Advancing Global Health Equity: Investing in Integrated HIV, HPV and Cervical Cancer Initiatives.

Co-Sponsors:

amfAR
MAKING AIDS HISTORY

fre
FUNDERS for REPRODUCTIVE EQUITY

Logistics

- We encourage you to introduce yourself in the chat with **your name, pronouns and where you're joining from today.**
- We will be **recording this conversation.**
- **Captions** are also enabled at bottom of screen.
- We will be monitoring activity in the Q&A and ask that attendees prioritize **rights-based** and **inclusive language in your interactions.**
- This is a **non-solicitation space**, and is a **dialogue intended foremost for donor institutions**. If you wear multiple hats at your institution, we ask that you consider your role as a funder in your questions.

Our Discussion Guides

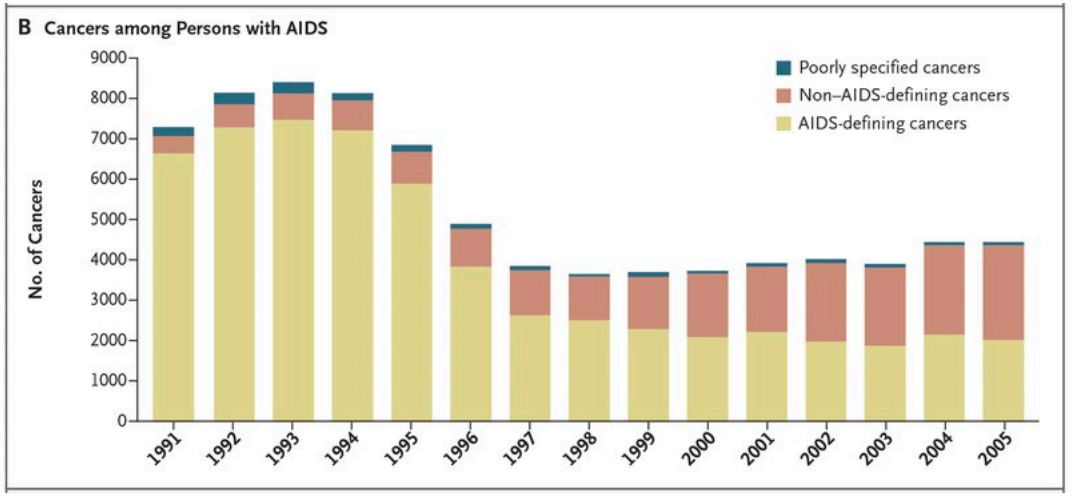
HPV and Cervical Cancer in Women Living with HIV

Carla Chibwesha, MD, MSc, FACOG
UNC Global Women's Health &
The Clinical HIV Research Unit, Wits Health Consortium

UNC SCHOOL OF MEDICINE

HIV and cancer

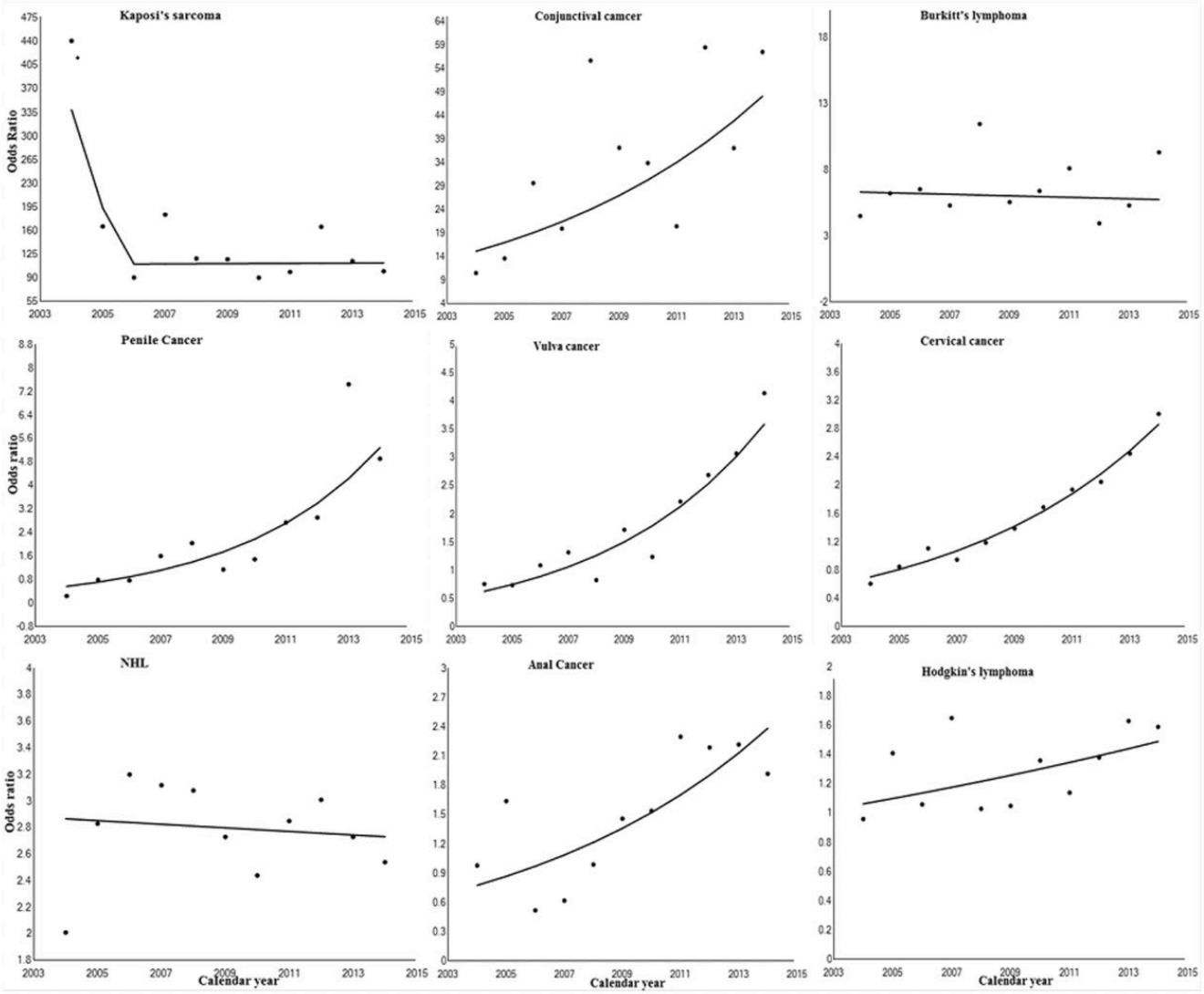
- People living with HIV have an increased risk of certain cancers
  - AIDS-defining cancers include Non-Hodgkin's lymphoma, Kaposi's sarcoma, and **cervical cancer**
  - Non-AIDs-defining cancers include Hodgkin's lymphoma, lung cancer, hepatocellular cancer, **oropharyngeal cancer**, **vulvar cancer**, **penile cancer**, and **anal cancer**
- Since the introduction of antiretroviral treatment, rates of NHL and KS have declined dramatically
  - Rates of HPV-associated cancers and other non-AIDS-defining cancers are either stable or increasing globally



Trends in cancer among PLWH in the United States (1990-2005)

Yarchoan (2018)

