



# ELIMINATION OF CERVICAL CANCER AS A GLOBAL PUBLIC HEALTH PROBLEM

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World Health  
Organization

# 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

# Elimination Strategy

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## 2030 CONTROL TARGETS

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# ACHIEVING 70% COVERAGE OF SCREENING AND TREATMENT OF PRECANCER LESIONS



## WHO recommendations

- Women aged 30-49 be screened at least once in their lifetime for cervical cancer, and rescreened every 5 years.
- Women living with HIV should be screened every 3 years
- Immediate treatment where possible



## Challenges

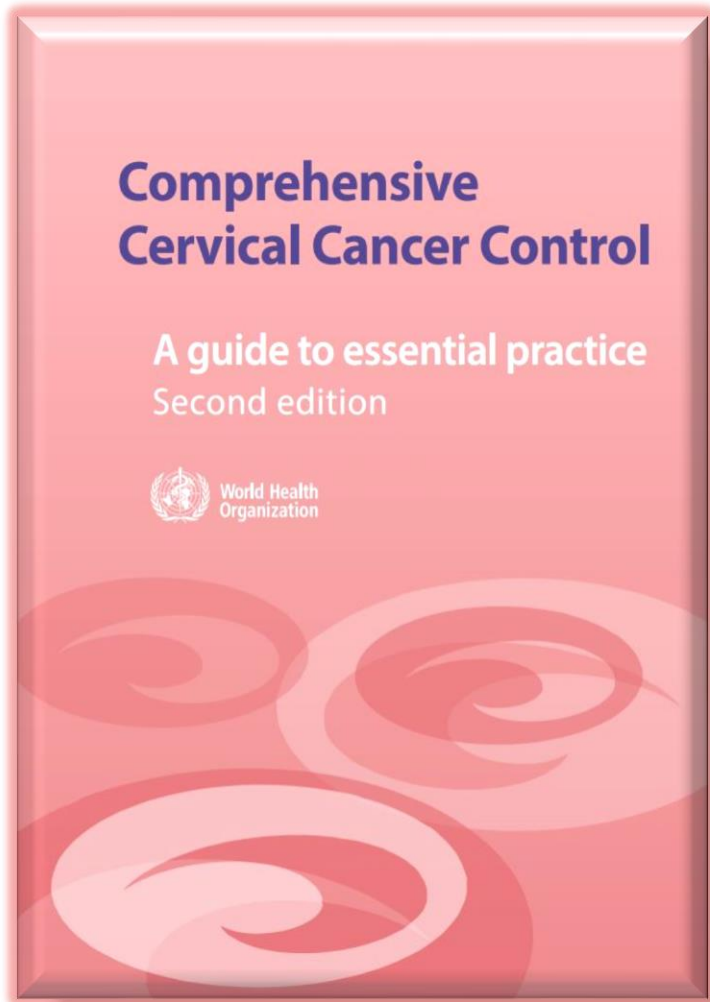
- *Expensive and complex screen and treat technologies complicate scaling-up*
- *New or optimized service delivery methods required for LMIC contexts*

## Accelerators

- **Sufficient, affordable supply of screen and treat technologies & products**
  - Prompt certification of new products
  - Price reductions
- **National scale-up of screen & treat**
  - Simple algorithms need to be introduced for different settings
- **Increased quality and coverage of service delivery**
  - Countries detailed implementation plans to introduce and scale-up products and delivery models
  - Strengthen patient retention and linkage to treatment



