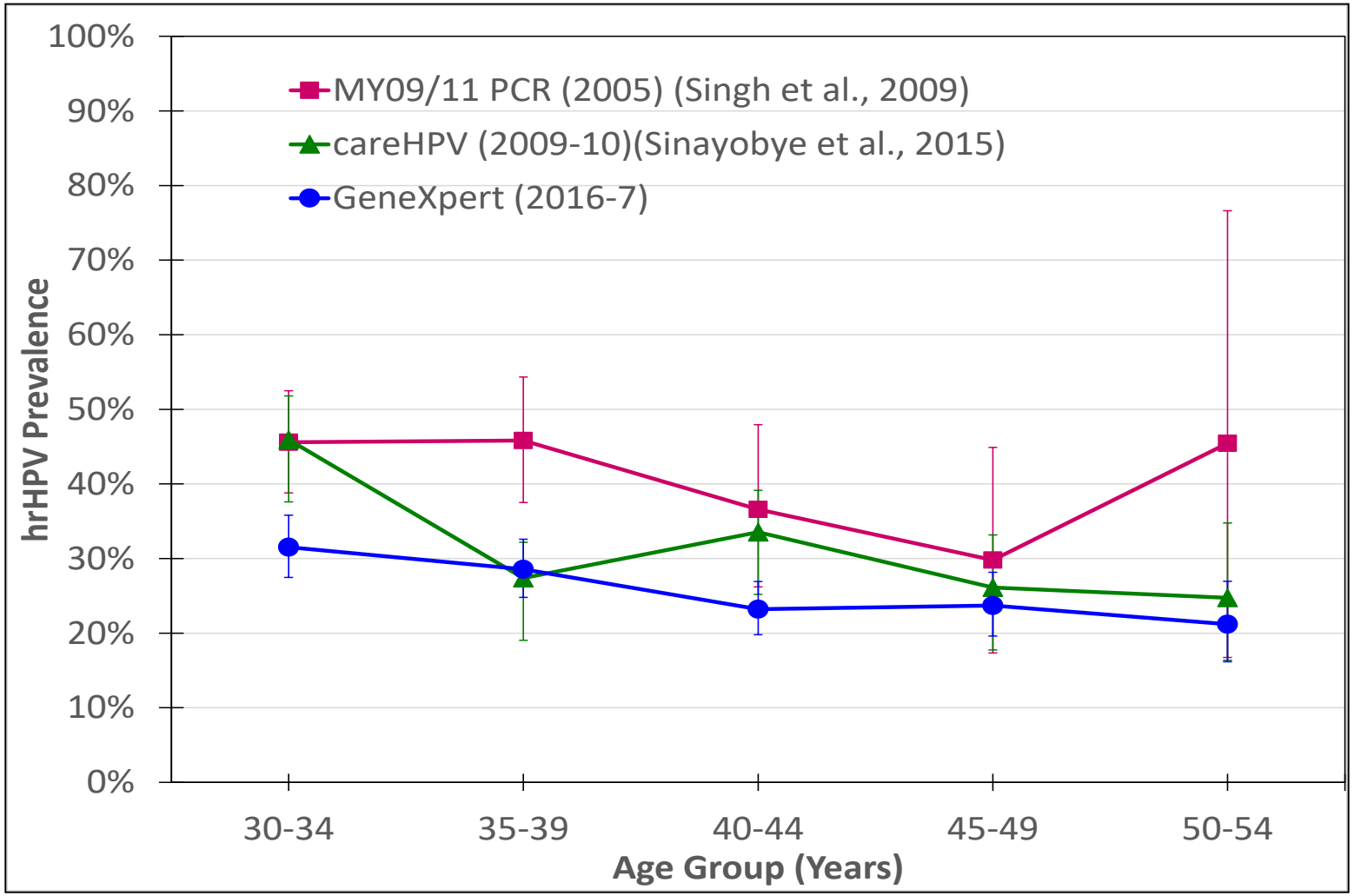
*** Ratio of HIV-/HIV+ within vaccinated women

UNPUBLISHED DATA, DO NOT COPY

HIV control is critical for HPV control

- HPV prevalence and types in WLWH globally not fully defined
- High HPV prevalence with HPV 16/18 (most carcinogenic) continuing to be the most prevalent, although HPV16 might evade immune surveillance
- **HPV35 more prevalent/persistent in women of African descent, *not included in any of the currently available vaccines***
- Antiretroviral treatment for women with HIV is critically important:
  - HIV control to control HPV prevalence
  - HIV control to control HPV persistence
  - Triage is therefore key
  - High HPV prevalence may lead to overtreatment