Cervical Cancer and NAD Cancers are Increasing in PLWH in LMICs

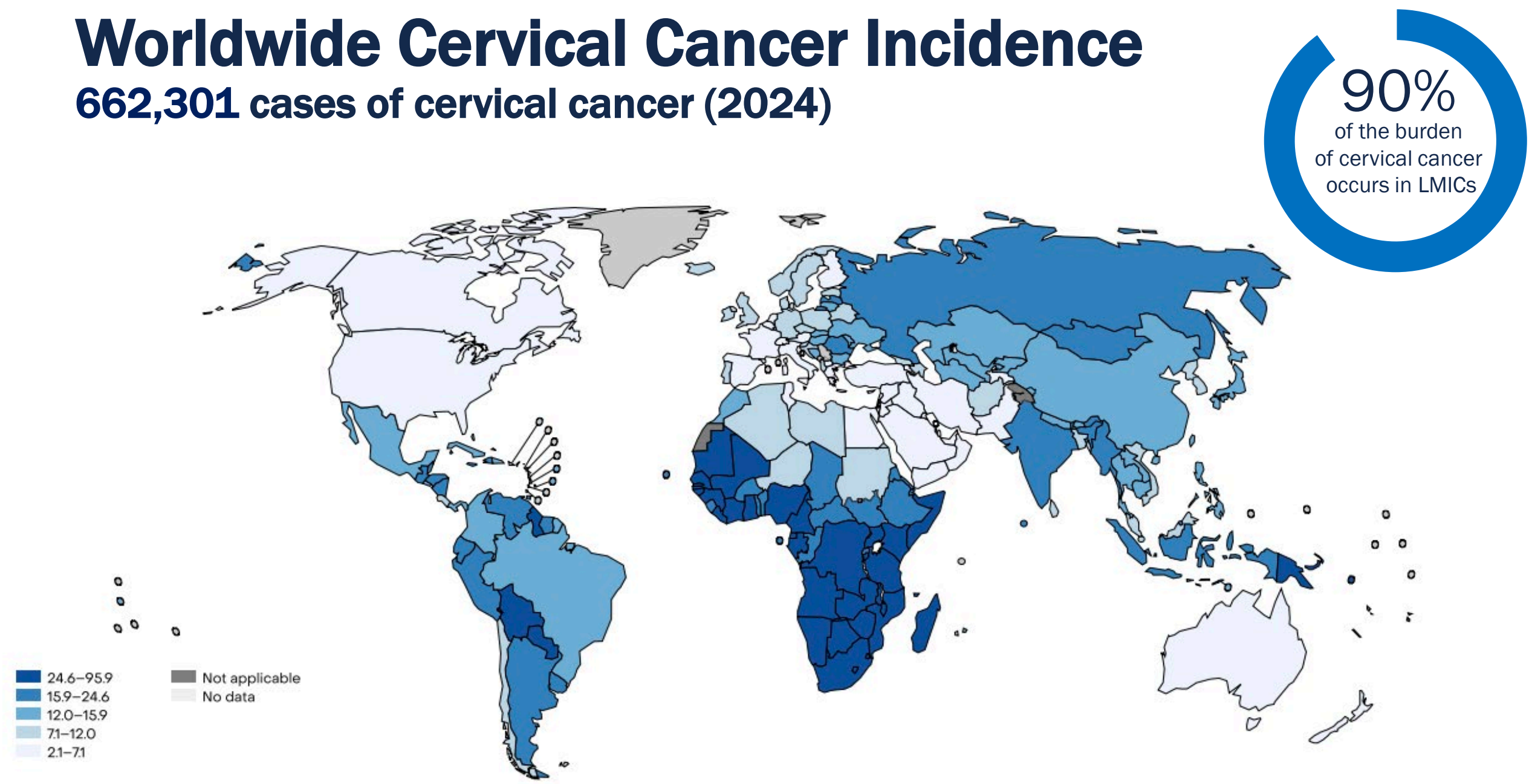


Trends in cancers among PLWH in South Africa (2004-2014)

Dhokotera (2019)

Worldwide Cervical Cancer Incidence

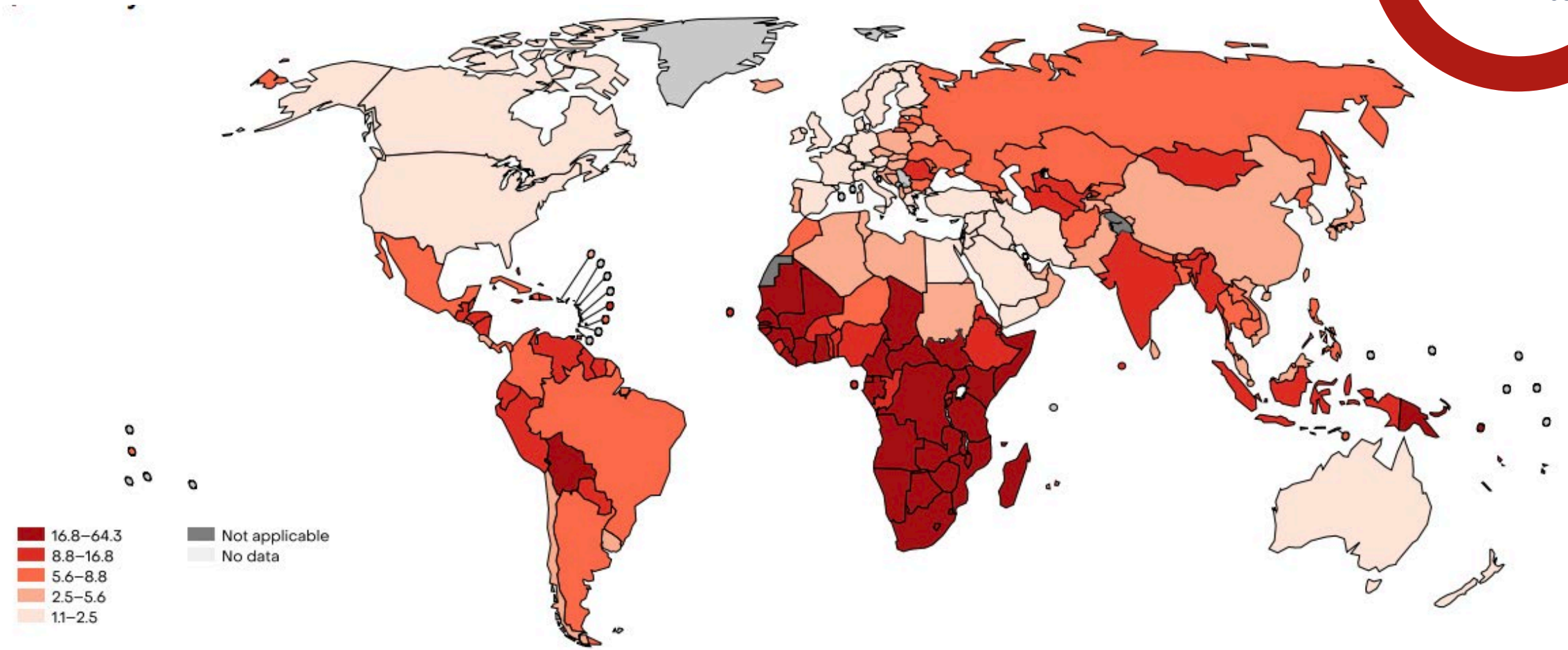
662,301 cases of cervical cancer (2024)

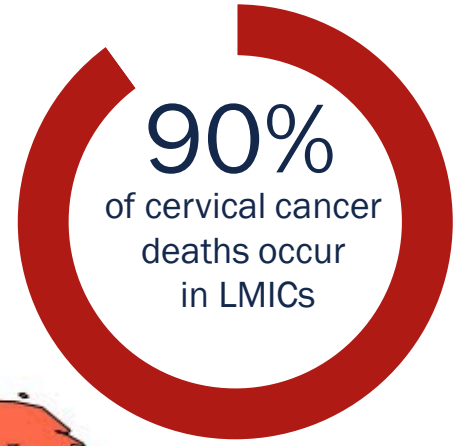


GLOBOCAN, 2024

Worldwide Cervical Cancer Deaths

348,874 cases of cervical cancer (2024)

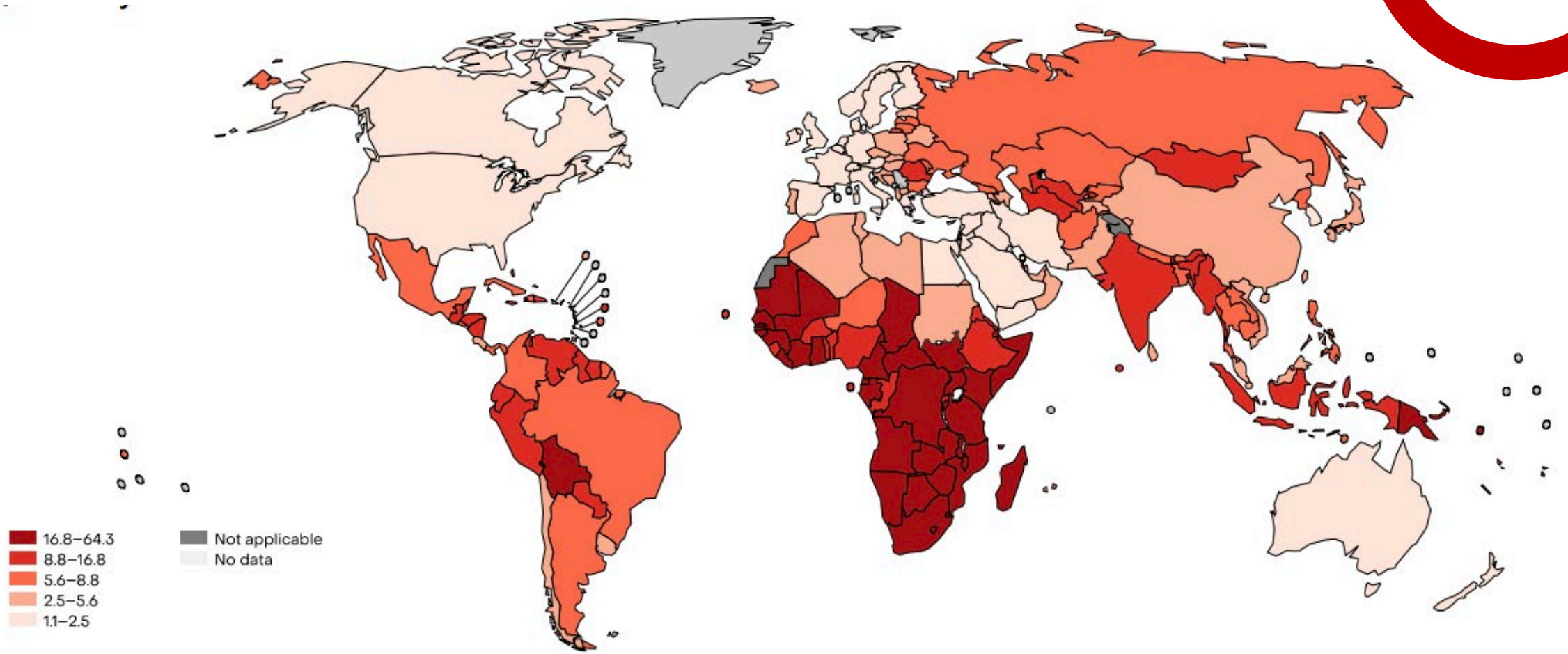




GLOBOCAN, 2024

Worldwide HIV Prevalence

20 million women and girls living with HIV (2023)



