Rolling Out HPV Testing for Cervical Cancer Screening and Treatment: Experience from a Multi-Country Project

TogetHER Webinar Series
February 23, 2023

Thank you for joining the webinar! We will begin momentarily. Please note that all attendees are automatically muted.

Expanding access to cervical cancer screening with HPV testing

Experience and lessons learnt from a multi-country Unitaid-funded project

Unitaid
Innovation in Global Health

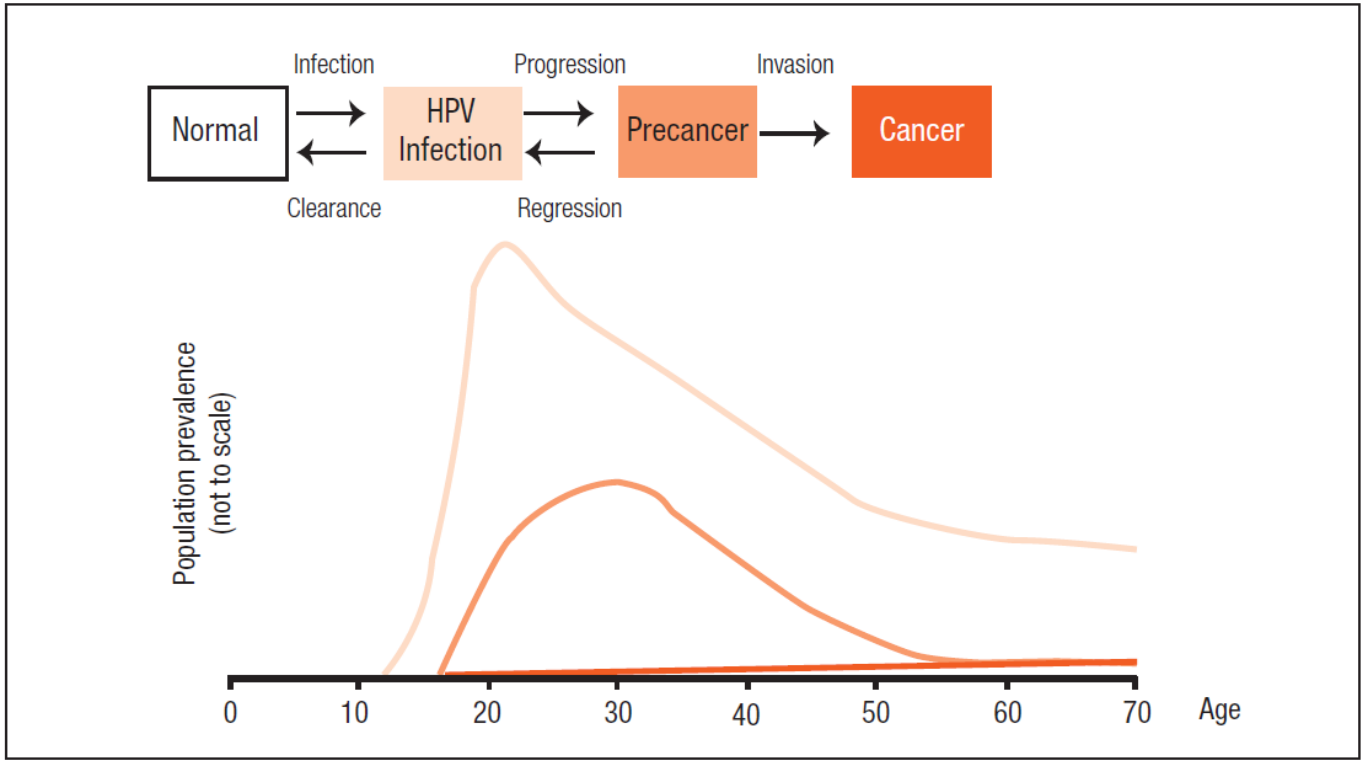
CLINTON HEALTH ACCESS INITIATIVE

Agenda

1	Overview of the challenge and Unitaid-funded CHAIs program response (3’)
2	Expanding access to screening with HPV testing (7’)
3	**Uganda**: Experience & lessons learnt from **point-of-care HPV testing model** (15’)
4	**Zimbabwe**: Experience & lessons learnt from **centralized HPV testing model** (15’)

Cervical cancer develops gradually, with opportunities at multiple points in time to interrupt disease progression and prevent death from invasive cancer…

Natural history of cervical cancer in HIV-negative women[1]



Opportunities to prevent deaths from cervical cancer:

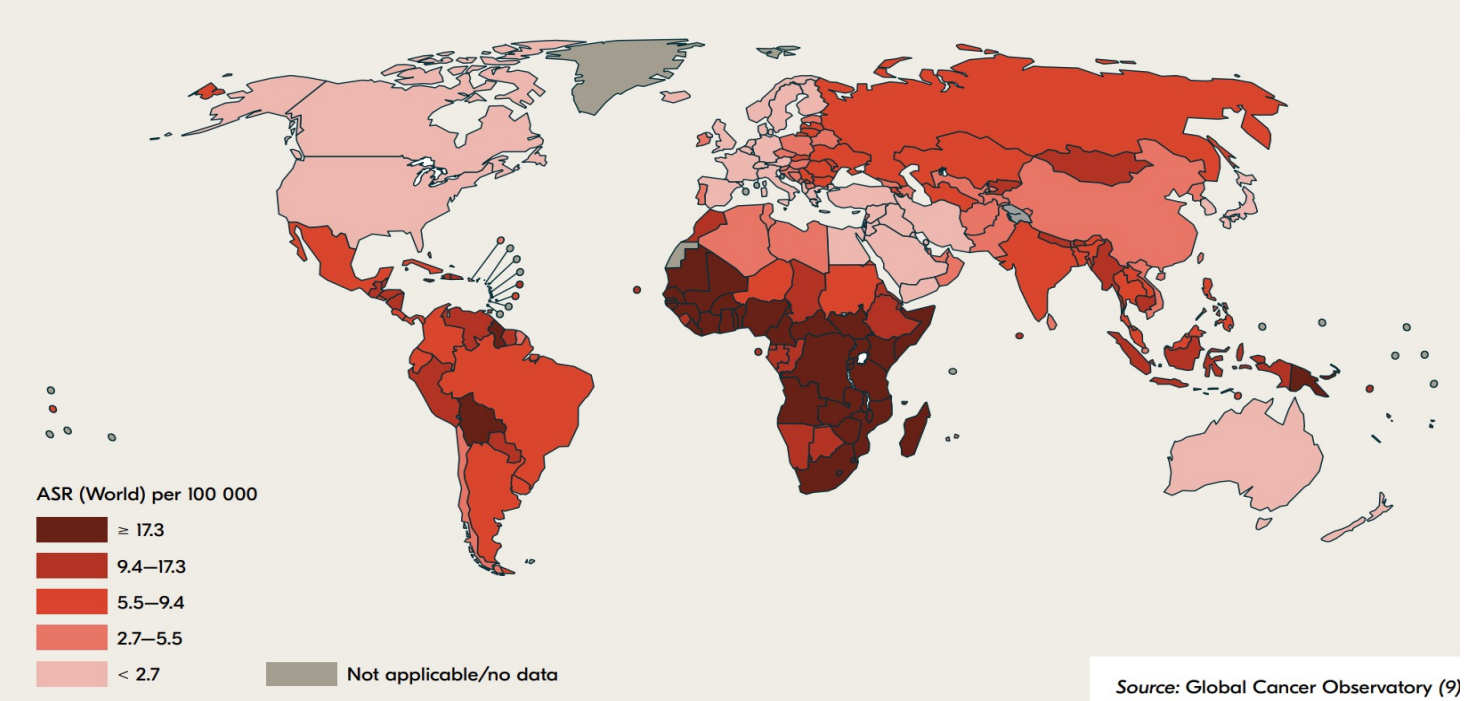
- HPV vaccination ("primary prevention")
- Screening and treatment for pre-cancer ("secondary prevention")
- Treatment for invasive cancer ("tertiary prevention")

Women living with HIV are **six times** more likely to develop cervical cancer than women who are HIV negative[2]: they are both more susceptible to HPV infection and experience more rapid progression from HPV infection to invasive cancer. The same prevention tools can save the lives of women living with HIV.

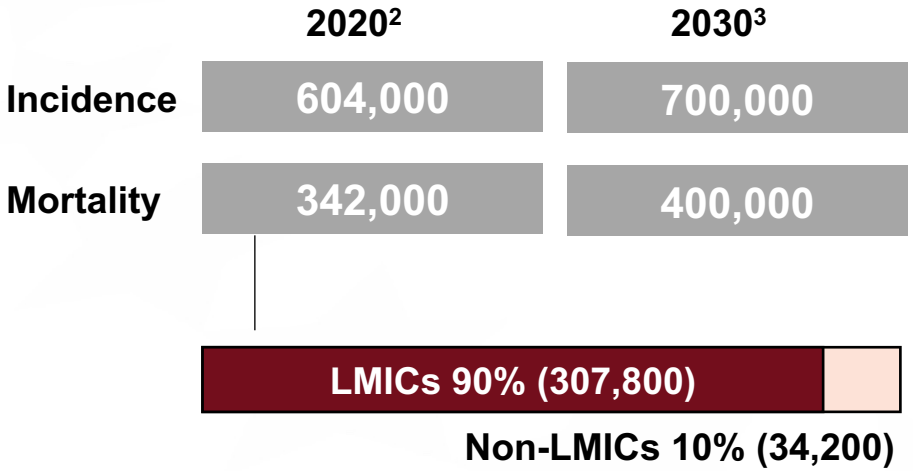
[1] *Comprehensive cervical cancer control: a guide to essential practice – 2nd ed. Geneva: World Health Organization; 2014.*
[2] *Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020.*