Time Trends in hrHPV Prevalence

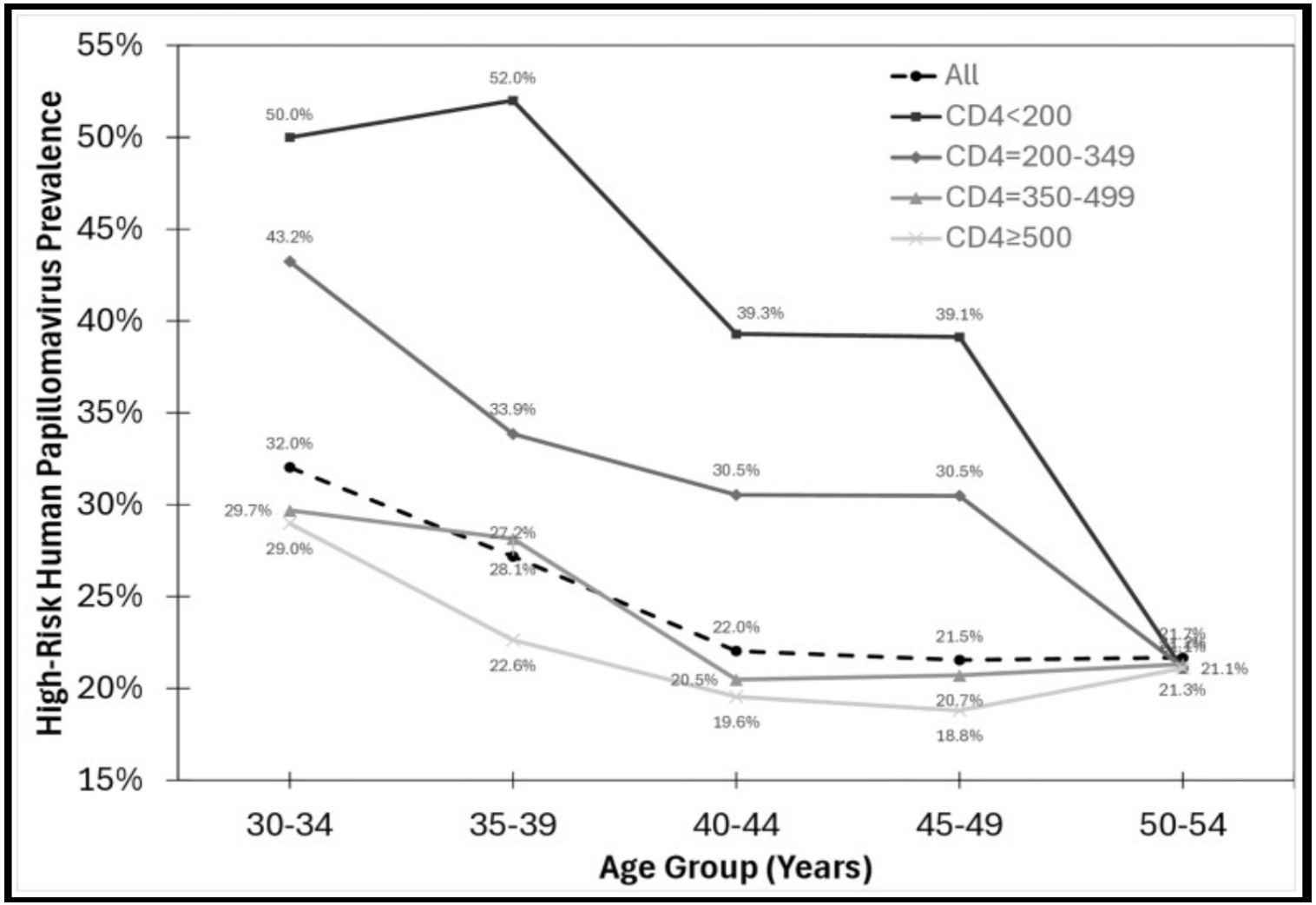


Twelve-Year Trend in the Prevalence of High-Risk Human Papillomavirus Infection Among Rwandan Women Living With HIV