UNAIDS/WHO, 2018

Intersecting Epidemics of Cervical Cancer and HIV

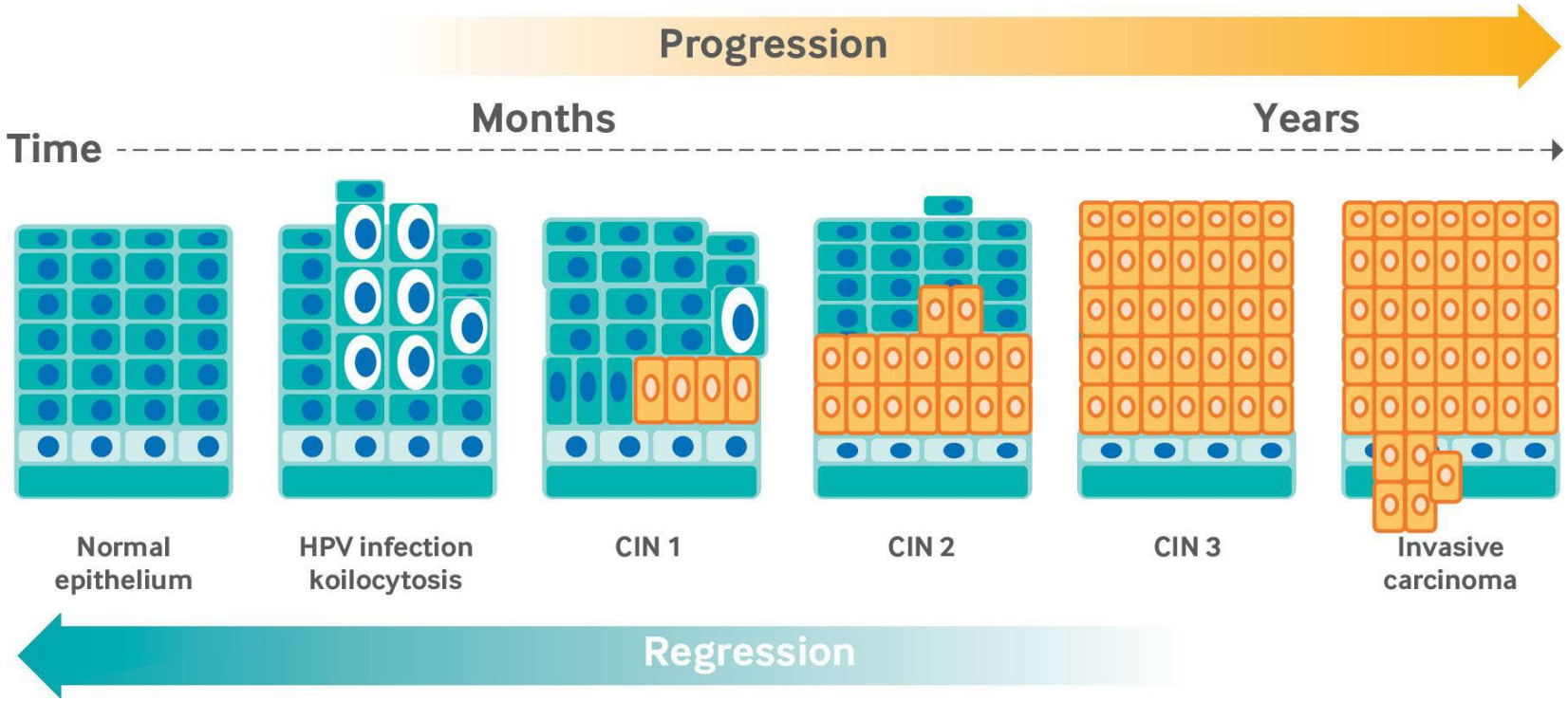
UNC SCHOOL OF MEDICINE

- The prevalence of hrHPV is high (45–90%) in women with HIV
  - Co-infection with multiple HPV types is also more common
  - HPV infection more is more likely to persist
- Rates of cervical precancer (CIN2/3) are 2-3 times higher than in women without HIV
- Rates of invasive cervical cancer are 6 times higher than in women without HIV
- Both precancer and invasive cervical cancer are harder to treat in women with HIV

Heard, 2005; Sahasrabuddhe, 2007; Heard, 2009; Castle, 2021

Progression from HPV Infection to Cervical Disease

UNC SCHOOL OF MEDICINE



Primary prevention:
HPV vaccination

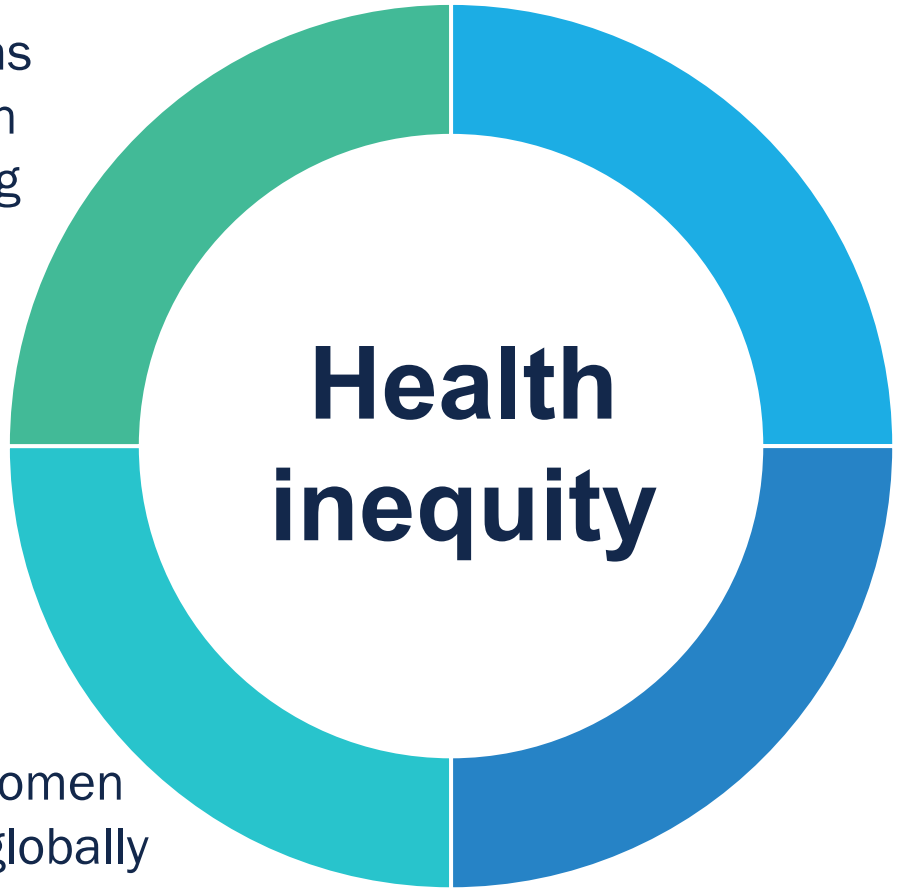
Secondary prevention:
Cervical screening & treatment

Low Health Literacy

- Traditional misconceptions about cancer are common
- Stigma limits help seeking

Imprecise Screening Tests

- Three approaches (visual, cytology, molecular)
- All with pros and cons
- All require organized health systems



Limited Access to Prevention

- 20% of girls and young women vaccinated against HPV globally
- 32-36% of women in LMICs screened for cervical cancer

Precancer Treatment Hard to Scale

- Two approaches (excision, ablation)
- Excision requires more training than ablation
- 30-50% of women with HIV experience treatment failure