# WHO Recommendations for Screening and Treatment

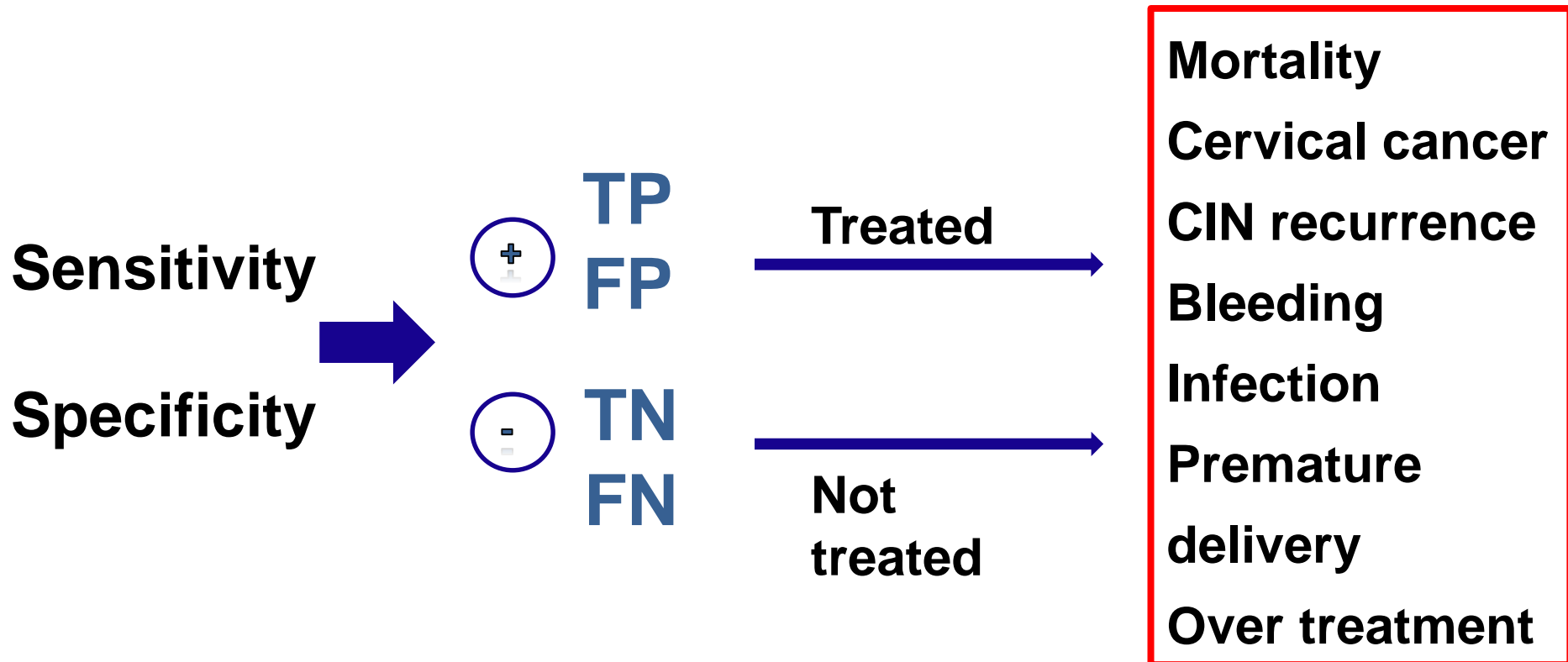


**Screening should start at 30 years of age.**

- The magnitude of the net benefit will differ by age
- Benefits may extend to younger and older women, depending on their baseline risk.

**HIV + women should be screened immediately** upon learning their HIV status, if they are sexually active.

# What are the downstream consequences of screening and treatment?



# Performance and characteristics of different screening methods (CIN2+)<sup>1</sup>

## Current screening tests recommended

Screening test	Sensitivity	Specificity	Characteristics
Conventional cytology	Moderate (44-78%)	High (91-96%)	Requires adequate healthcare infrastructure; laboratory based; stringent training and quality control
