



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

VISION: A world without cervical cancer

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

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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

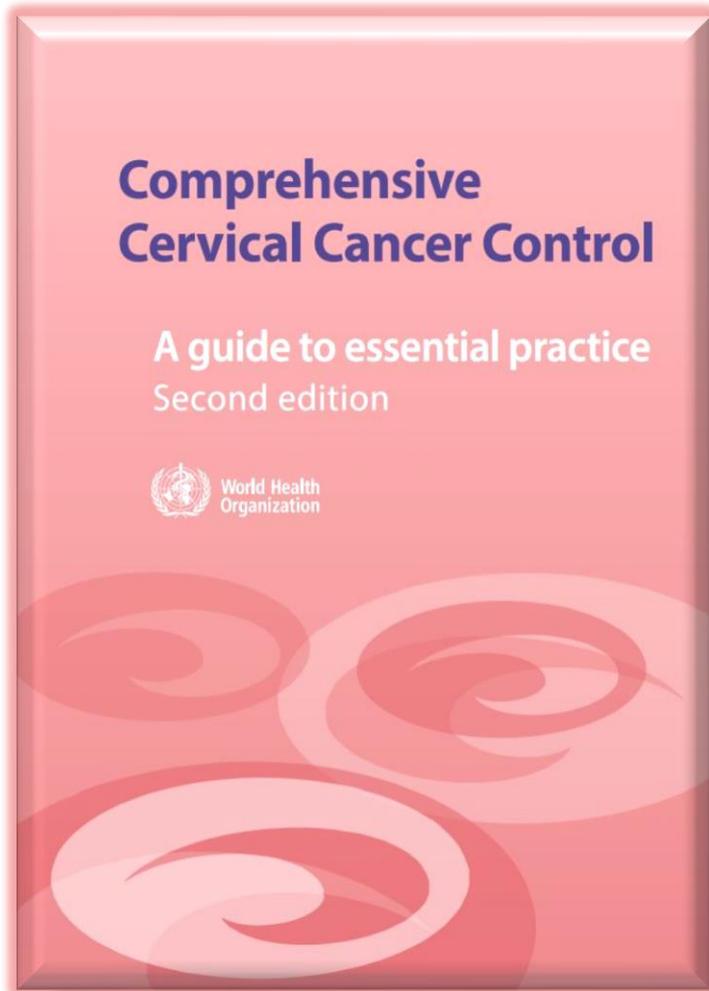
- *Expensive and complex screen and treat technologies complicate scaling-up*
- *New or optimized service delivery methods required for LMIC contexts*

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



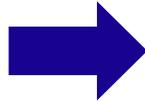
Screening should start at 30 years of age.

- 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?

Sensitivity



TP
FP

Treated



Mortality

Cervical cancer

CIN recurrence

Bleeding

Infection

Premature

delivery

Over treatment

Specificity



TN
FN

Not

treated



Performance and characteristics of different screening methods (CIN2+)¹

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 ² -79%)	Low (49-86%)	Low technology; low cost Linkage to immediate treatment possible

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

² Labani *et al.*, *EurJOGRB* (2014)

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

Ablative treatment (of women screened positive and eligible)

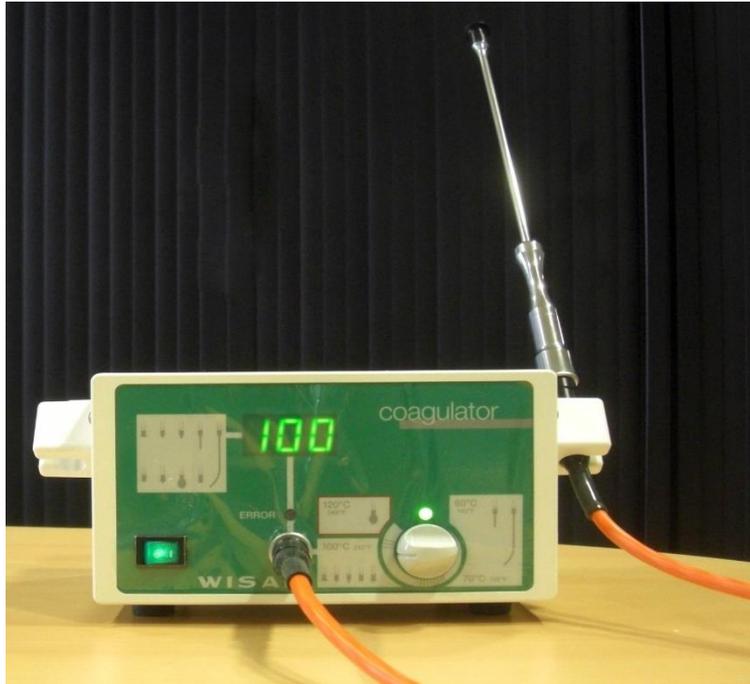
- Cryotherapy
- Thermal Ablation (now WHO recommended)