Improving Cervical Cancer Screening and Treatment in Women with HIV

UNC SCHOOL OF MEDICINE

- Secondary prevention is feasible and cost-effective, especially in LMICs
  - Primary HPV screening can be scaled by leveraging existing cervical screening programs that use cytology (Pap smears) or visual screening (VIA/VILI)
  - HPV tests can also be self-collected
  - Ablative treatments allow for same-day screening and treatment
- Women with HIV are at increased risk of cervical disease as standard surgical treatment for cervical precancer fails in 30-50% of cases
  - This may be due to residual CIN2/3 that is not completely removed during surgery
  - Due to re-infection with another HPV type
  - Due to reactivation of underlying HPV infection in the genital tract

Improving Cervical Precancer Treatment Outcomes in Women with HIV

UNC SCHOOL OF MEDICINE

- **AMC-099 / COVENANT** NCT03284866
  - **Rationale**: HPV vaccination in combination with standard treatment for cervical precancer may improve outcomes by providing protection against new HPV infections
  - **Design**: Double blind RCT of 9vHPV vaccination vs. placebo in combination with standard treatment in 536 women with HIV
  - **Setting**: 5 clinical trial sites in Malawi, Uganda, South Africa, and Zimbabwe
  - **Status**: Closed to enrollment

- **IGHID-12046 / ACT 2** NCT05413811
  - **Rationale**: 5-fluorouracil (5FU) cream in combination with standard treatment for cervical precancer may improve outcomes by treating residual disease
  - **Design**: Double blind RCT of 5FU vs. placebo cream in combination with standard treatment in 180 women with HIV
  - **Setting**: 1 clinical trial sites in South Africa
  - **Status**: Enrolling

THE ARCHITECTURE TO ELIMINATE CERVICAL CANCER:

VISION: A world without cervical cancer

THRESHOLD: All countries to reach < 4 cases 100,000 women-years

2030 CONTROL TARGETS

90%

of girls fully vaccinated with HPV vaccine by 15 years of age

70%

of women screened with an high precision test at 35 and 45 years of age

90%

of women identified with cervical disease receive treatment and care

SDG 2030: Target 3.4 – 30% reduction in mortality from cervical cancer

The 2030 targets and elimination threshold are subject to revision depending on the outcomes of the modeling and the WHO approval process

World Health Organization

WHO, 2020

Summary

UNC SCHOOL OF MEDICINE

- Sociodemographic, behavioral, and biological overlap between HIV and HPV result in high burden of cervical cancer in women with HIV
- HPV vaccination is safe and highly effective in individuals with HIV
- HPV screening prevents cervical cancer and is cost-effective
- However, additional research is needed to develop more effective precancer treatments for women with HIV
- Integration of cervical cancer prevention services into HIV care is imperative to expand access for women living with HIV

Unitaid
SAVE LIVES FASTER

Tools to advance the package of care to reach women with life saving preventive services for cervical cancer in high HIV burden settings

30 May 2024

Investments in cervical cancer response

Focus on laying the groundwork for cervical cancer screening and treatment programs and introducing new tools and technologies, in partnership with CHAI, Expertise France, Jhpiego, UICC and WHO.

With more than US$80 million invested so far, Unitaid remains the largest funder of innovative tools to find and treat women with precancer living in low-resource settings.

Unitaid

Represents work across 14 countries: Burkina Faso, Cote d'Ivoire, Guatemala, India, Kenya, Malawi, Nigeria, Rwanda, Philippines, Senegal, South Africa, Uganda, Zambia, Zimbabwe

Key highlights

BEFORE

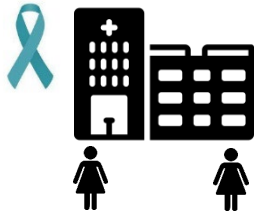
Women visiting primary health center/ HIV+ woman visiting ART center **often not offered** screening

Eligible population

Where screening is offered, the test used is **visual inspection with acetic acid (VIA)**: subjective visual test with high rate of false negatives

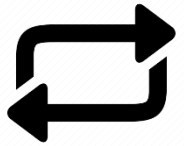
Screening

For those screening positive, need to travel **long distances** to secondary/ tertiary hospital for treatment using **cryotherapy** – bulky, dependent on gas supply, expensive, often out of service



Treatment

Sub-optimal follow-up care for women who screen positive or lack of attendance to referral visit if suspected cancer



Referral & follow up care

AFTER

Women visiting PHC, FP/ MCH clinic or HIV+ woman visiting ART offered screening

Screening offered using either gold-standard HPV DNA test, if available, or VIA with improved capacity of HCWs to carry out VIA

For women screening positive (& found eligible upon triage), lesion treated on same day at same facility using TA devices, or referred to close by facility for Tx using TA/ LEEP

Client tracking mechanisms ensure appropriate follow-up care

RESULTS

1,000+
Sites offering integrated service delivery

11,400+
HCWs- nurses, midwives, clinicians, CHWs trained; **Task shifting now** possible

1.5 M
Women screened
530K w/ HPV tests

>87%
Tx completion rate among women w/ eligible pre-cancerous lesions

5,700+
TA devices deployed in 26 countries

81%
Referral visit completion rate for suspected cancer

CLINTON HEALTH ACCESS INITIATIVE

EXPERTISE FRANCE

SUCCESS

40%
Median price reduction in HPV tests improving affordability, accessibility

HPV testing implementation

- Across the five countries, CHAI saw the following for testing & treatment cascade:

15,766 Tests conducted	92% Valid results	32% HPV-positive	66% Received results	71% Received VIA	26% VIA-positive	87% Treated

*Some steps may not include all countries due to relevant local policies.

5 countries implemented >**15,000 HPV tests** between Sep 2019 & Jan 2021, with programs continuing to-date.

**Predominantly WLHIV, except for Senegal*

Results of study

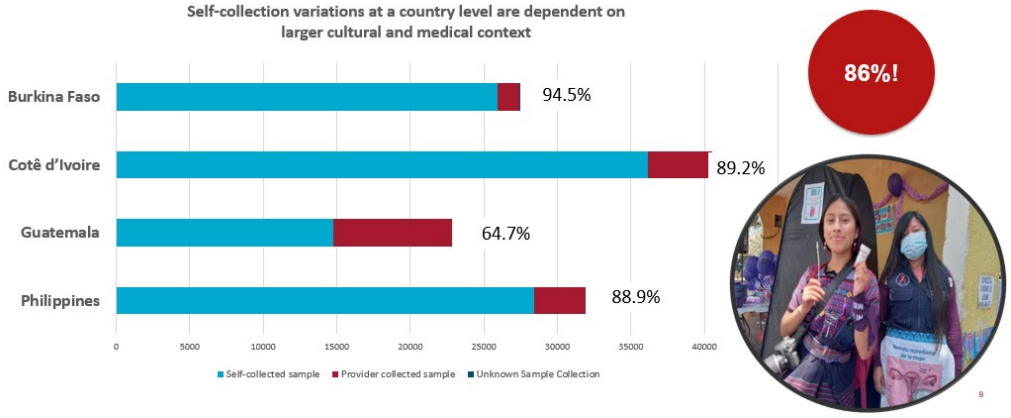
1. In countries that offered both clinician- & **self-sampling, the latter was found to be feasible & acceptable**
2. Integration of HPV testing on existing testing platforms systems was feasible & was achieved **without additional resources** (HR, supply chain, infrastructure, lab support etc.)
3. **Same-day Test-triage-treat was very difficult to achieve** due to HPV testing not being prioritized on POC devices; however, same-day triage-treat was possible

http://dx.doi.org/10.1136/bmjopen-2022-065074

Self-collection

- Most countries offered choice of either self- or clinician-collected at facilities
- Self-collection of HPV tests by clients found feasible, acceptable, allowing for greater flexibility in future screening programs
- Task shifting made possible w/ self collection thus freeing up HCW capacity – sample collected by woman vs. HCW
- Self-collection has begun expansion into community settings
- There is need to explore if community based self-collection models of HPV testing result in improved linkage-to-care alongside improving coverage **(focus of the second wave of investments)**

Empowering women through self-sampling: self-sampling is feasible and acceptable



45%
Ceiling price reduction of TA devices improving affordability, accessibility

Benefits of using thermal ablation

- **Ease of use:** Portable, battery operated, easy operation intuitive automated timer & visual/ audio indicators
- **Ease of clinical rollout:** Straight forward requirements for rollout, easy to use & train HCWs; broader range of HCWs can operate- Task shifting possible
- **Improved access & health equity:** Enabled decentralization of treatment with portable TA devices can be placed at lower-level facilities. Helps deliver services in hard to reach/ remote/ rural areas
- **Ease of procurement:** Single supplier from which device+ consumables are procured. Logistically easier to procure than cryotherapy that comes with the challenge & variability involved with supply of gas cylinder & its refills
- **Reduction in service delivery time & Cost:** 1-2 min to conduct TA procedure vs. ~10-20 min for cryotherapy, thus saving precious HCW time; Cost per Tx cut by ~75% vis-à-vis cryotherapy

Total cost per treatment using TA devices

CRYOTHERAPY		THERMAL ABLATION	
At full utilization	At 80% utilization	At full utilization	At 80% utilization
~$16	~$21	~$4	~$5

~75% reduction in cost per Tx using TA vs. Cryo

- **Device cost per TA treatment is 1/2 that of using Cryotherapy:** Cheaper upfront cost, lower cost of probes
- **TA does away with requirement of** costly gas to carry out Tx, which contributed **~60%** of total cost using cryo
- **Service delivery time, HCW costs lower by ~50%** in TA procedure vs. cryotherapy

Total cost per Tx using TA is average cost across 4 countries Kenya, Zambia, Senegal, Zimbabwe (unpublished program data) comprising: 1) Device cost, including procurement supply chain costs; 2) Reagents (gas for cryotherapy, NA for TA), 3) General Consumables, 4) Service delivery cost, 5) Training & site activation cost.

