

Cervical Precancer Treatment

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Disclosures

- None

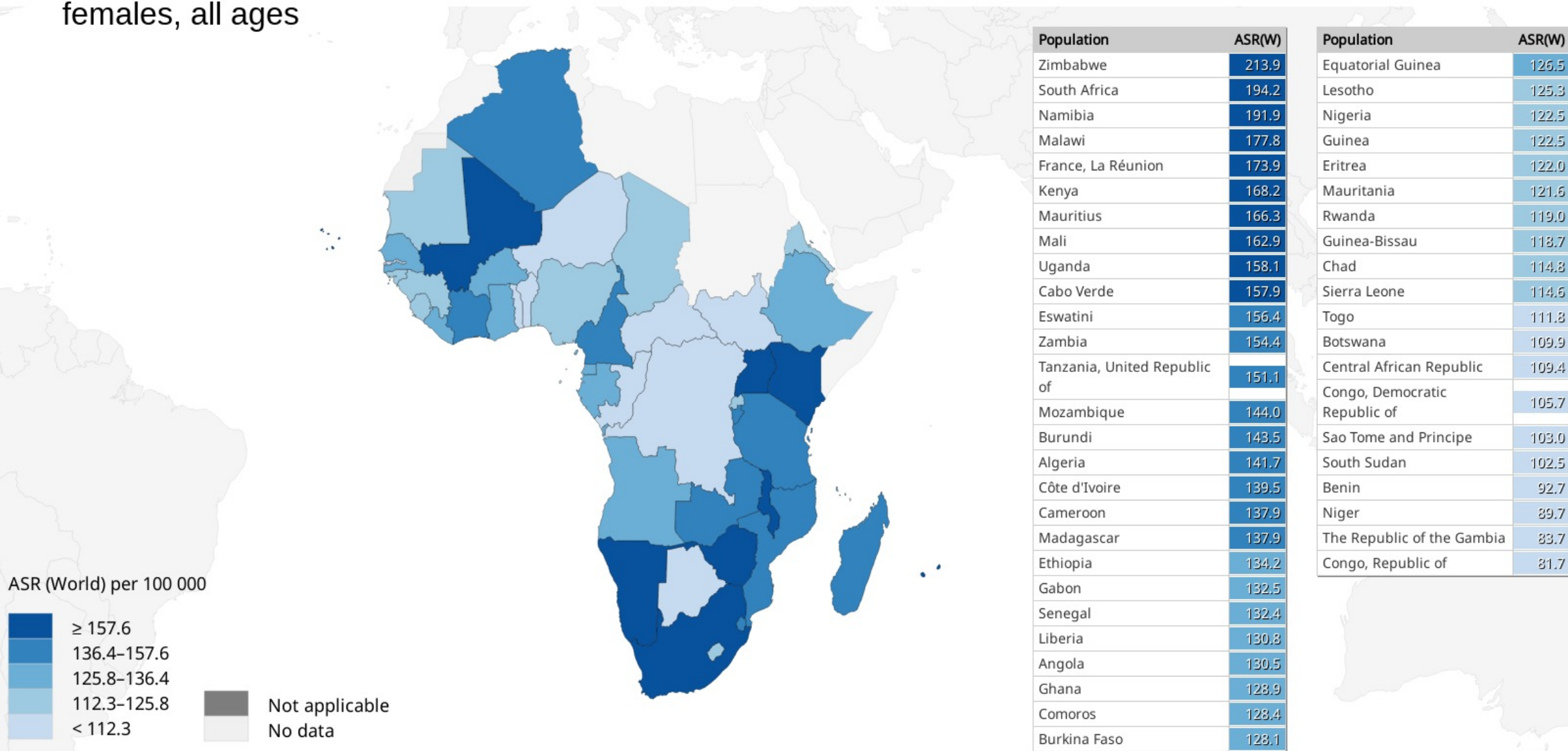
Outline

- Epidemiology of cervical cancer
- WHO Elimination cervical cancer elimination plan
- Treatment of preinvasive disease
- Ongoing research
- Conclusion