HPV DNA testing	High (66-100%)	Moderate (61-96%)	Laboratory-based; high throughput; objective, reproducible and robust; currently expensive
VIA	Low - Moderate (22 <sup>2</sup> -79%)	Low (49-86%)	Low technology; low cost Linkage to immediate treatment possible

<sup>1</sup> Cuzick *et al.*, Vaccine 26S (2008) K29-K41

<sup>2</sup> Labani *et al.*, EurJOGRB (2014)

# CERVICAL CANCER SCREENING AND TREATMENT: TREATMENT METHODS FOR CIN2/3

## **Ablative treatment (of women screened positive and eligible)**

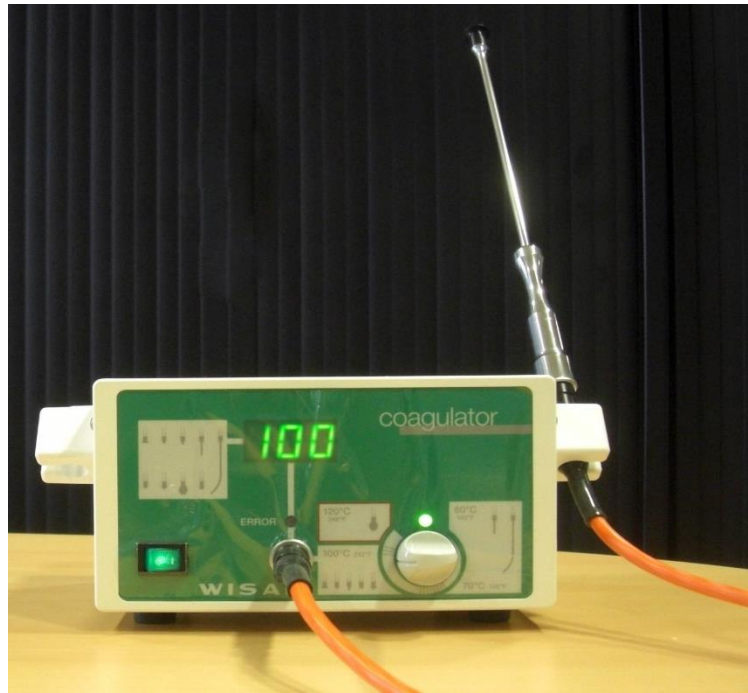
- Cryotherapy
- Thermal Ablation (now WHO recommended)

## **Excision treatment**

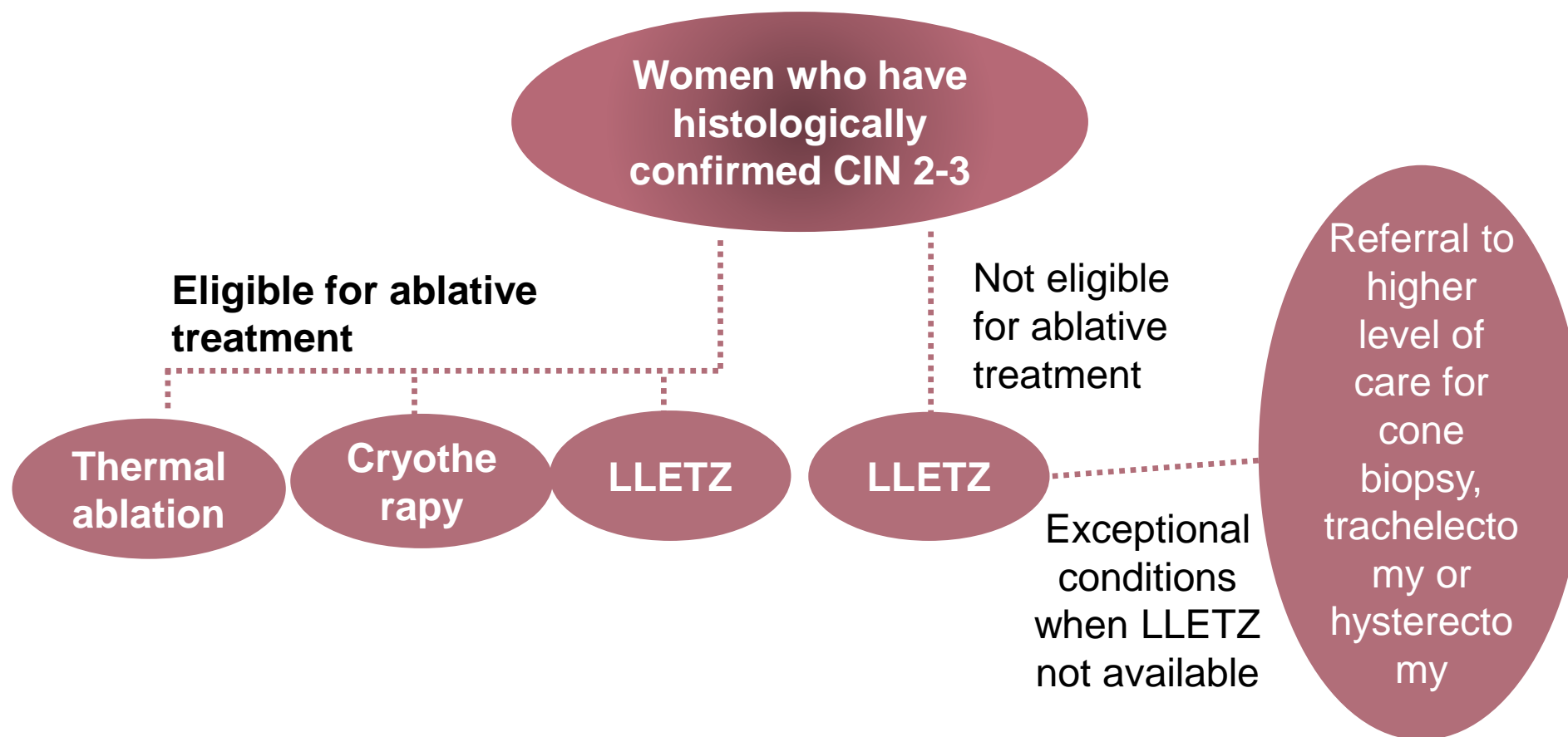
- LEEP (Loop Electrosurgical Excision Procedure) / LLETZ (Large Loop Excision of the Transformation Zone)
- Cold knife conization
- Hysterectomy