Unitaid

SAVE LIVES FASTER

Integrating HIV and Cervical Cancer Prevention: Essential Steps Toward Eliminating Cervical Cancer in Lesotho

By: Dr OL Akintade,MD

Elizabeth Glaser Pediatric AIDS Foundation (EGPAF)

Date: 30th May 2024

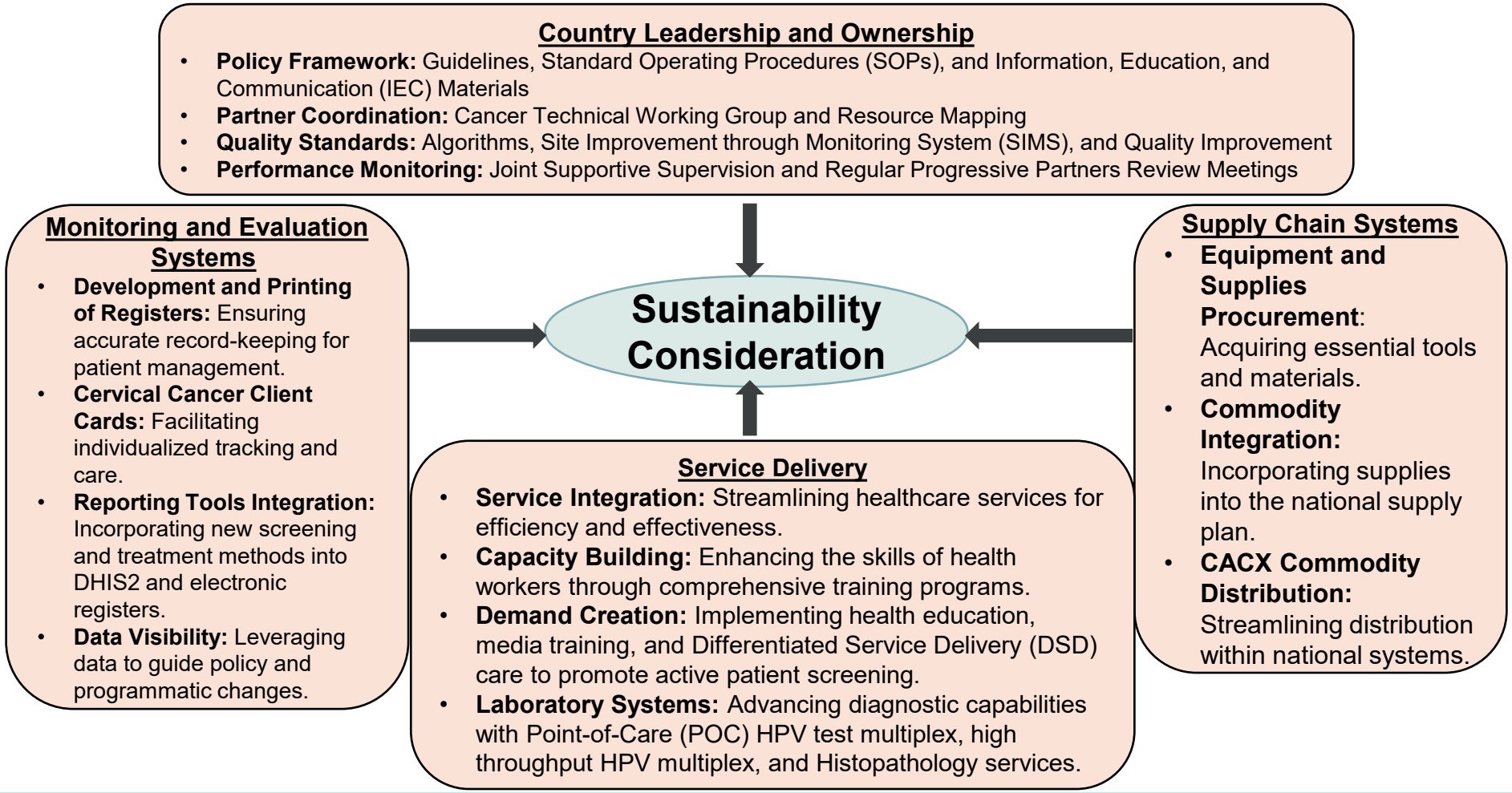
Integrating HIV and Cervical Cancer Screening: A Synergistic and Pragmatic Approach to Accelerate Cervical Cancer Elimination and Promote Holistic Women's Healthcare in Resource-Limited Settings

EGPAF Nurse, Sister Mamofolo Khamokha," **"Prevention is better than cure"**

Photo Description: Nurse accompanied by a student who undertook cervical cancer screening initiatives after their health education training.

Photo Credit: Makopano Makopano Letsatsi/EGPAF 2022

EGPAF's Health System Approach



Process Implementing Cervical Cancer Initiatives in Lesotho

Strategic Engagement: Initiate strategic meetings with program managers in HIV, Sexual and Reproductive Health, and Non-Communicable Disease sectors, along with ministry leadership, to explore opportunities for integrated approaches.

Resource Transparency: Engage in open discussions regarding available resources, ensuring a mutual understanding of their allocation and utilization.

Collaborative Planning: Address concerns collaboratively, fostering a shared vision and plan to enhance efficiency and effectiveness in tackling cervical cancer.

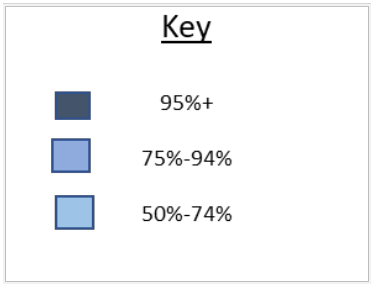
Stakeholder Involvement: Actively involve technical working groups and stakeholders to leverage diverse insights, skills, and resources for a comprehensive approach.

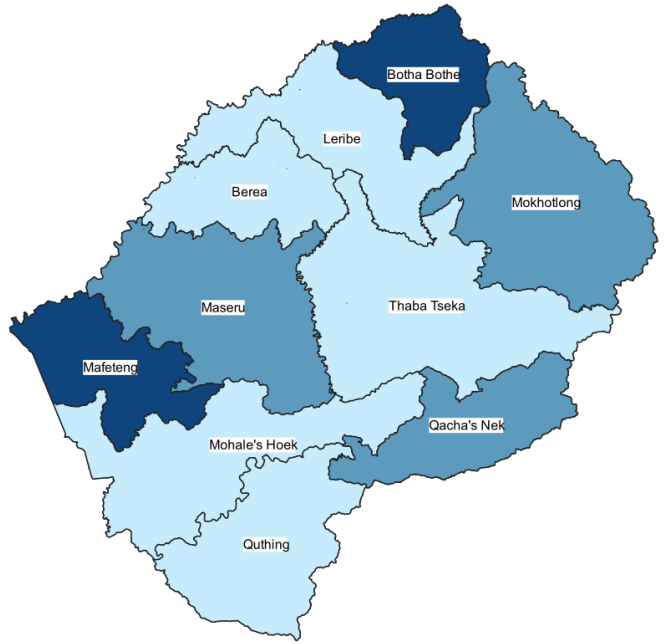
Resource Development: Develop detailed program implementation resources to ensure consistency, quality, and impact across all initiatives.

Implementation & Reporting: Execute the plan with precision and regularly report progress to donors, the Ministry of Health, and stakeholders to maintain transparency and accountability.

High-Level Advocacy: Engage with Director Generals, the Parliament Health Cluster, and the Prime Minister's Office to garner endorsement and support for cervical cancer initiatives.