INTRODUCTION

- Cervical cancer is a global public health problem especially in LMICs
- Globally an estimated 604 127 new cases of cervical cancer and 341 831 deaths occurred in 2020
- Cervical cancer morbidity and mortality is a preventable
- Reduction in cervical cancer incidence and mortality, has thus far been observed predominantly in countries with a high Human Development Index (HDI)

Estimated age-standardized incidence rates (World) in 2020, all cancers, females, all ages



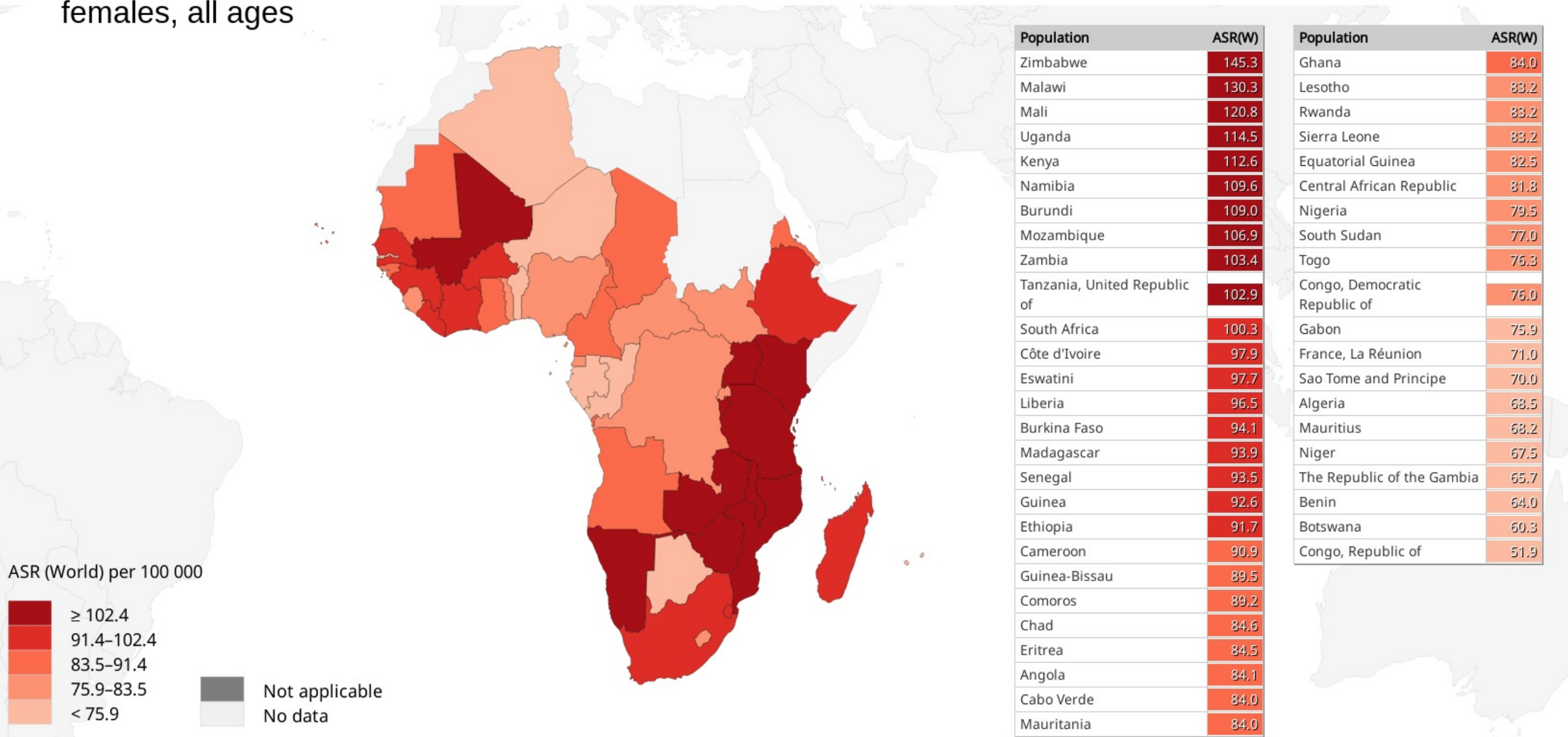
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Data source: GLOBOCAN 2020
 Map production: IARC
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 World Health Organization