Limited access to prevention services drives a highly inequitable burden of disease, with more than 90% of the >340,000 annual deaths from cervical cancer occurring in LMICs

Estimated age-standardised mortality rates (World) 2018, cervix, all ages[1]



Source: Global Cancer Observatory (9)



[1]*Global Cancer Observatory. Estimated cancer incidence, mortality and prevalence worldwide in 2018: cervical cancer. International Agency for Research on Cancer, World Health Organization; 2018*
[2]*World Health Organization fact sheet 22 February 2022* **Cervical cancer (who.int)**
[3]*Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020.*

WHO's elimination strategy[1] calls for mobilization towards specific targets that would result in >62 million cervical cancer deaths averted in the next 100 years

Adaptation of WHOs strategy for cervical cancer elimination

90% OF ALL girls fully vaccinated7 with HPV vaccine by 15 years of age *Primary Prevention*	70% **OF ALL** women screened using a high-performance test by 35 years of age and again by 45 years of age ***Secondary Prevention***	90% OF ALL women identified with cervical disease are treated *Tertiary Prevention*
Vaccination & Communication  • HPV vaccination for 9–14-year-olds • Sexuality education • Condom promotion/provision • Male circumcision	**Screening & Treatment of pre-cancerous legions**  • Screening with HPV and/or VIA • On-site treatment for eligible lesions with TA or Cryotherapy • Referral for LEEP for other precancerous lesions • Referral for diagnosis of suspected cancer	**Cancer Treatment**  • Ablative surgery • Radiotherapy • Chemotherapy • Palliative care

[1] *Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020.*

In response to the WHO Call to Action, Unitaid has invested in increasing access to life-saving screening and treatment tools by addressing key access barriers

Multifaceted approach to address critical access barriers

Improve affordability of screening tools & establish sustainable supply of handheld treatment devices

Affordability

Demonstrate effective delivery models for screening, treatment & linkage to continuum of care

Supply & Delivery

Create conditions for scale-up of effective, affordable models & tools

Demand & adoption

Prepare AVE algorithm & accompanying tools for regulatory approval, in-country intro & sustainable continued use

Innovation & availability

Access barriers

Unitaid-funded CHAI program scope

1. Expand access to HPV testing & VIA screening
2. Improve access to treatment of cervical pre-cancer using thermal ablation & LEEP devices
3. Strengthen patient Management, referral & patient tracking systems
4. Create conditions for scale-up & sustainability

Countries in scope: *India, Kenya, Malawi, Nigeria, Rwanda, Senegal, South Africa, Uganda, Zambia, Zimbabwe*

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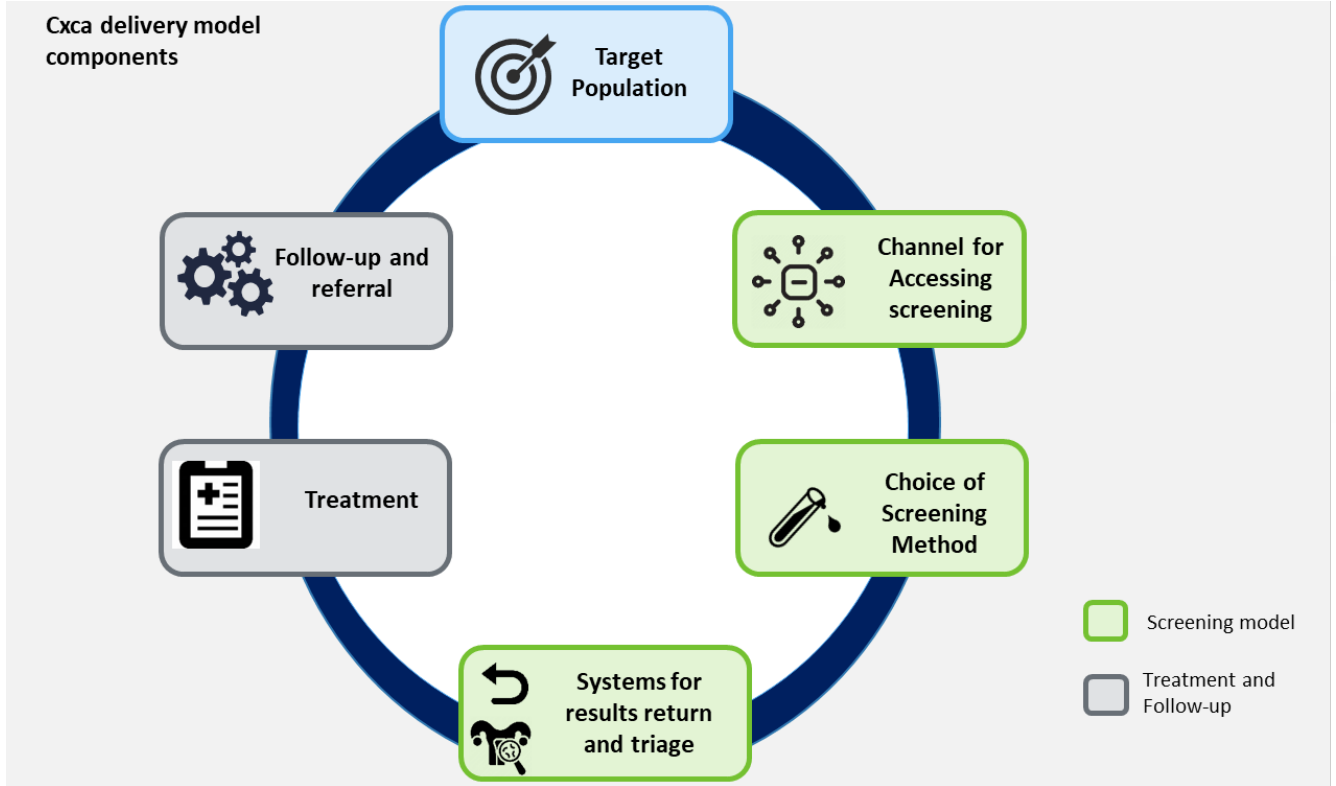
The project worked with national and state government partners across 10 countries to map out appropriate delivery models to reach women for cervical cancer prevention