HPV Vaccine Coverage in Lesotho by Districts



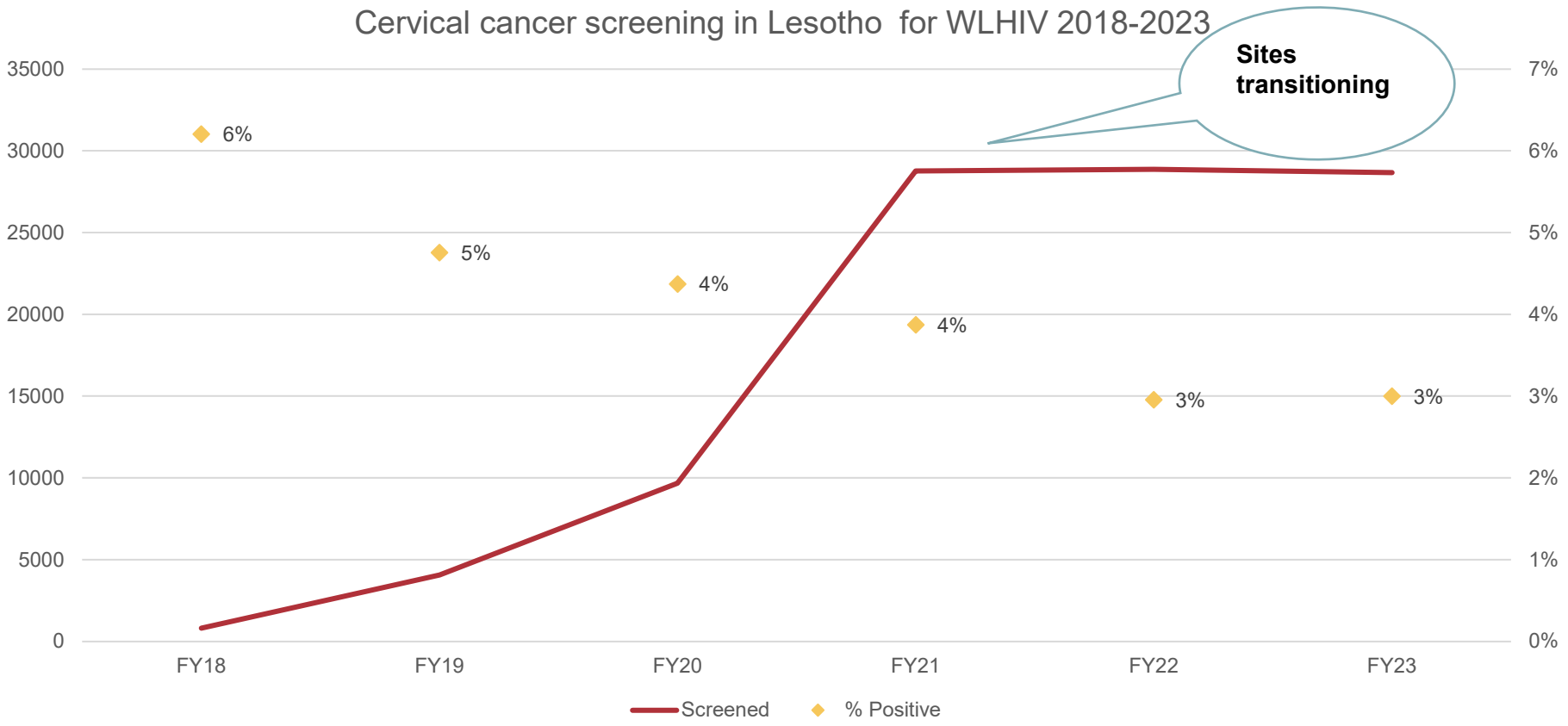


Total No. of eligible girls vaccinated, as of April 2024 – All districts

District	Total Target (HPV1 and HPV2, for all age groups) (A)	No. of girls vaccinated by district, as at 25th February 2024 (B)	Percentage (%)
Berea	7223	5134	71
Botha-Bothe	2806	3191	114
Leribe	12900	7872	61
Mafeteng	3636	4918	135
Maseru	28063	21616	77
Mohales Hoek	5455	3973	73
Mokhotlong	3996	3511	88
Qachas Nek	2207	1902	86
Quthing	3572	2442	68
Thaba-Tseka	6564	3538	54
TOTALS (National)	**76422**	**58097**	76

Source: BoS Projections and DHIS2

Cervical Cancer Screening in Lesotho for Women Living with HIV 2018-2023



Navigating Challenges in Cervical Cancer Initiatives in Lesotho

Ensuring Sustainability: Addressing concerns about the enduring impact and continuity of cervical cancer programs to secure lasting health outcomes.

Redefining Workload: Transforming the perception of additional work by integrating new initiatives into existing systems, streamlining efforts for maximum efficiency.

Closing the Skill Gap: Identifying and addressing the skill gap among service providers through targeted training, ensuring high-quality care and expertise in cervical cancer management.

Cervical Cancer Screening Saves Lives

Makhothatso Matsela

- As she was referred for cervical cancer screening by her neighbor, she feels that it is her responsibility to educate other women to go for cervical cancer screening.

- She therefore talks to her neighbors, her work mates and her family members about cervical cancer screening.

Elizabeth Glaser Pediatric AIDS Foundation

Fighting for an AIDS-free generation

HPV, Cervical Cancer, and HIV: The Importance of Advocacy

Alison Footman, PhD, MPH
Senior Program Manager, STIs
AVAC
May 30, 2024

AVAC
Advocacy. Access. Equity.

HPV, Cervical Cancer, and HIV

Why we should care

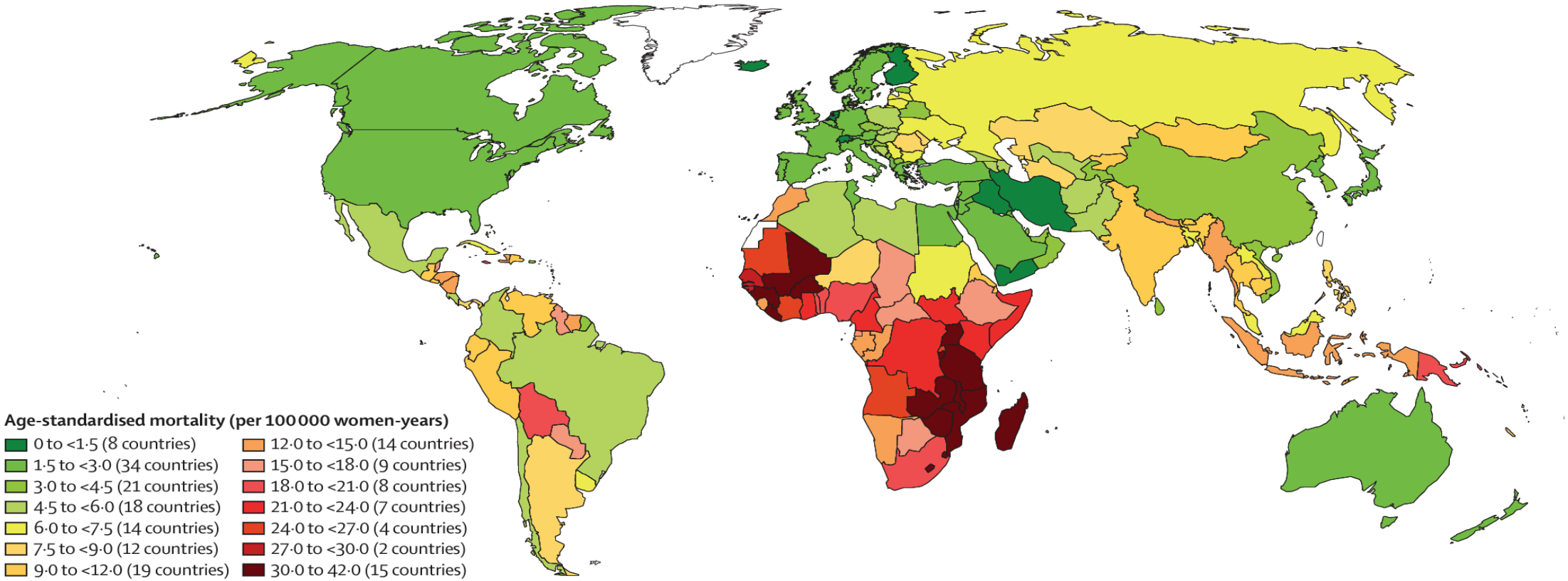
- Long-lasting, persistent, human papillomavirus (HPV) infections lead to cervical cancer.
- Cervical cancer is the **fourth** most common cancer in women, globally.
- In 2022, there were around 660,000 new cases and around 350,000 deaths related to cervical cancer.
- Women living with HIV are **six** times more likely to develop cervical cancer compared to women who are HIV-negative.
- Highest rates of cervical cancer incidence and mortality are in low- and middle-income countries, similar to HIV.
- Service integration is needed to better prevent and treat HPV, cervical cancer, and HIV

https://www.who.int/news-room/fact-sheets/detail/human-papilloma-virus-and-cancer

AVAC
Advocacy. Access. Equity.