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Zimbabwe National Cancer Registry Data

FIGURE 25

INCIDENCE: 2015

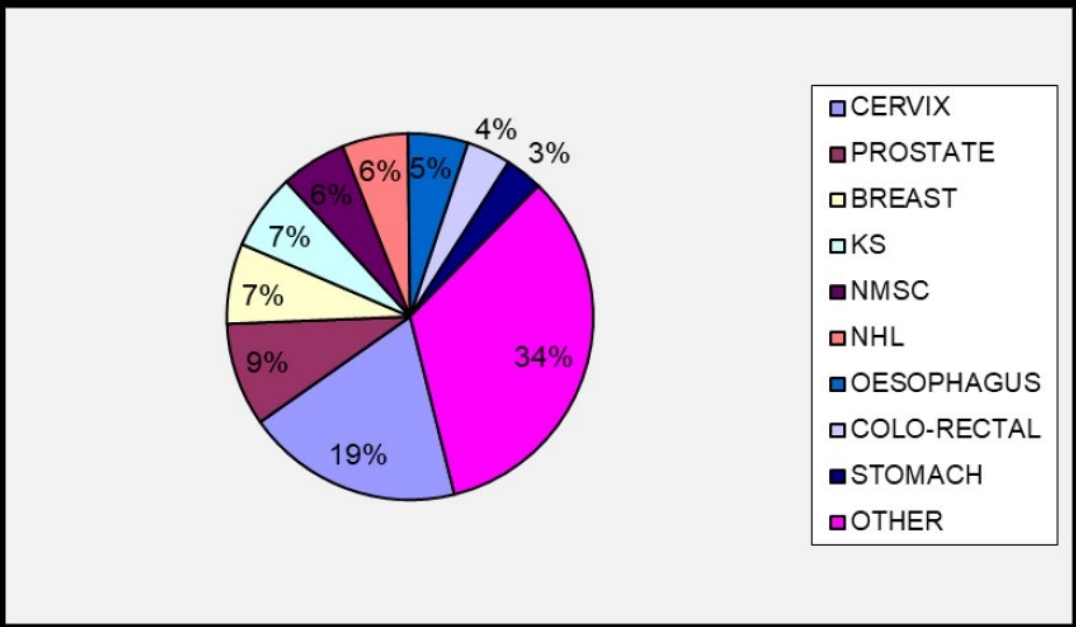
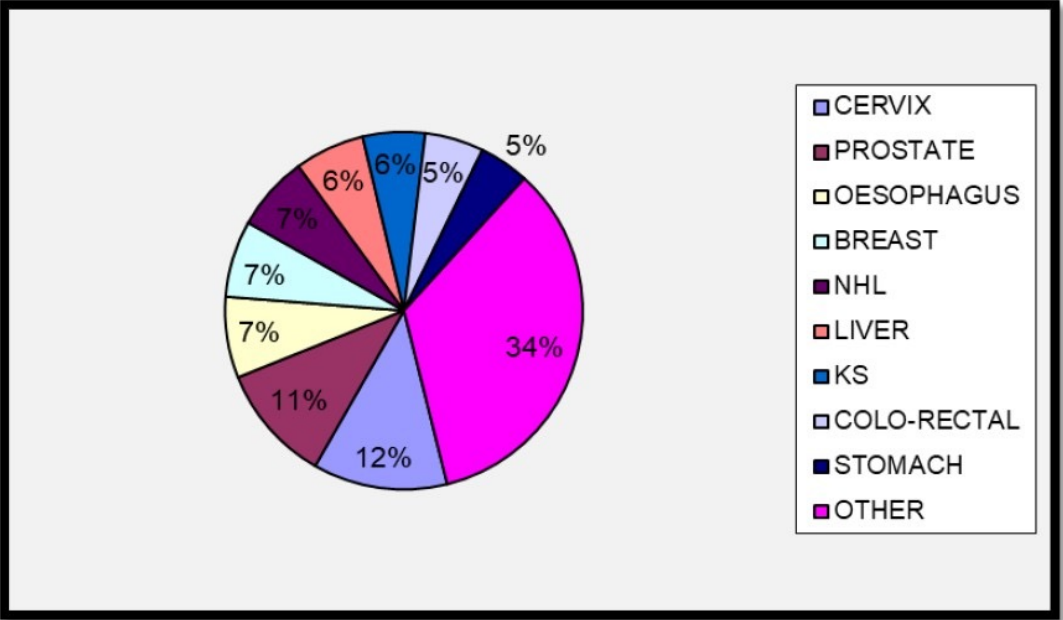