Gad Murenzi,[1] Faustin Kanyabwisha,[1] Anthere Murangwa,[1] Gallican Kubwimana,[1] Leon Mutesa,[2] Robert D. Burk,[3] Kathryn Anastos,[3] and Philip E. Castle[3]

[1]Rwanda Military Hospital, Kigali, Rwanda, [2]Center for Human Genetics, College of Medicine and Health Sciences, University of Rwanda, Kigali, Rwanda, and [3]Albert Einstein College of Medicine, Bronx, New York, USA

JID, 2020



PLOS One

RESEARCH ARTICLE

Determinants of cervical high-risk human papillomavirus positivity among Rwandan women living with human immunodeficiency virus

Gad Murenzi[1*], Faustin Kanyabwisha[1], Maria Demarco[2], Benjamin Muhoza[1], Kristen Hansen[2], Jean Paul Mivumbi[1], Anthere Murangwa[1], Theogene Rurangwa[3], Thierry Muvunyi Zawadi[1], Gallican Kubwimana[1], Julia C. Gage[2], Tiffany Hébert[2], Adebola Adedimeji[6], Laetitia Nyirazinyoye[7], Marcel Yotebieng[5], Leon Mutesa[8], Kathryn Anastos[5], Philip E. Castle[2]

PLOS One, 2025

Secondary prevention: Screening-- Second (70%) WHO target

- Secondary prevention: screening with HPV testing
- Sufficient data to show that HPV testing is the *optimal method* for screening
- How can we reach as many women as possible: Couple HPV testing with self-collection in addition to provider/office-based collection
- Opportunities for implementation: leverage cervical cancer screening with existing health infrastructure:
  - pharmacy networks
  - ART delivery sites, primary care sites
  - community centers
  - Others

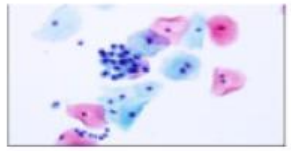
Triage of screen-positive women

- Partial type assays (HPV16 and 18 separately)
- E6/E7 oncoproteins testing: commercially available assay with 8 HPV types (does not include HPV35)
- Methylation can work on self collected samples
- Automated Visual Evaluation (AVE): uses machine learning to analyze images of cervix to identify cervical precancers or cancer
  - Evidence of differences by HIV status
  - Machine learning for AVE must include images specifically for WLWH
  - Differences in epithelial changes in WLWH due to “field effect”
- Strength: Utilize same screening specimen (easily implemented) Minimize overtreatment and improve reassurance of lack of disease
- Challenge/weakness: Some require significant lab infrastructure, limiting point-of-care deployment

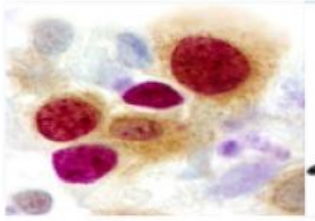
"Enduring" guidelines (American Society for Colposcopy and Cervical pathology) Accommodate new tests in development