# New Recommendations

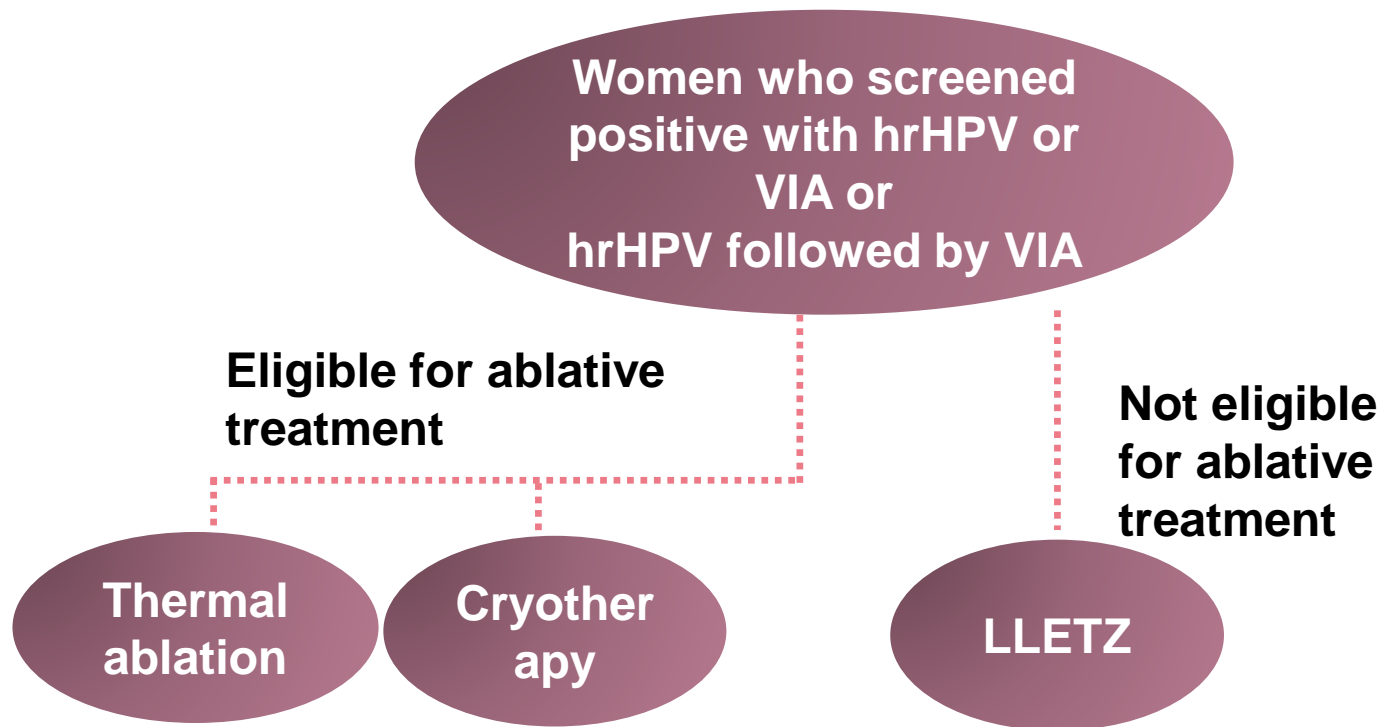
# New Recommendations on thermal ablation



# Histologically confirmed CIN 2-3



# Screen and Treat programme



**WHO suggests thermal ablation be provided at a minimum of 100 °C for 20–30 seconds using as many applications as needed to cover the entire transformation zone in overlapping fields.**

Very few studies comparing different modalities for use of thermal ablation

## **Indications / eligibility:**

As for cryotherapy:

- any CIN lesion;
- SCJ completely visible;
- no endocervical involvement;
- <75% ectocervix; no signs invasive cancer

Different from cryotherapy:

- possibility to treat lesions that are larger than the probe

# Important research

- Comparison of thermal ablation to other treatments for histologically confirmed CIN2-3 or screen positive women
  - evidence based primarily on studies following one group of women receiving thermal ablation
  - few outcomes measured (need for fertility and reproductive health outcomes)
  - no studies in WHIV
  - important outcomes in WHIV (HIV shedding or risk of transmission after treatment)
- Compare the use of a **2-probe method**, treatment of the visible glandular epithelium with a small conical probe followed by treatment of the ectocervix with a flat probe versus a **one-probe method**

# New Recommendation on HPV Self-Sampling

**HPV self-sampling** should be made available as an additional approach to sampling in cervical cancer screening services for women aged 30–60 years.