HPV, Cervical Cancer, and HIV

Geographical distribution of world age-standardised mortality rate of cervical cancer by country, estimated for 2018

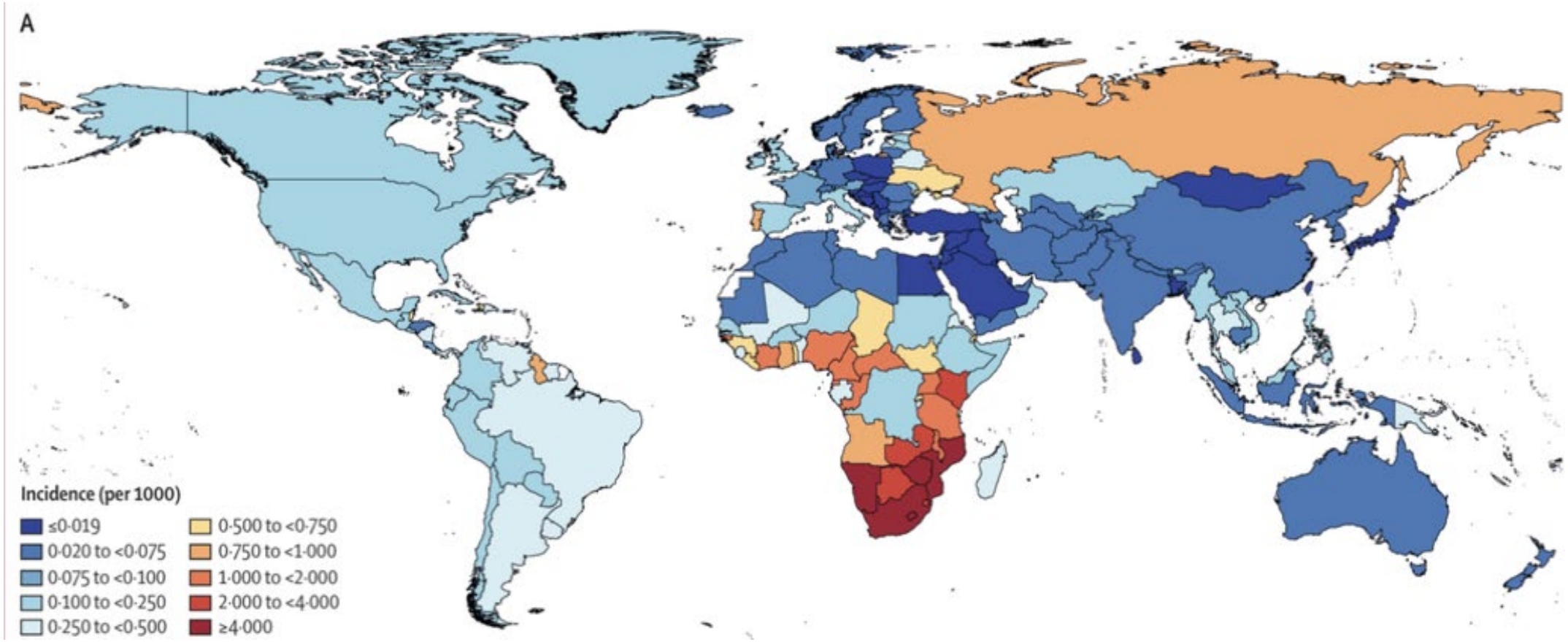


Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M., Ferlay, J., & Bray, F. (2020). Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. The Lancet. Global health, 8(2), e191–e203. https://doi.org/10.1016/S2214-109X(19)30482-6

AVAC
Advocacy. Access. Equity.

HPV, Cervical Cancer, and HIV

Age-standardised HIV incidence for both sexes, 2017



GBD 2017 HIV collaborators (2019). Global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2017, and forecasts to 2030, for 195 countries and territories: a systematic analysis for the Global Burden of Diseases, Injuries, and Risk Factors Study 2017. The lancet. HIV, 6(12), e831–e859. https://doi.org/10.1016/S2352-3018(19)30196-1

AVAC
Advocacy. Access. Equity.

HPV, Cervical Cancer, and HIV

Prevention

- Cervical cancer and HIV are preventable.
- The HPV vaccine can prevent six types of cancer (anal, cervical, oropharyngeal, penile, vaginal, and vulvar) and genital warts.
- In 2024, researchers in Scotland found,
  - No cases of cervical cancer in women born between 1988 and 1996 who were fully vaccinated against HPV at ages 12 to 13 years.
- If women living with HIV or in communities with high HIV incidence rates were vaccinated, could we see similar results?

"The vaccine is extremely effective": no cases of invasive cervical cancer found in Scottish women vaccinated against HPV

Real-world data suggests the HPV vaccine dramatically cuts cancer risk among women who received it during adolescence.

The New York Times

GLOBAL HEALTH

Millions of Girls in Africa Will Miss HPV Shots After Merck Production Problem

The company has told countries that it can supply only 18.8 million of the 29.6 million doses it was contracted to deliver this year.

Palmer, T. J., Kavanagh, K., Cuschieri, K., Cameron, R., Graham, C., Wilson, A., & Roy, K. (2024). Invasive cervical cancer incidence following bivalent human papillomavirus vaccination: a population-based observational study of age at immunization, dose, and deprivation. Journal of the National Cancer Institute, djad263. Advance online publication. https://doi.org/10.1093/jnci/djad263
https://www.gavi.org/vaccineswork/vaccine-extremely-effective-no-cases-invasive-cervical-cancer-found-scottish-women
https://www.nytimes.com/2024/04/18/health/hpv-vaccine-africa-merck.html

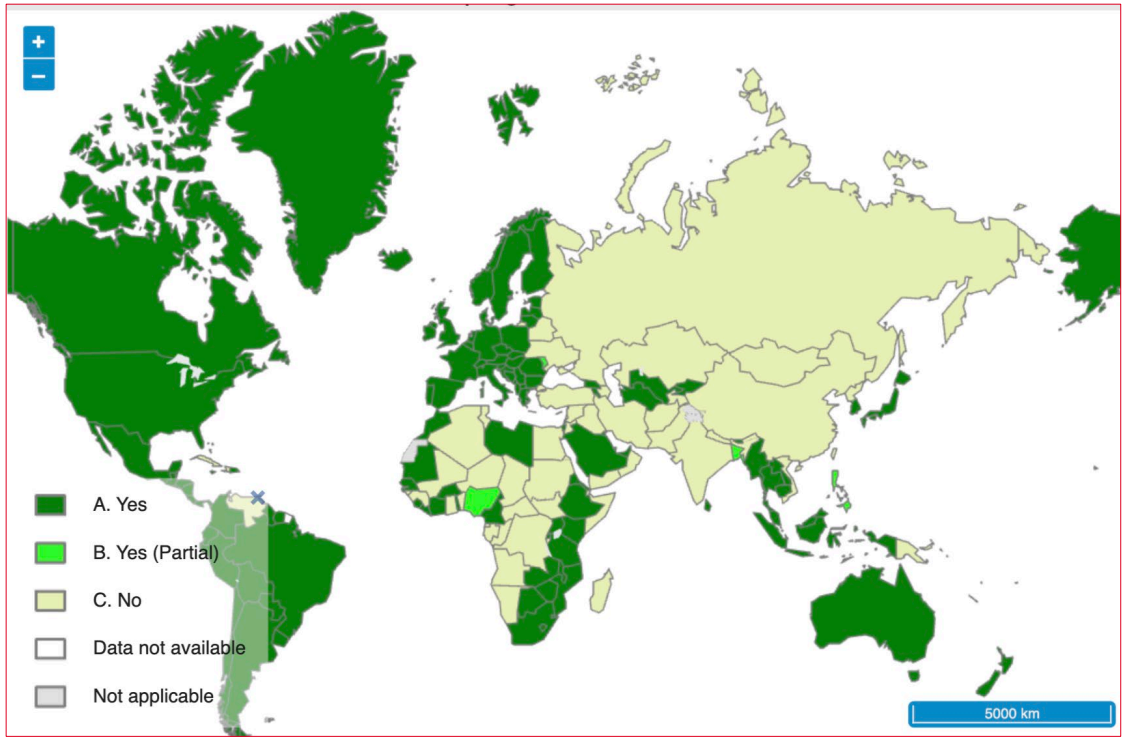
AVAC
Advocacy. Access. Equity.

If we build it, will they come?

AVAC
Advocacy. Access. Equity.