Key enablers/ success factors

- National Strategic Plans
- Demand Generation
- Training, Mentoring & Supervision
- Info systems for patient tracking

Key results

>950,000
Women screened

<$9 HPV DNA test
~40% price reduction

~80%
Screen-positive women receiving treatment

$920
Thermal Ablation device*
~45% price reduction

97%
Sites offering integrated service delivery

90%
Sensitivity** of AVE algorithm to screen for pre-cancer

Program countries in order of flag appearance: Kenya, Rwanda, Malawi, Zambia, Uganda, South Africa, Zimbabwe, Nigeria, Senegal, India

Estimated grant level results as of 31 Dec 2022

* Average of Liger TA product $925 and Wisap TA product Euro 904/ 938
** Based on results of training and validation study; performance studies underway

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The project leveraged existing lab network capacity to offer HPV testing through an integrated approach

Key PCR Platforms conducting HPV Tests

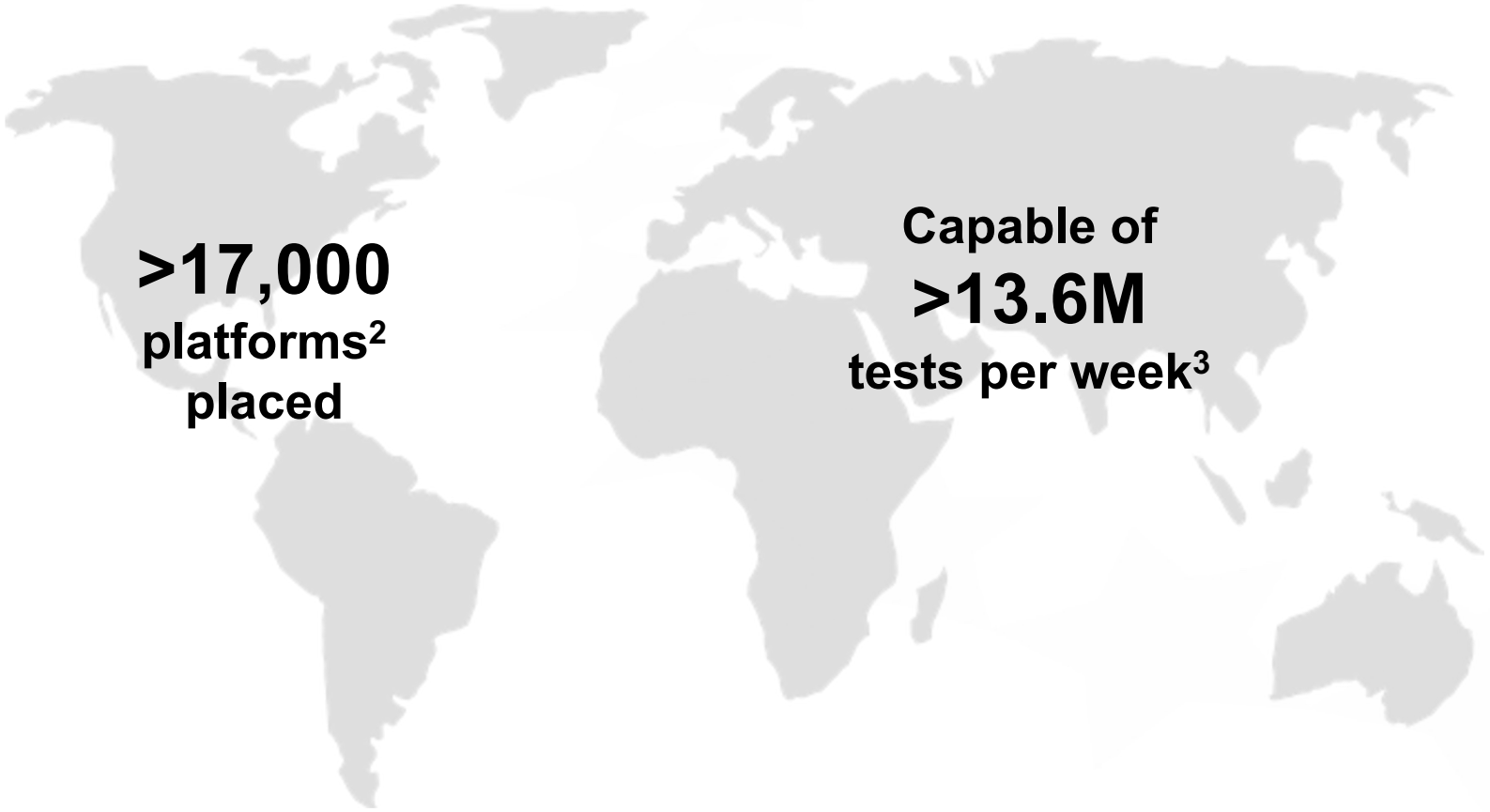
- Abbott Laboratories
- Becton Dickinson
- Bio-Rad Laboratories
- Hologic
- Roche
- ThermoFisher
- Qiagen[4]
- Cepheid[5]
- MolBio[6]