FIGURE 26

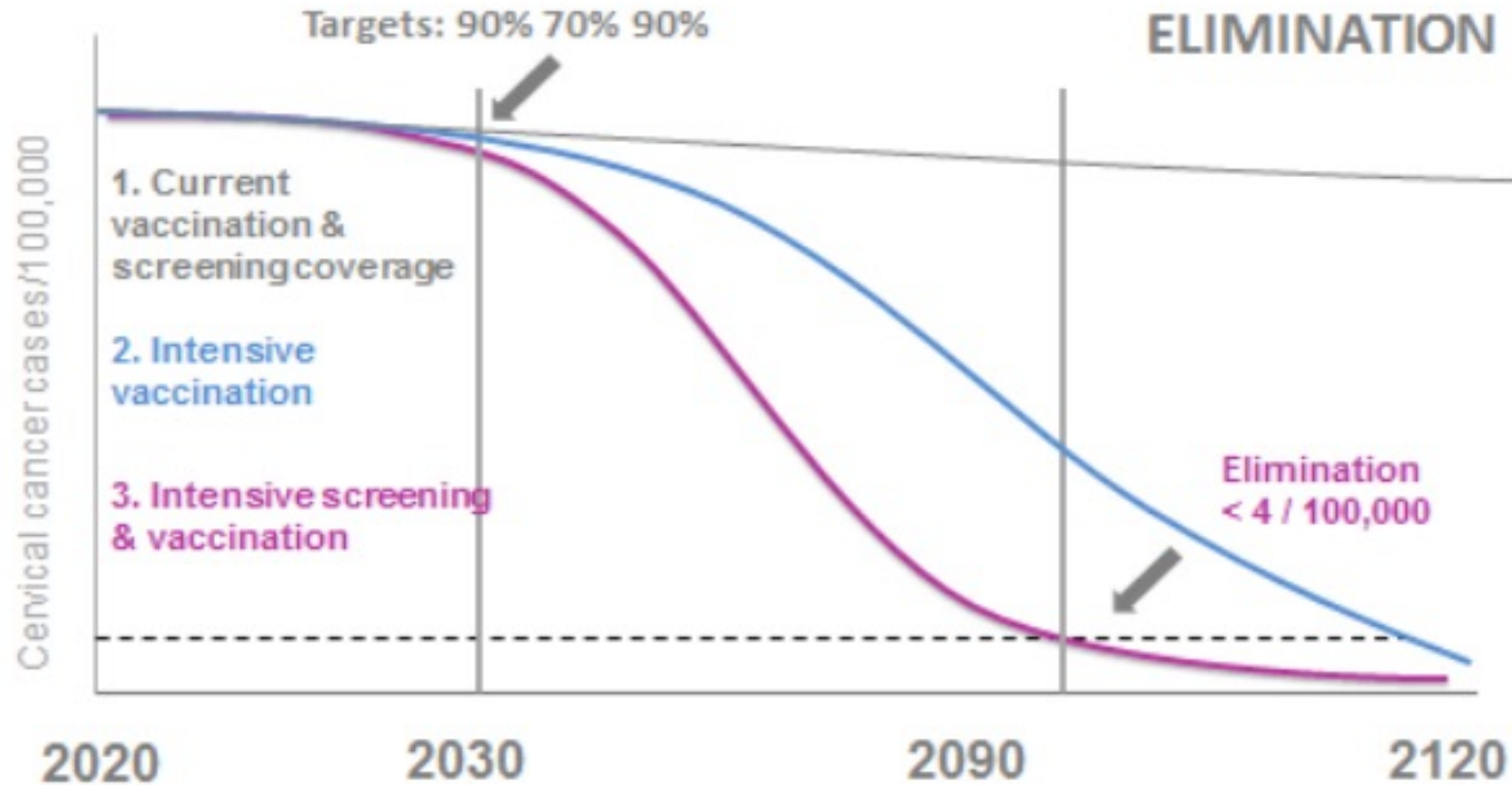
MORTALITY: 2015



KS = Kaposi sarcoma NHL = Non-Hodgkin lymphoma NMSC = Non-melanoma skin cancer

GLOBAL STRATEGY TOWARDS THE ELIMINATION OF CERVICAL CANCER AS A PUBLIC HEALTH PROBLEM

FIGURE 3: CONCEPTUAL FRAMEWORK OF THE GLOBAL CERVICAL CANCER ELIMINATION



WHO INITIATIVE ON CERVICAL CANCER ELIMINATION



WHO'S ELIMINATION STRATEGY 3 PILLARS*

- 1 Prevention through vaccination**
HPV vaccination offers long-term protection against cervical cancer.
- 2 Screening and treatment of precancerous lesions**
can prevent pre-cancer from developing into cancer.
- 3 Timely treatment and palliative care for invasive cervical cancer**
can save lives and palliative care can greatly reduce pain and suffering.

*To eliminate cervical cancer, all countries must reach and maintain an incidence rate below four per 100 000 women.

90-70-90 To Eliminate Cervical Cancer



#GlowTeal

GET INFORMED. GET SCREENED. GET VACCINATED.
LEARN MORE AT WWW.WHO.INT

Summary Recommendations: WHO suggests using the following strategy for cervical cancer prevention

For the general population of women

Screen and Treat **OR** Screen, Triage and Treat

- HPV DNA as primary screening test