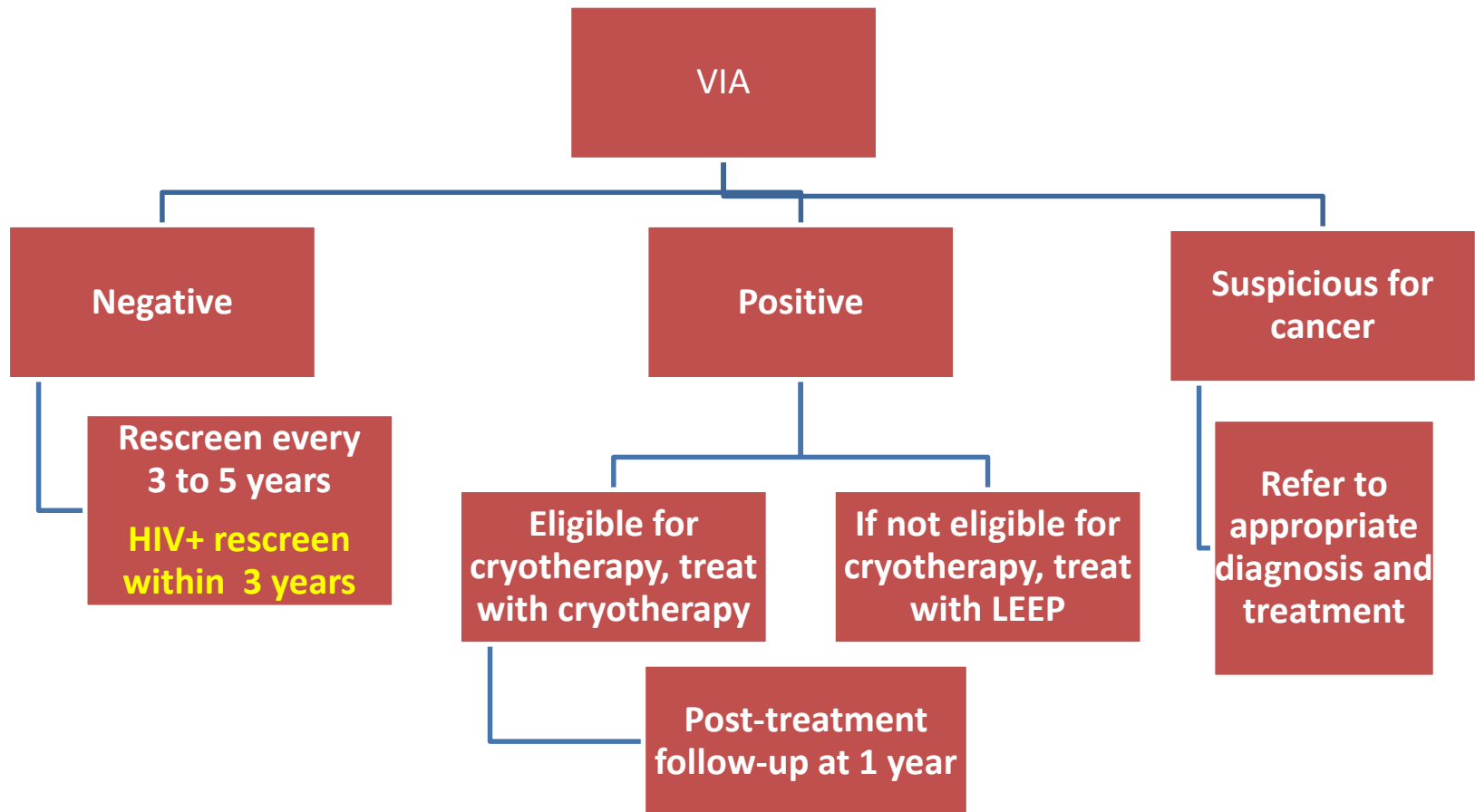
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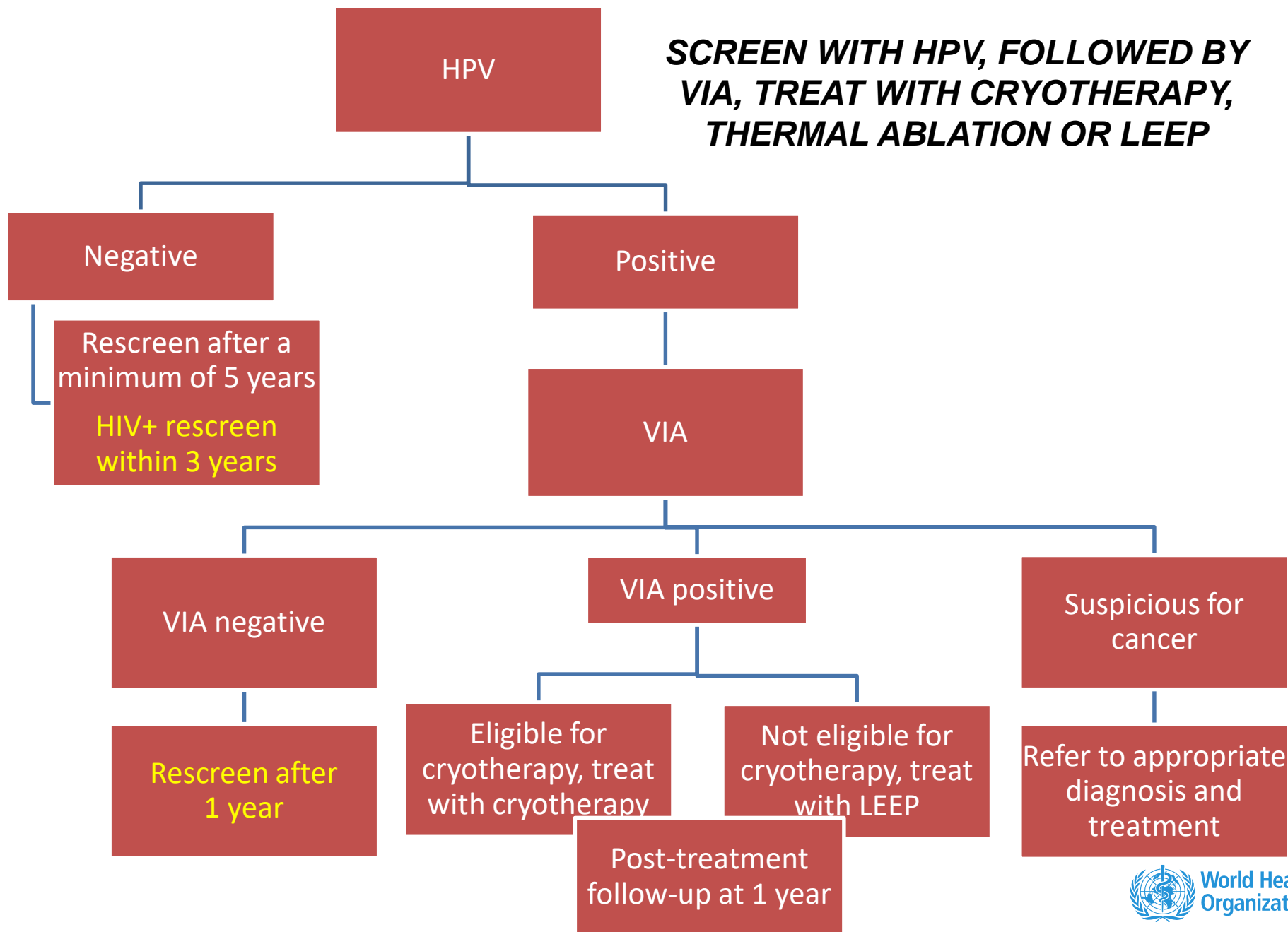
WHO Consolidated Guideline on Self-Care Interventions for Health: *Sexual and Reproductive Health Rights*