Centralized

Near Point-of-Care

Not comprehensive

LMIC Automated and Manual Testing Infrastructure[1]



>17,000 platforms[2] placed

Capable of >13.6M tests per week[3]

1. Non-comprehensive mapping of footprint data. Data as of October 2021. 2. Platforms indicative of individual amplification platforms (thermocycler, automated amplification platform, GeneXpert I, II, IV, XVI, etc). Gx data based on platform devices assumes average of 4 modules/platform. 3. Capacity calculations based on observed manual testing throughput during Covid period through May 2021, supplier estimated testing throughput for GeneXpert and other automated devices, observed number of shifts per days and days per week for lab operation observed through May 2021. 4. Multiple platform offerings for both centralized and near-POC. 5. Cepheid Omni and Edge HPV products in pipeline. 6. Currently available in India, though not yet available globally

Swift and substantial price reductions were achieved for HPV assays across Abbott, Roche, and Hologic, ranging from 25-50%

	Abbott	Roche	Hologic [1]	Cepheid[5]
POST-negotiation	**HPV $5.69** [2] EXW	**HPV $7.90** [3] CPT	**HPV $9.00** DAP	**HPV $14.90** EXW
	33 SSA countries	89 LMICs	8 African countries [4]	145 countries
PRE-negotiation	$12	$9.4	$12	
	-53%	*-16%*	*-25%*	

Price reductions achieved even at low volumes

CHAI-negotiated lower pricing for LMICs was made possible by manufacturers **leveraging economies of scale achieved through large volumes in HICs** and intending to **catalyze high demand in LMICs**

[1] All-inclusive
[2] Instrument included $7.99
[3] Different prices may apply for special projects/grants, please contact Roche directly
[4] $11.28 pricing available to 50 countries
[5] Part of all-in GX 16 program

With available guidance and existing testing capacity, CHAI conducted HPV testing pilots within public healthcare programs for 5 countries

- Across the five countries, we saw the following for testing and treatment cascade:

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

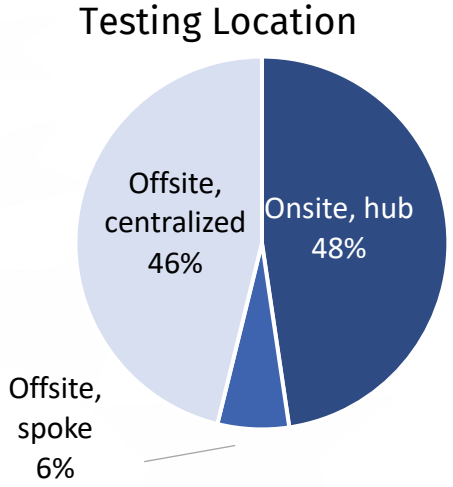
*Some steps may not include all countries due to relevant local policies.

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

**Predominantly WLHIV, except for Senegal*

- Turnaround times and patient results receipt, by testing location

	Hub	Spoke	Centralized	p-value
Median turnaround time from sample collection to patient receipt	9 days (IQR: 2-43)	11 days (IQR: 6-38)	56 days (IQR: 39-91)	p<0.001
Same-day results receipt	11%	0%	0%	p=0.091
180 days results receipt	**72%**	**63%**	**67%**	**p=0.587**



Impact

1. In countries that offered both clinician- and **self-sampling, the latter was found to be feasible and acceptable**, allowing greater flexibility in future screening programs.
2. Integration of HPV testing on existing testing platforms systems was feasible and 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.