HPV Vaccination

- In 2022, it was estimated that 21% of adolescent girls had received at least one dose of HPV vaccine a 5% increase from 2021.
- 73% of countries (142 out of 194) include HPV vaccination in national immunization program.
- HPV vaccine introduction, coverage, and scale-up is impacted by
  - Cost
  - Health system constraints
  - Patient and policy barriers
  - Supply chain issues



HPV vaccine included in national immunization programme

https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/human-papillomavirus-vaccines-(HPV)/hpv-clearing-house/hpv-dashboard
https://www.who.int/news-room/fact-sheets/detail/immunization-coverage#:~:text=One%20hundred%20thirty%20Member%20States,programmes%20that%20resumed%20after%20interruptions.

AVAC
Advocacy. Access. Equity.

If we build it, will they come?

Maybe

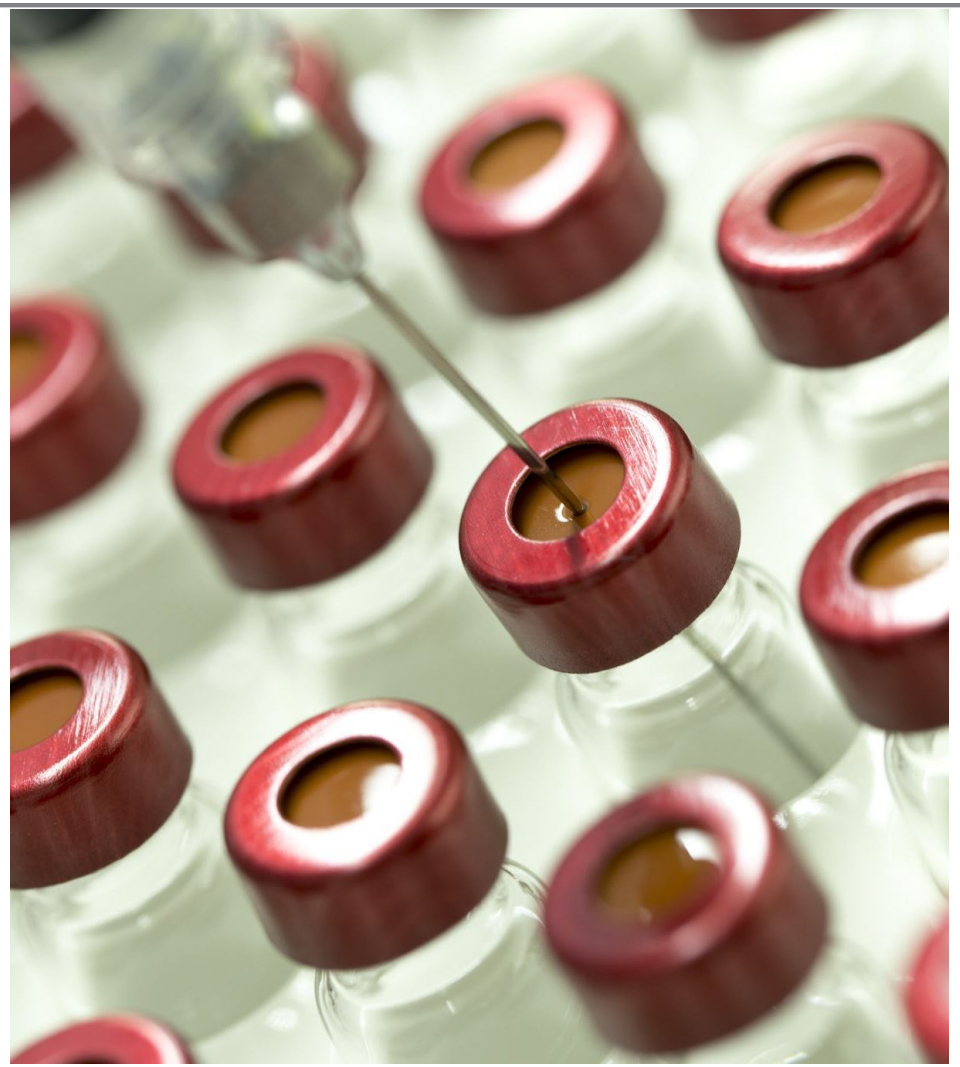
AVAC
Advocacy. Access. Equity.

If we build it, will we make it accessible?

AVAC
Advocacy. Access. Equity.

Advocacy Questions

- Is the vaccine accessible?
- Is the vaccine affordable?
- Have we communicated why people should get vaccinated?
- Do people trust us and the messages we are delivering?
- Have we proven to people that the vaccine will benefit them and protect their health?
- What policies are needed to promote vaccine introduction?
- Is this the vaccine that people want?



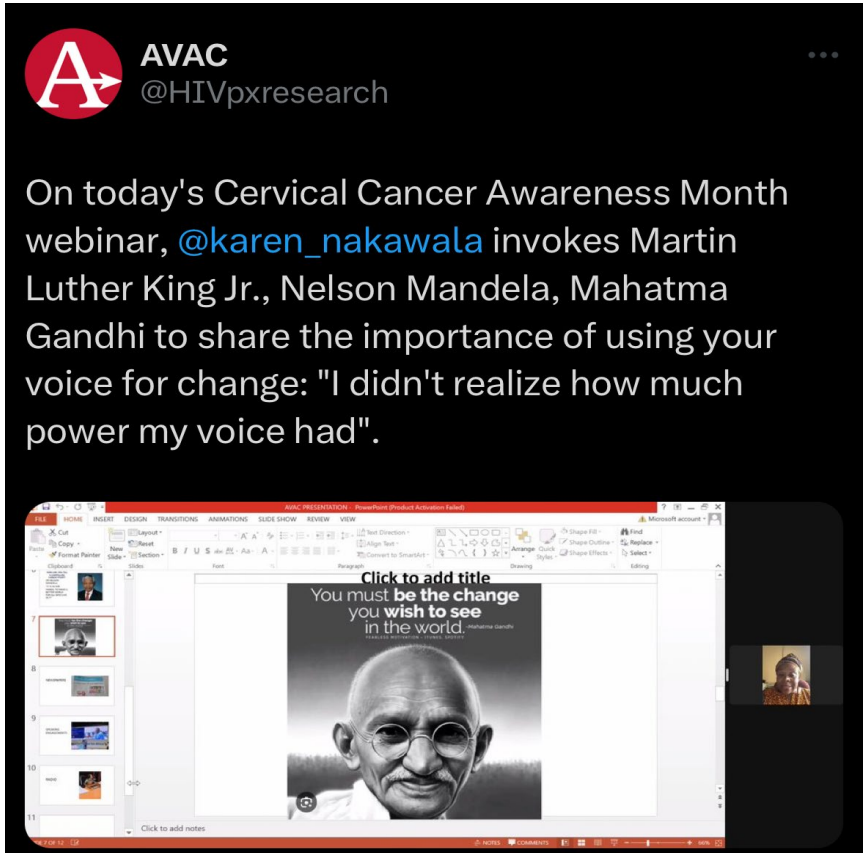
AVAC
Advocacy. Access. Equity.

If we build it, will we make it accessible?

We should

AVAC
Advocacy. Access. Equity.

Advocacy is Important



"We all contribute to the elimination of cervical cancer." – Tamika Felder, Founder, Cervivor, United States

"I didn't realize how much power my voice had." – Karen Nakawala, Founder, Teal Sisters Foundation, Zambia

https://avac.org/event/cervical-cancer-awareness-month-webinar-series/
https://cervivor.org/
https://www.tealsistersfoundation.org/

AVAC
Advocacy. Access. Equity.

Advocacy is Important

"STI prevention, diagnostics and vaccines costs are MUCH LOWER THAN DEALING WITH neonatal deaths, deaths associated with cervical cancer and AMR (STI Prevention - IS AN EMERGENCY)." – Mandisa Dukashe, Founder, HIV Survivors and Partners Network, South Africa

"There are significant opportunities to improve STI prevention, ensure equitable access to vaccines and diagnostics, and advocate for sexual health rights in Kenya through policy changes, community mobilization, public-private partnerships, and comprehensive educational campaigns." – Simon Odiwuor K'Ondiek, Associate Community Advisor, Nyanza Reproductive Health Society, Kenya

"Key population civil society organisations play a key role in information dissemination about STIs to their community members." - Henry Muzuwandile Sakala, Executive Director, Latu Human Rights Foundation, Zambia

https://avac.org/resource/results-from-sti-landscaping-analyses-in-east-and-southern-africa-parts-1-and-2/

AVAC
Advocacy. Access. Equity.

We can prevent cervical cancer among women living with HIV.

AVAC
Advocacy. Access. Equity.

How can we work together to prevent cervical cancer among women living with HIV?

AVAC
Advocacy. Access. Equity.

Alison Footman, PhD, MPH
Senior Program Manager, STIs

alison@avac.org

@AlisonFootman

@HIVpxresearch

AVAC
Advocacy. Access. Equity.