Cytology-based

Cytology / Automation

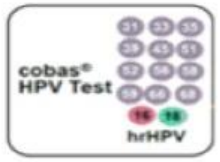


p16/Ki-67 / Automation



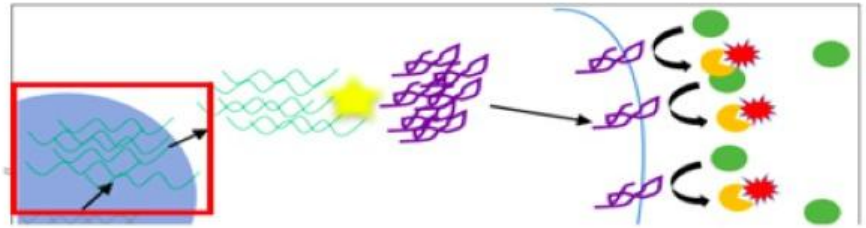
Molecular

HPV genotyping



Methylation

In-vivo imaging

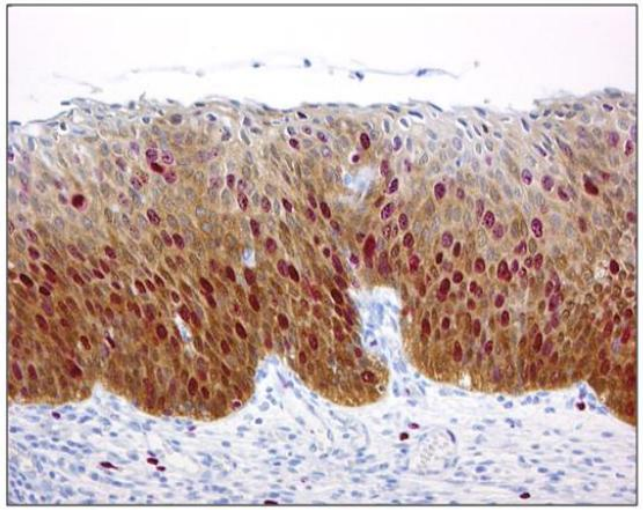


Visual

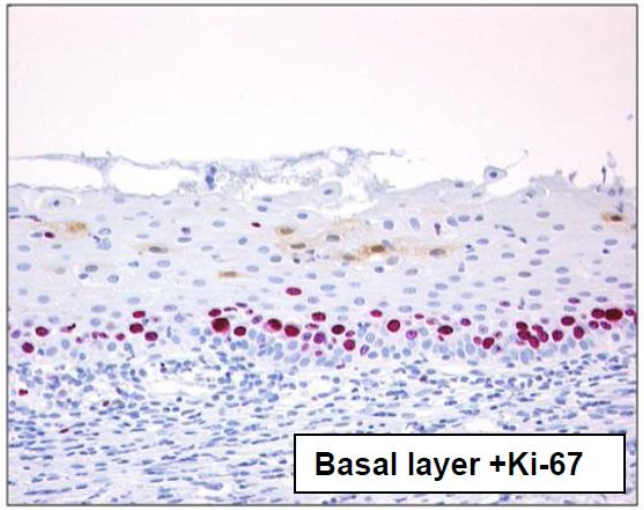
VIA / Automation

Courtesy of Mark Einstein

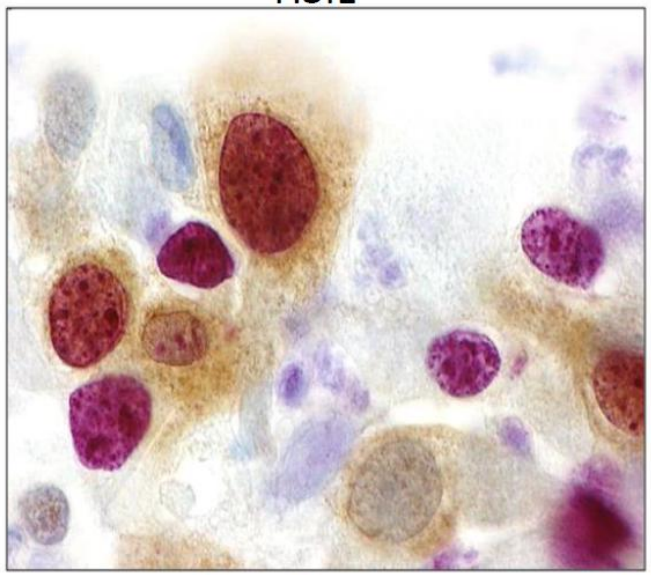
Biomarkers: p16 and Ki-67 dual staining

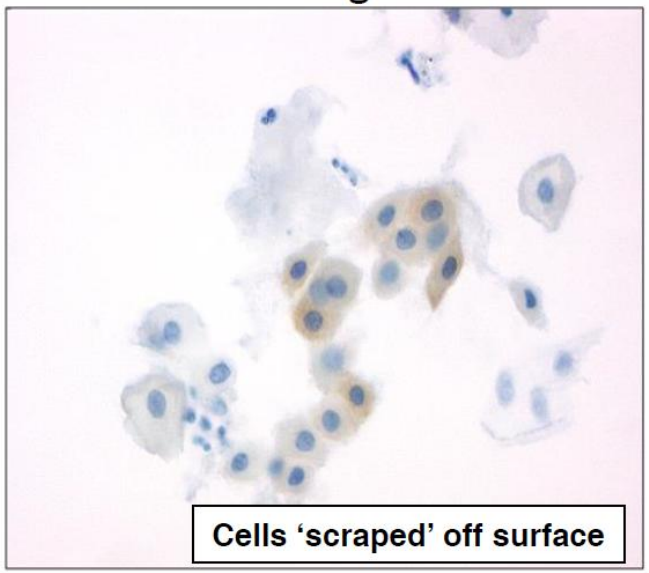


HSIL



Benign





Red nuclear stain: Ki-67 / Brown cytoplasmic stain: p16

- In HPV-transformed cells:
  - E7 oncoprotein leads to accumulation of p16
  - Ki-67 marker for proliferation or mitotic activity
- **Histology:** 2-d architecture
  - Really only need p16
  - Ki-67 adds little
- **Cytology:** *Need both stains*
  - "Individual" cells
  - Can't see the block positivity