At program implementation level, 9 countries instituted various approaches across different core areas of service delivery to improve the efficiency of HPV testing models

	Service delivery approach	Challenges & Learnings
1 **Sample Collection**	• Most countries **offered the choice of either self- or clinician-collected** at facilities • Self-collection has begun expansion into community settings	• In 2 countries, **~60% of women opted for self-sampling** – when offered a choice • In another SSA country, **split was driven by the supply purchased** w/ increased self-sampling kit supply leading to increased use. • **100% of women** surveyed recommended self-sampling.
2 **Near-POC vs. Centralized**	• Countries offered **integrated testing** leveraging platforms with available capacity • Programs relied on existing sample transport and referral systems	• Same-day results return possible under near-POC models, though **difficult to achieve** due to lower prioritization of HPV tests • **In-lab backlogs** impacted turnaround times and volumes, caused by breakdowns, limited staff time, and high demand for other tests
3 **Results Return**	• HCWs **scheduled appointments for women** to receive results when results were likely to be ready • ART staff **applied stickers to patients' files** to remind staff of available results on patients' return	• Turnaround times **did not appear to significantly impact patient result return** rates • **Competing space on devices** made timelines for receiving results to clinic unclear. One country ensured dedicated lab time for HPV results (before 10am) to better plan for result availability
4 **Market Conditions**	• HPV test prices negotiated to reduce **average cost of HPV tests to $11.92** within pilot programs. • As program expanded, average pricing per test procured dropped **under $9/ test**	• **Country-led negotiations** and clear, funded country-demand helped to achieve even lower country-specific pricing • **Near-POC pricing is higher,** countries may consider the lower costs for centralized testing relative to programmatic outcomes

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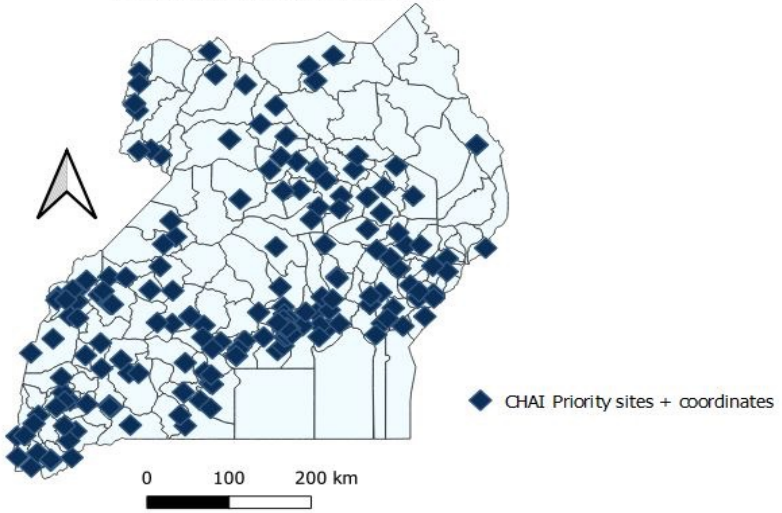
Cervical cancer is the leading cause of cancer deaths & most common gynaecological malignancy in Uganda. CHAI partnered with MoH to integrate scalable models of screening & treatment

A Map of Uganda Showing CHAI/UNITAID Supported Sites



- Uganda's cervical cancer burden is staggering. **With an ASIR* at 56.2 per 100,000**, it is among top 15 countries w/ highest rates of cervical cancer attributable to HIV.
- **National Screening target** by 2027: 50% of women aged 25-49 years screened; 90% of screen+ women getting treatment
- **Current national screening rate** at 10%
- **CHAI has been partnering since 2019 w/ the MoH** to expand HPV testing as the **primary cervical cancer screening modality,** by building scalable screening & treatment models, inc. self-testing of HPV, **using near point-of-care (POC) & centralized testing models**

RESULTS

Optimal tools for screening & treatment – **HPV tests ,TA & LEEP devices** included in **National guidelines**

2 **Integrated HPV testing models** established – Near POC using GeneXpert & centralized using Hologic

32,000 **Women screened** using **HPV tests** and
53,000 **VIA** respectively

89% **Treatment linkage**
250+ Lower-level health facilities equipped w/ **portable TA devices**

* ASIR = Age Standardized Incidence Ratio. Data from WHO IARC GLOBOCON 2020 Cancer Today (iarc.fr)

Uganda program was successful in delivering HPV testing under near-POC approach that resulted in highlighting logistical benefits associated with this model, although more costly to procure

NEAR-POC HPV TESTING MODEL: PROCESS FLOW

WLHIV screened for eligibility for CxCa screening at ART clinic

Eligible women **counselled** & consent obtained

Woman **taught to self-collect** her sample at ART clinic

Midwife **delivers samples** collectively to the lab **same day**

Depending on workload on GeneXpert, samples processed & **results sent to ART clinic within 1-3 days**