- Starting at age 30
- Every 5 to 10 years screening interval

For women living with HIV

Screen, Triage and Treat - **ONLY**

- HPV DNA as primary screening test
- Starting at age 25
- Every 3 to 5 years screening interval

ARE ALL SCREEN POSITIVE WOMEN GETTING TREATED

Percentage of women with precancerous lesions who received treatment

Baseline (2016)	Midterm (2019)	Target (2020)
53%	66%	80%

Means of verification: Programme data

- To reduce the incidence of cervical cancer it is imperative that all women with precancerous lesions are treated
- Increase to 66% is an achievement
- ? are we really treating women with HSIL, PPV of VIAC is 10-20%
- ? no stage shift at diagnosis at tertiary unit in Harare (key informant)

Treatment of preinvasive lesions

- **EXCISIONAL**

- ✓ LEEP

- ✓ Cone biopsy

- ✓ Hysterectomy

- **ABLATIVE**

- ✓ Cryotherapy

- ✓ Thermal Ablation

- ✓ LASER



LEEP/LLETZ (type 1 and 2 excision)

- Since the early 1990s, LEEP is widely used for treatment as it allows histological audit of the colposcopy diagnosis, and can be performed under LA
- Challenges in LMICs
 - ✓ Cost
 - ✓ Equipment
 - ✓ trained personal (can only be done by trained doctors)