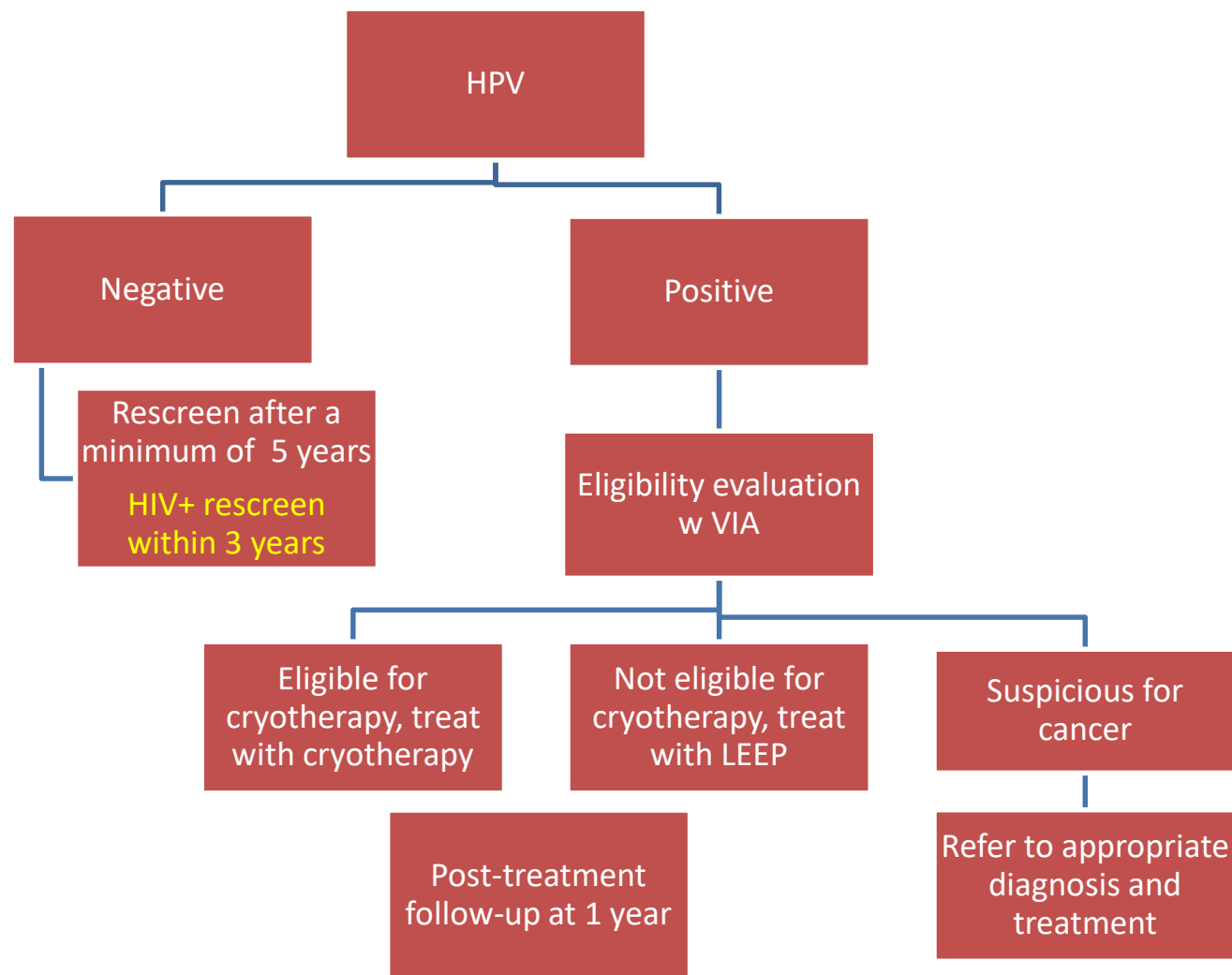
**No changes in the  
Algorithms**

# ***SCREEN WITH VIA, TREAT WITH CRYOTHERAPY, THERMAL ABLATION OR LEEP***

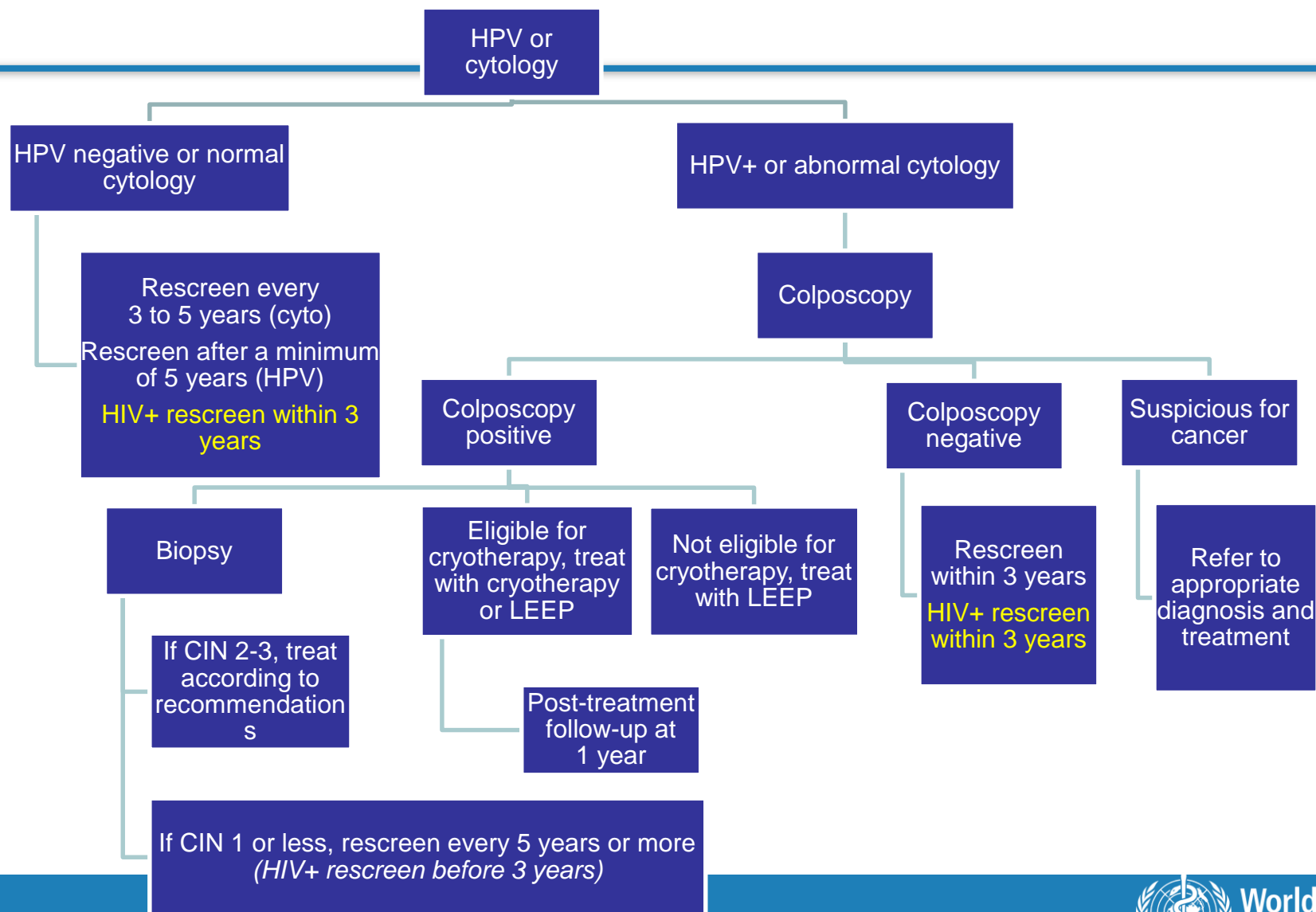




# ***SCREEN WITH HPV, USE VIA TO DETERMINE ELIGIBILITY, TREAT WITH CRYOTHERAPY , THERMAL ABLATION OR LEEP***



# SCREEN WITH HPV OR CYTOLOGY, FOLLOWED BY COLPOSCOPY, TREAT WITH CRYOTHERAPY OR LEEP



# In the context of the elimination initiative

# To Accelerate Access We Need to Move Toward High Performance Tests

## Complex or Low-Sensitivity

### Cytology:

Successful in high-resource countries, but implementing quality cytology screening is challenging in middle and low resource countries

### VIA:

Naked eye visual inspection with 3-5% acetic acid



## High Performance Alternatives

- **HPV Testing**
  - Plus triage with VIA, cyto or other tests
  - Followed by treatment with cryotherapy or thermal ablation
- **HPV Testing**
  - No triage
  - Followed by treatment with cryotherapy or thermal ablation

# To Accelerate Access We Need to Move Toward High Performance Tests

**High sensitivity is an important requirement for early detection in low-resource settings**

# Advantages and disadvantages of triage of HPV positives

- Reduction in overtreatment
- Reduction in sensitivity
- High need of training and quality control of VIA or cytology

However:

- **Very limited data available on impact**

# Review of Future Tests Under Development

- **Biomarkers for cell transformation**
  - HPV E6/E7 messenger RNA
  - HPV E6 oncoprotein
  - Cellular p16INKa/Ki-67 (immunostaining on cytology/biopsy)
  - Methylation markers
- **Non-molecular testing**
  - Automated Visual Evaluation (AVE): screening or triage
  - (Digital) cervicography