Midwife contacts women to return for their results, priority given to HPV+ women for contact

Near-POC testing platforms provide the opportunity to shorten wait time for the woman to receive her result back & be linked to appropriate treatment/ care

- **Same-day results return to women is possible** under this model, albeit with intensive efforts as HCWs often have competing priorities
- **Minimizes delays due to transportion** as collection & testing sites are in the same facility
- **Tracking samples is easier** in case results are not received at the ART clinic

The program adopted innovative strategies to overcome challenges associated with lab workflows, results return a& sample collection

	Challenges	Approach adopted
1 **In-lab workflows**	• **Limited capacity of GeneXpert to test for HPV samples**; HPV samples often deprioritized due to competing priorities. • **In-lab backlogs** impacted turnaround times & volumes, caused by breakdowns, limited staff time, and high demand for other tests.	• Guidance to health facilities to **dedicate 25% GeneXpert capacity to HPV testing** • MoH been able to obtain **higher capacity GeneXpert machines (16 modular)** for high burden facilities • Some health facilities **dedicated 2 days a week** to prioritize HPV testing
2 **Results return**	• **Same-day results return to the women wasn't possible in most cases** even though results were available at the facility due to constrained bandwidth of staff & healthcare • **Linkage to treatment challenge** when same day result-return is not feasible	• **Stickers placed on patient files** to identify those due treatment based on HPV test result • Piloting **automated SMS notification** to both woman & clinician prompting them to follow up for their results once ready from lab • Partner support in form of **airtime to ART clinic** to follow up women to come for their results
3 **Sample collection**	• Self sampling could sometimes be challenging **among uneducated women** leading to some samples getting rejected	• **Health worker aided self sampling** where necessary to ensure a fit for purpose sample is collected

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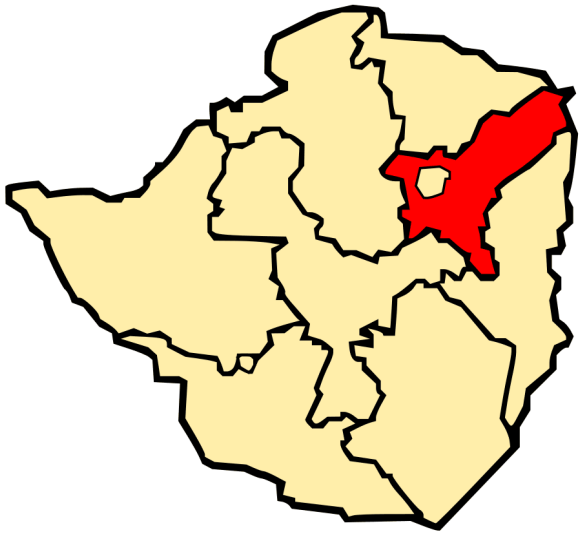
Cervical cancer is most common cancer among women in Zimbabwe with current infrastructure posing serious limitations to achieve screening targets. The project has made significant strides since 2019

CHA/ Unitaid implementation sites have been concentrated in Mashonaland East province



- Zimbabwe has among the highest burden of cervical cancer in the world. **With an ASIR* at 61.7 per 100,000**, it is among top 10 countries with highest rates of cervical cancer attributable to HIV.
- **Current national screening rate** at 20%, with only an estimated 10% of women in the **rural areas** having ever accessed a screen by 2021
- National screening target: 400,000 / year
- **CHAI has been partnering since 2019 with the MoH to scale HPV testing as the primary cervical cancer screening modality,** establishing scalable models of screening & treatment that leverage the existing deep penetration of **Hologic platforms** in the country

Optimal tools for screening & treatment – **HPV tests and TA devices** included in **National guidelines**

25,000 **Women screened** using **HPV tests;**

15,000 Women using **self-sampling**

80% **Treatment linkage** rate

138 …of 212 screening sites **across all 10 provinces offering treatment using TA**

RESULTS

* ASIR = Age Standardized Incidence Ratio. Data from WHO IARC GLOBOCON 2020 Cancer Today (iarc.fr)

Zimbabwe was successful in delivering HPV testing using the centralized approach, showcasing the potential it holds to maximize testing potential for HPV screening

CENTRALIZED TESTING MODEL: PROCESS FLOW

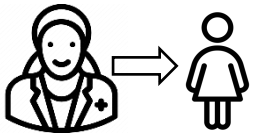
Samples collected at different points – Clinic, outreach in community by nurses & Village health workers

Samples **transported to hub** & forwarded to **testing lab**

Samples **processed alongside viral load samples** & tested on Hologic machine

Results returned to patients utilizing **LIMS frontline SMS system**

Village health workers follow up clients not presenting themselves for treatment



Centralized testing models offer the opportunity to maximize testing potential for HPV screening