Courtesy of Tere Darragh, MD UCSF
Presented at ASCCP 2024 Meeting

Emerging visualization technology for detection of CIN (cervical intraepithelial neoplasia)

- AI based technology

OXFORD

JNCI J Natl Cancer Inst (2019) 111(9): djy225

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First published online January 10, 2019
Article

ARTICLE

An Observational Study of Deep Learning and Automated Evaluation of Cervical Images for Cancer Screening

Liming Hu, David Bell, Sameer Antani, Zhiyun Xue, Kai Yu, Matthew P. Horning, Noni Gachuhi, Benjamin Wilson, Mayoore S. Jaiswal, Brian Befano, L. Rodney Long, Rolando Herrero, Mark H. Einstein, Robert D. Burk, Maria Demarco, Julia C. Gage, Ana Cecilia Rodriguez, Nicolas Wentzensen, Mark Schiffman

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CANCER EPIDEMIOLOGY

IJC International Journal of Cancer

A demonstration of automated visual evaluation of cervical images taken with a smartphone camera

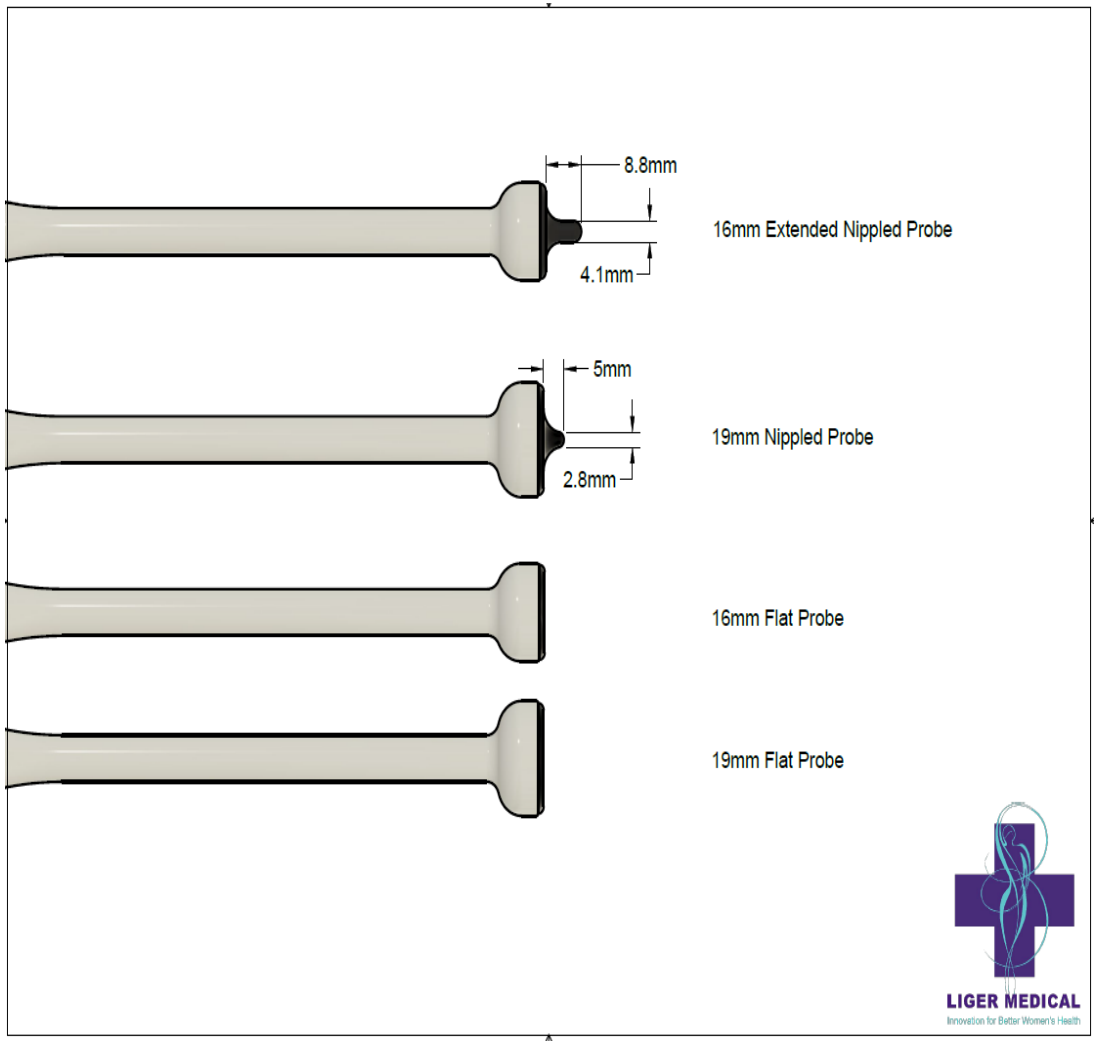
Zhiyun Xue[1] | Akiva P. Novetsky[2] | Mark H. Einstein[2] | Jenna Z. Marcus[2] | Brian Befano[3] | Peng Guo[1] | Maria Demarco[4] | Nicolas Wentzensen[4] | Leonard Rodney Long[1] | Mark Schiffman[4] | Sameer Antani[1]