Excision treatment

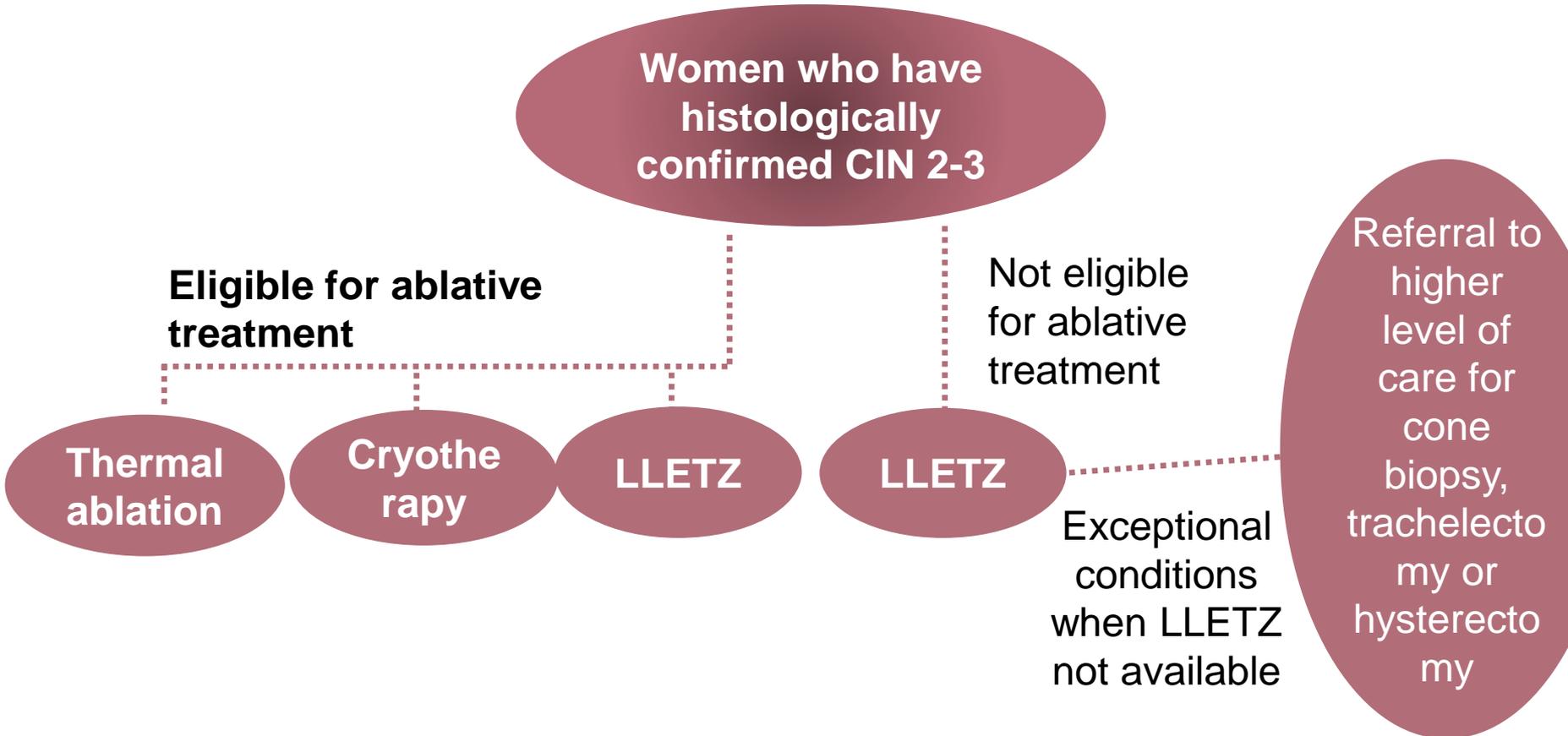
- LEEP (Loop Electrosurgical Excision Procedure) / LLETZ (Large Loop Excision of the Transformation Zone)
- Cold knife conization
- Hysterectomy