- **Efficient** as it **leverages on existing** platforms, lab workflows, sample referral systems & results return used for viral load testing
- **Lower pricing** as compared to near-POC tests
- Flexible, **allows differentiated delivery models** for different use cases
- Offers best **mass screening potential** for low-resource settings
- **Higher throughput**

Effective interventions were implemented targeting demand creation, maximizing testing potential of existing platforms & streamlining sample referral & result return processes

	Challenge	Approach adopted
1 **Demand generation**	• **Hesitance among women** to screen especially WLHIV, given fear of stigma • Women who are healthy **rarely visit health facilities**/ seek screening	• Set up **community-based initiatives** **leveraging CSO's, CHCW's** to increase program visibility • **Screening program tailored** to WLHIV, & other women who are otherwise healthy but rarely seek screening
2 **In-lab workflow**	• **Inadequate testing capacity & lack of prioritization** to test HPV samples given competing priorities for platform (HIV, TB, Covid)	• Engaging with HIV viral load program to **create dedicated capacity** for HPV testing on validated platforms to meet desired targets (25% capacity should be utilized for HPV testing)
3 **Sample referral systems & results return**	• **Still-evolving processes to ensure results return to facility/ women** especially given newer models of self-collection	• **Developed LIMS based results return system**- clients get SMS as soon as test results validated & published • **Document modifications to sample referral workflows** that enable integration of HPV samples into existing transport systems + **National endorsement & dissemination** of the modifications to secure buy-in

We leave you with two images here – First is a lab technician testing an HPV sample at a lab in Zimbabwe; and happy faces from Uganda after using the thermal ablation device for treatment of pre-cancerous lesions.
Thank you for listening!

Zimbabwe – HPV testing being carried out on the Hologic Panther machine at Marondera Laboratory

Uganda – Cervical Cancer Focal Person in Mbarara RRH showcasing Unitaid-CHAI donated TA device for precancer treatment of HPV positive women

ANNEX

At program implementation level, HPV testing in 9 countries utilized integration on existing systems, with delivery models inc. from routine-facility screening, campaign models & community self-sampling

	Kenya	Malawi	Nigeria	Rwanda	South Africa	Zambia	Senegal	Uganda	Zimbabwe	SUMMARY
Testing model used	**Centralized & Near-POC**	**Near-POC hub and spoke**	**Centralized & Near-POC**	**Centralized**	**Centralized**	**Centralized & Near-POC**	**Near-POC hub and spoke**	**Centralized & Near-POC**	**Centralized**	• 7 Centralized • 6 Near-POC • 2 Spoke
Deployment model used (HPV) ***Deployment model***	Country referral hospitals to service as COE for HPV roll-out & community self sampling	Health center routine screening	Offered at sites with FP, ART and ANC services with community mobilization	Health centers using routine screening and campaigns	integrating HPV testing at LBC collection sites in pilot provinces	Passive demand through existing channels (ART clinics, FP, etc)	Hub & spoke testing with test & treat model	Testing offered at ART for 62 hub sites for routine-screening	Routine screening & Community self sampling through CHCWs	• 9 routine screening • 2 campaign • 2 community self-sampling
Results Return	-Facility return integrated into HIV LMIS system. -Scheduled return visits for clients	Health Surveillance Assistants for follow-up	Direct follow-up to HPV+ women by HCWs and CHAI teams	Direct follow-up with HPV+ often through CHAI outreach	Integration within existing LBC systems (TrakCare/email sent to site)	Women to return to facility for results	Scheduled return visits for when result availability is expected	Calling HPV+ and returning results on ART return visits	ART visits and CHCW follow-up with results	• Proactive outreach • ART return • Scheduled visits
HPV Testing Model	Gx integration if capacity, otherwise using Roche/Abbott	Gx16 & Gx4 integration with lab time set-aside for HPV	Integration at PEPFAR mega labs & GeneXpert sites	Integration with existing centralized device capacity	Dedicated devices for HPV testing used at NHLS sites	Centralized testing where Hologic exists; Gx in other regions	Integration with Gx4 platforms	Integration on on-site GeneXpert for most sites	Community and facility samples sent to integrated centralized labs	• 8 integrated • 1 dedicated
Target population	WLHIV (5%) and general population (95%)	WLHIV and general population	WLHIV (20%) & general population (80%)	WLHIV (15%) & Gen Pop (85%) Gen Pop receive HPV tests only if available	Same target population as existing LBC program	WLHIV, particularly under CDC and PEPFAR support	WLHIV and general population at all sites	WLHIV at ART sites	WLHIV and target populations (e.g sex workers)	• 8 WLHIV • 6 General population • 1 targeted
Models of sample collection	**Self collection HCW collection**	**Self collection HCW collection**	**Self collection HCW collection**	**Self collection HCW collection**	**HCW collection**	**Self collection HCW collection**	**Self collection HCW collection**	**Self collection**	**Self collection HCW collection**	**~50% self ~ 50% HCW**

Question & Answer

TogetHER Webinar Series

February 23, 2023