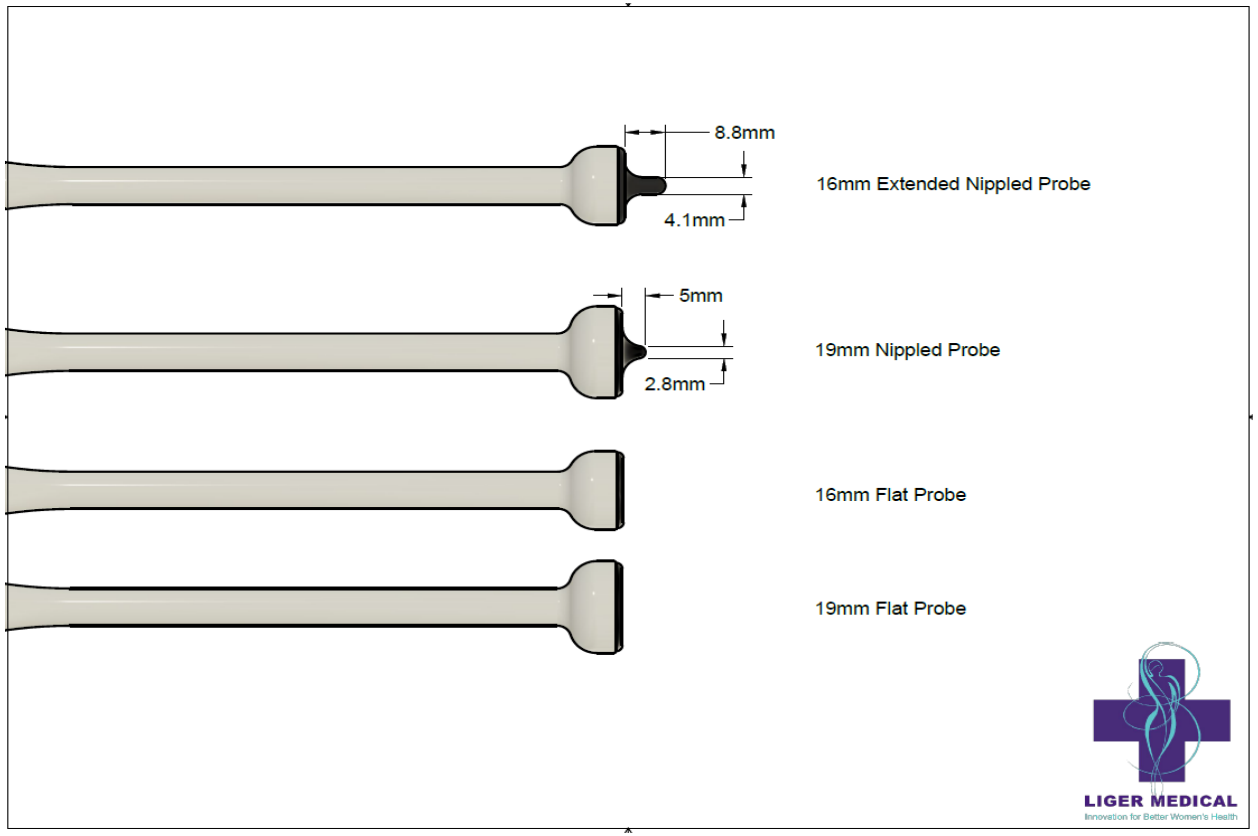
Courtesy of Mark Einstein

Treatment of precancerous lesions:

Third (90%) WHO target

- Most difficult goal to achieve as it requires patient tracking and follow-up, provider training, post treatment surveillance
- Rolling out Thermoablation (TA) for treatment in Africa is key to achieving this goal for treating WLWH with HPV16/18
- Effectiveness of current TA probes, possibly not reaching the endocervix where reserve cells that supply the ectocervix harbor residual HPV





SoftBiopsy

SoftBiopsy® - Gynecological Biopsy Device

Soft-ECC

Soft-ECC® - Endocervical Curette

HISTOLOGICS

Novel approaches in development

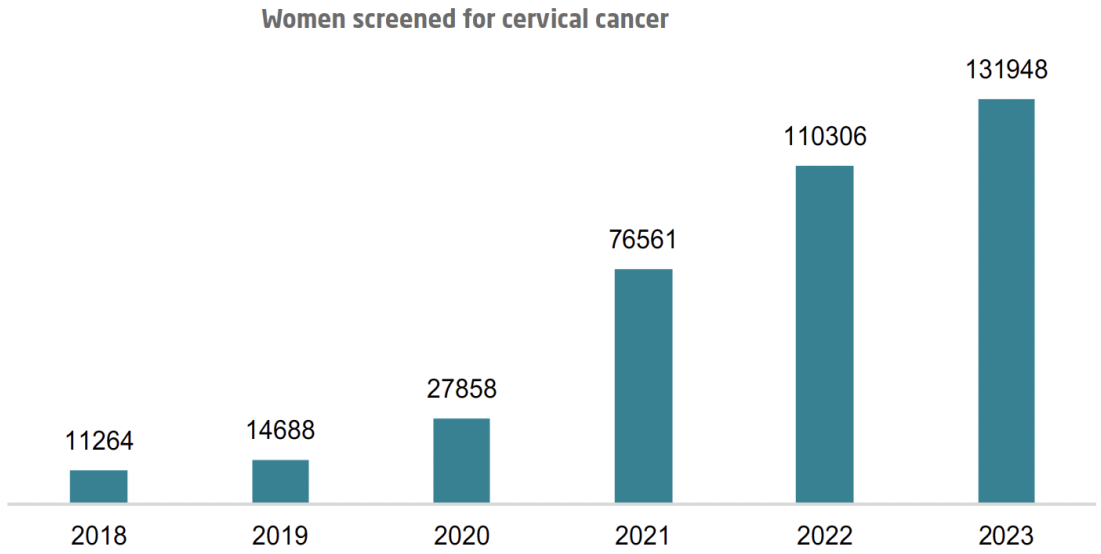
- Therapeutic vaccine: efficacy, timing?
- Direct acting HPV antivirals: lopinavir/ritonavir vaginal gel to treat precancer
- Implementation science research is critically needed: Many evidence-based interventions are not effectively implemented to improve people's health in real-world settings
  - What are the barriers: individual, systemic, environmental
- Implementation science approaches to improve prevention of cervical cancer
  - Self-collection can be transformative, globally
  - Community outreach and other platforms for delivering HPV tests such as pharmacies
  - Integration into HIV services