# Accelerate Research

- Need for randomized trials
  - Evaluation of screen-and-treat strategies and patient-important outcomes w new screening or triage tests
  - Few studies that assessed the strategies that the guideline development group ranked as clinically relevant (e.g. HPV test followed by VIA)
- Need for accelerated R&D
  - Encourage manufacturers to implement trials for new rapid point-of-care tests in LMIC;

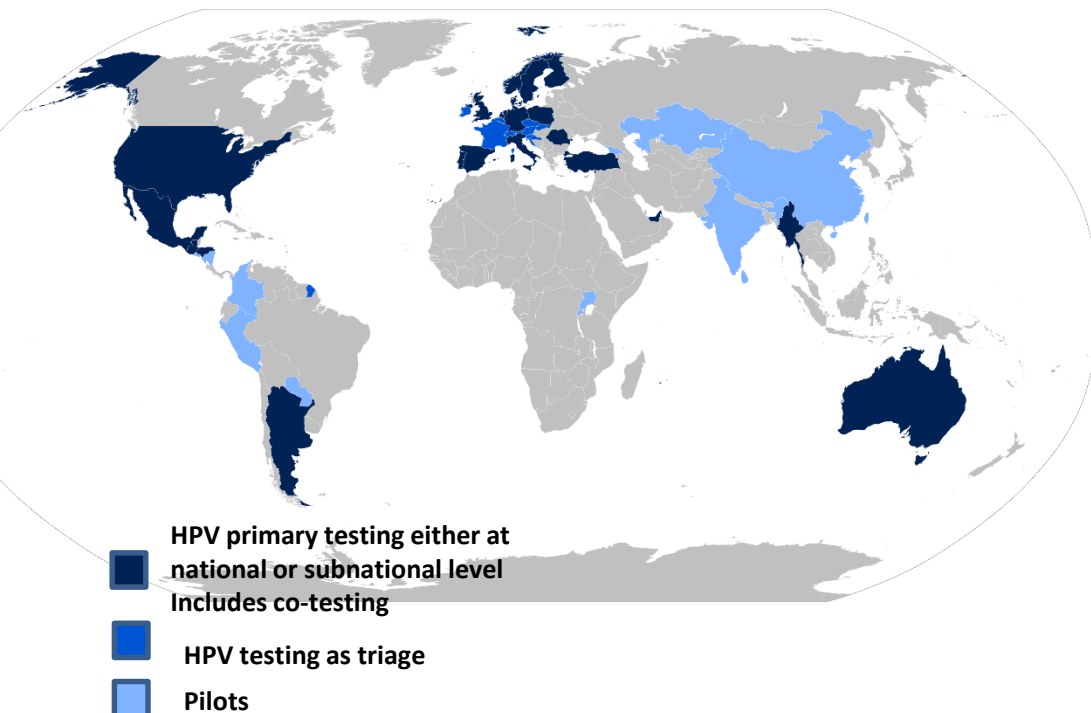
# Update of WHO Guidelines related to cervical cancer prevention and control

- **For women with HIV (by mid 2020):**
  - Age at first screening
  - Frequency of screening
  
- **Update Screen and Treat algorithm (by the end of 2020)**
  - Revise existing PICO questions: delete, review, new ones
  - Determine living recommendations
  - Which screening (and triage) test (VIA, HPV test, cytology, other tests)
  - Treatment: efficacy and potential harm of overtreatment

# The need for HPV tests

# Countries Introducing Screening with HPV Testing and VIA Testing

## Global Progress in **HPV DNA** Testing for Cervical Cancer Screening Status: June 2019



## Global Progress in **Visual Inspection (VIA)** for Cervical Cancer Screening Status: June 2019



\*\*<sub>41</sub> Work in progress, some geographical regions not fully updated

Data sources: Cervical Cancer Action, HPV Information Centre, Chrysostomou 2018, Personal communications

# Global HPV Tests Need Estimation for screening

## Short-list of key assumptions

### Population

**Country population:**

HIV+ and low risk women  
age 30-49

**Yearly adjustments:**

- New 30 year age group
- Follow-up need  
mortality adjusted

### Time Period

**Need calculated over 5  
year time period:**

(2018 = Y0; 2023 = Y5)

**Year 1 need covers total  
eligible population**

### Rates

**Previous cervical cancer  
screening coverage rates:**

- applied for HICs only
- other regions assume  
baseline of zero

**HPV prevalence:**

weighted average by  
region and high/low risk

### Screening

**Screening algorithm:**

For HPV-

- 3 year testing for HIV+
- >5 year testing for HIV-

For HPV+

- 1 year follow-up for all

## High/Low Risk Groups

**A**

### HIV+ Populations

Each year's screening need includes:

- All HIV+ women 30-49 that have not been  
previously screened for HPV
- HIV+ women screened positive preceding year
- HIV+ women screened negative 3 years prior