New Recommendations

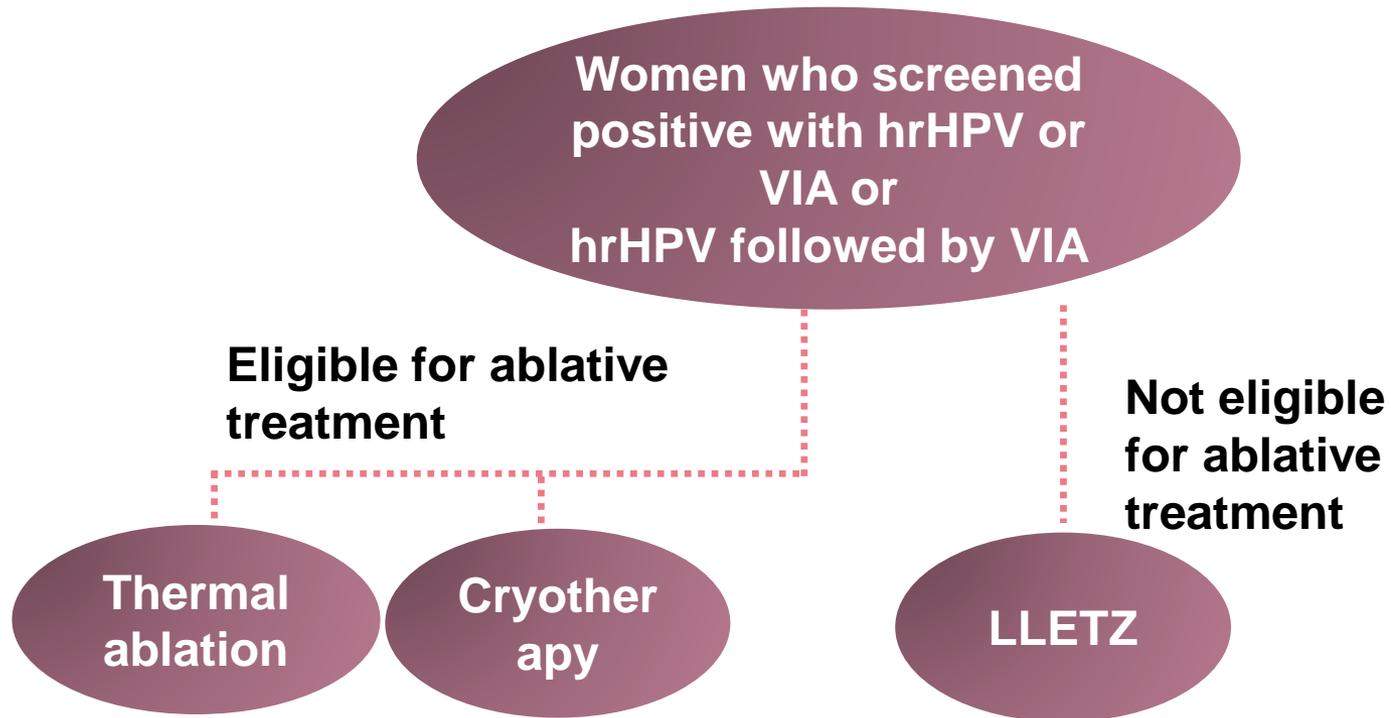
New Recommendations on thermal ablation



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.