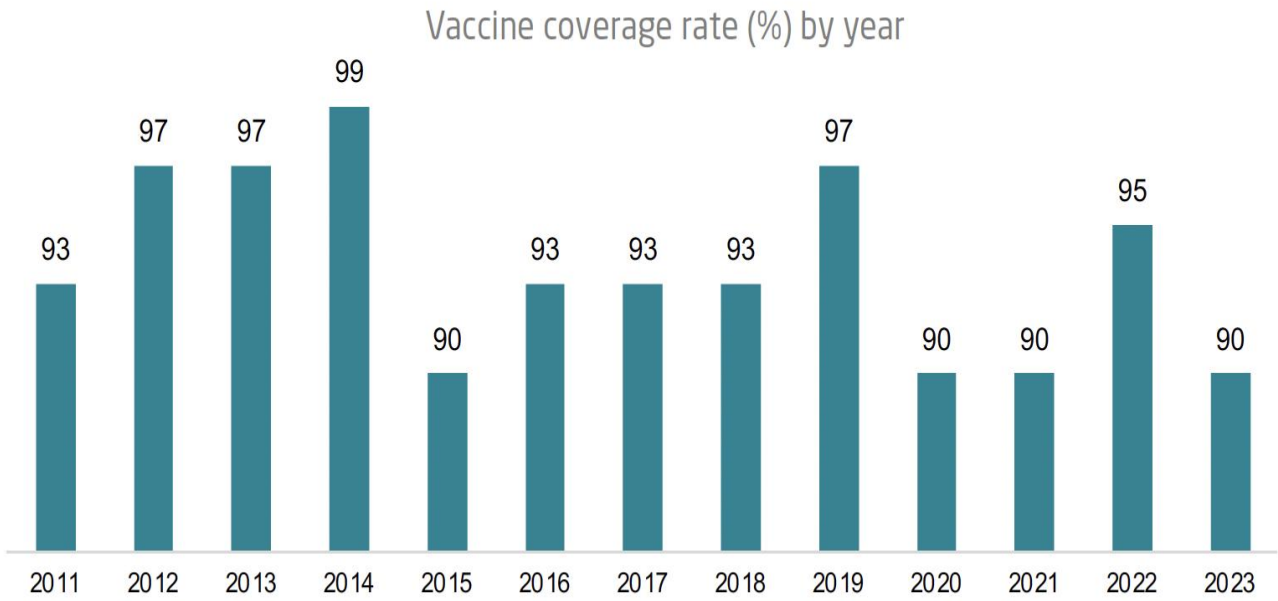
Rwanda's Mission 2027

Republic of Rwanda
Ministry of Health

Accelerated Plan for Elimination of Cervical Cancer in Rwanda

2024-2027





4.1. Vision, Mission and Goal

Vision: A Rwanda where cervical cancer is prevented, detected early, and effectively managed, for a healthier future for all women and girls.

Mission: To eliminate cervical cancer as a public health problem in Rwanda by providing equitable, accessible, and high-quality prevention, screening, and treatment services, ensuring that all women and girls are protected from cervical cancer through education, vaccination, early detection, and timely management.

Goal: To reduce the incidence and mortality of cervical cancer in Rwanda by maintaining 90% HPV vaccination coverage among 12-year girls, achieving 70% cervical cancer screening coverage among women aged 30 to 49 years old, and ensuring 90% of women diagnosed with cervical pre-cancer or cancer receive effective treatment by 2027, in alignment with the WHO Global Strategy for cervical cancer elimination. The long-term impact goal is to reduce and maintain cervical cancer incidence to less than 4 cases per 100,000 women.

4.3. Strategic Objectives

The reduction of cervical cancer incidence and related mortality will be achieved through implementing the following strategic objectives.

- Strengthen cervical cancer **program organization, governance, and coordination**
- Strengthen cervical cancer **primary prevention through awareness, information, education, and HPV immunization** to maintain vaccination coverage above 90%
- Increase cervical cancer **screening coverage in eligible women using high performance tests** to attain population coverage of **70% and 90%** treatment of pre-cancerous lesions by 2027
- Improve access to cervical cancer **diagnosis, treatment of invasive cancer, rehabilitation, and palliative care** to reach 90% treatment coverage by 2027
- Enhance the **monitoring and evaluation system** for cervical cancer prevention and control services to track the performance, data systems and research
- Promote **intersectoral collaboration, partnerships and create resource mobilization strategies** for a sustainable financing of cervical cancer elimination

Take home message

- In order to achieve the 2030 WHO targets, we need to scale up vaccination and screening and treatment of precancer for WLWH, in turn decrease M&M due to a preventable disease
- WLWH have highest HPV burden: prevalence and persistence
- HPV testing after self collection is key
- Triage with partial typing, biomarkers and leveraging artificial intelligence
- Scale up of TA and continuing to assess its effectiveness
- Implementation science methods critical to improve uptake and follow up

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  - Philip Castle PhD
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MURAKOZE CYANE

THANK YOU