**B**

### Low Risk Populations

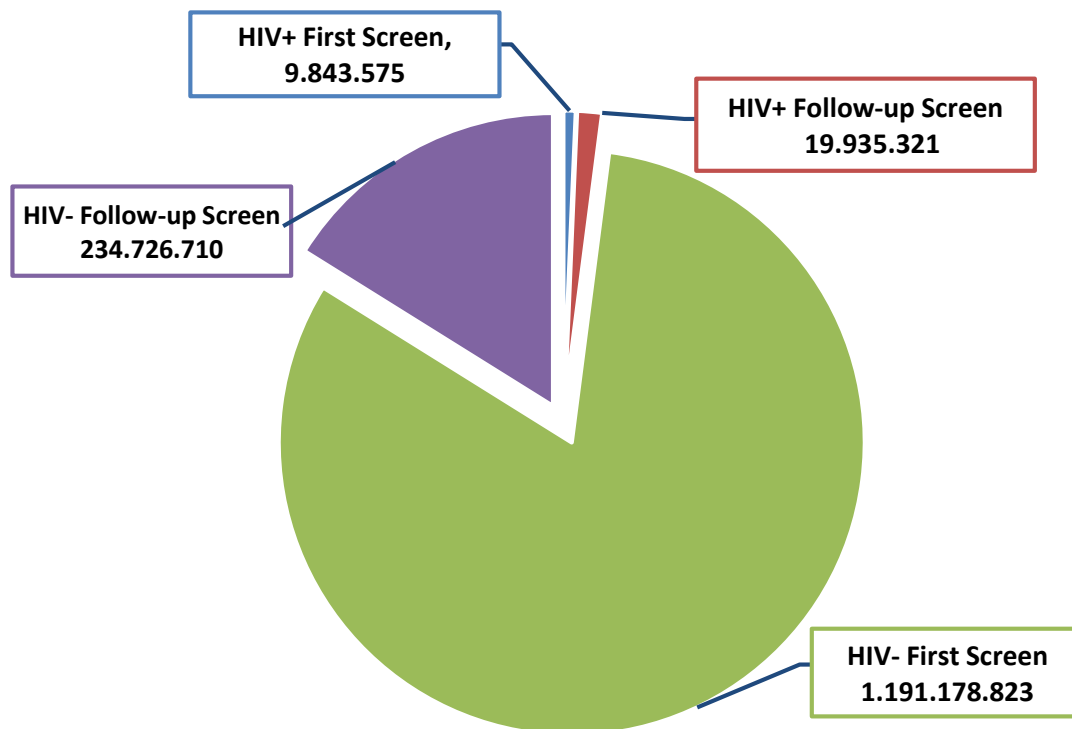
Each year's screening need includes:

- All HIV neg women 30-49 that have not been  
previously screened for HPV
- HIV neg women screened positive preceding year

# Preliminary Global HPV Screening Need

Global HPV  
screening need  
over 5 year period

**>1.4 billion tests**

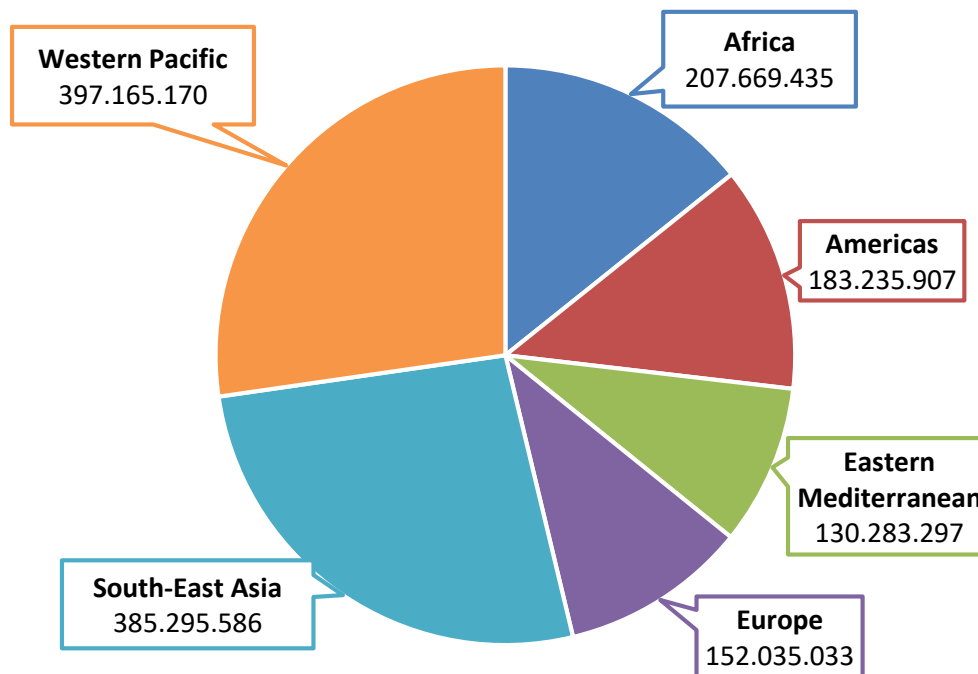


Summary			
	First Screen	Follow-up	Total Need
<b>Patient Need</b>			
Number of HIV+ Women to be Screened	9,843,575	19,935,321	29,778,896
Number of HIV neg Women to be Screened	1,191,178,823	234,726,710	1,425,905,533
<b>Number of Total HPV Tests</b>	<b>1,201,022,398</b>	<b>254,662,031</b>	<b>1,455,684,429</b>

# Preliminary HPV Screening Need by Region

Global HPV  
screening need  
over 5 year period

**>1.4 billion tests**



Summary					
Regions	HIV+ First Screen	HIV+ Follow-up Screen	HIV- First Screen	HIV- Follow-up Screen	Total HPV Screening Need
Africa	7,685,213	15,445,504	141,950,424	42,588,294	207,669,435
Americas	327,648	936,323	136,564,901	45,407,035	183,235,907
Eastern Mediterranean	164,733	282,202	115,306,643	14,529,719	130,283,297
Europe	466,763	1,138,406	122,330,852	28,099,012	152,035,033
South-East Asia	814,672	1,432,193	341,162,703	41,886,018	385,295,586
Western Pacific	384,546	700,693	333,863,299	62,216,632	397,165,170
<b>Total HPV Screening Need</b>	<b>9,843,575</b>	<b>19,935,321</b>	<b>1,191,178,823</b>	<b>234,726,710</b>	<b>1,455,684,429</b>

# There are currently only 2 Prequalified HPV tests

**CareHPV™ (Qiagen)**

**GeneXpert™ (Cepheid)**

[https://www.who.int/diagnostics\\_laboratory/evaluations/pq-list/public\\_report\\_hpv/en/](https://www.who.int/diagnostics_laboratory/evaluations/pq-list/public_report_hpv/en/)

## ... and one under evaluation

**Abbott RealTime High Risk HPV**

[https://www.who.int/diagnostics\\_laboratory/hpv.pdf?ua=1](https://www.who.int/diagnostics_laboratory/hpv.pdf?ua=1)

# Accelerators

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