Cone biopsy (type 3 excision)

- Upper margin of lesion not seen
- Discrepancy between cytology and colposcopy findings
- Suspicion of microinvasion
- Endocervical cell abnormalities
- ✓ Cold knife, hot loop or laser
- ✓ Challenges- trained personal, cost, theatre time, higher risk of adverse obstetric outcomes

CRYOTHERAPY

- Cryotherapy is still the most widely used ablative method
- It is a safe and acceptable, cure rates exceed 90% when HSIL is confined to the visible part of the cervix (1-4)
- Challenges in LMICs
 - ✓ Requires uninterrupted supply of refrigerant gases such as NO or medical quality CO₂
 - ✓ The refrigerant gas may be expensive or not available in certain LMICs such as many SSA countries
 - ✓ Outreach programmes difficult to implement
- Zimbabwe is currently transitioning towards TA

Thermal ablation

- Thermal ablation is a feasible alternative to cryotherapy as it uses light weight portable electrical generators
- No anaesthesia is recommended (20 vs 30-45s at 100 °C), overall cure rate= 93.8% (95% CI 90.8% to 96.0%) (5)
- Although there are few reports of patients discontinuing the procedure due to pain (5,6)
- Indian study, 61% of women treated with TA without any anaesthesia complained of some pain (though mild only in vast majority of them) and 1.5% complained of severe pain (7)

TADA STUDY

- Collaboration with IARC
- RCT- duration of treatment, need for analgesia
- Recruitment very slow, most VIAC positive patients have no disease
- Challenges of VIAC

CERVICAL CANCER TREATMENT

- Depends on stage, PS, fertility wishes of the patient
 - Modalities can be surgical or radiation therapy, or multimodal
-
- ✓ Cone biopsy
 - ✓ Trachelectomy
 - ✓ Simple hysterectomy and BPLND
 - ✓ Radical hysterectomy and BPLND
 - ✓ Radiation + chemotherapy

DISPARITIES IN HIGH AND -LOW INCOME COUNTRIES

- Advanced imaging not readily available for staging - CT, MRI or PET scans
- Staging primarily clinical with limited imaging investigations
- Challenges with resources and trained personnel for surgery (2 gynaecological oncologists in Zimbabwe)
- Chemoradiation not readily available in government
- NACT given may have inferior oncological outcomes

?PROPHYLACTIC AND THERAPEUTIC VACCINES

- Prophylactic vaccine in women undergoing LEEP (AMC 99)
- Most of the double blinded RCTs demonstrate that therapeutic HPV vaccination trend towards efficacy patients with CIN
- Challenge is most of the trials don't include WLHIV
- BMG modelling work to design an ideal vaccine and assess the best model to deploy it

Therapeutic vaccines

Summary of clinical HPV therapeutic vaccines.

Vaccine Platform	Vaccine	Antigen	Conditions	Phase/NCT Number	Study Start	Status
Bacterial vector Vaccine	ADXS11-001	HPV16 E7	EAs,UCC	Phase II/ NCT01266460	May 23,2011	Completed
			OC	Phase I/ NCT01598792	February 2012	Terminated
			AC,RC	Phase II/ NCT02399813	September 2015	Completed
			UCC,SCCHN	Phase I/Phase II NCT02291055	April 2015	Active, not recruiting
			SCCHN	Phase II/ NCT02002182	December 2013	Active, not recruiting
	Ad/MG1-E6E7	HPV16/18 E6/E7	HPV-Associated Cancers	Phase I/ NCT03618953	June 21,2018	Active, not recruiting

CASCADE trials network- WLHIV

- Thermal ablation vs follow-up
- Extended vs flat probes
- TA vs LEEP

CONCLUSION

- Most LMICs employ screen and treat
- Recent data showing high failure rates in WLHIV
- More studies needed to determine optimal treatment especially in WLHIV

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THANK YOU