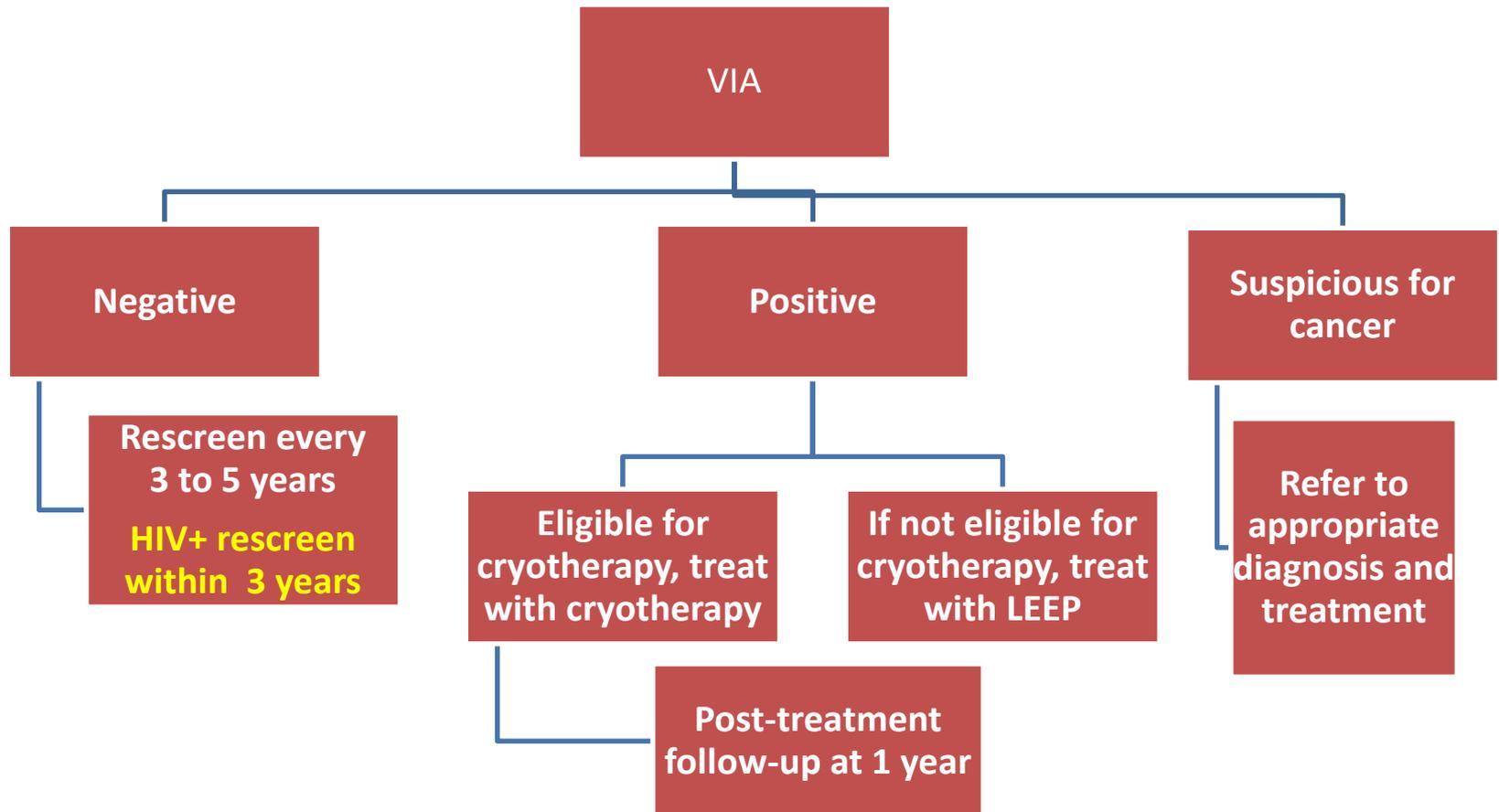
Source:

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

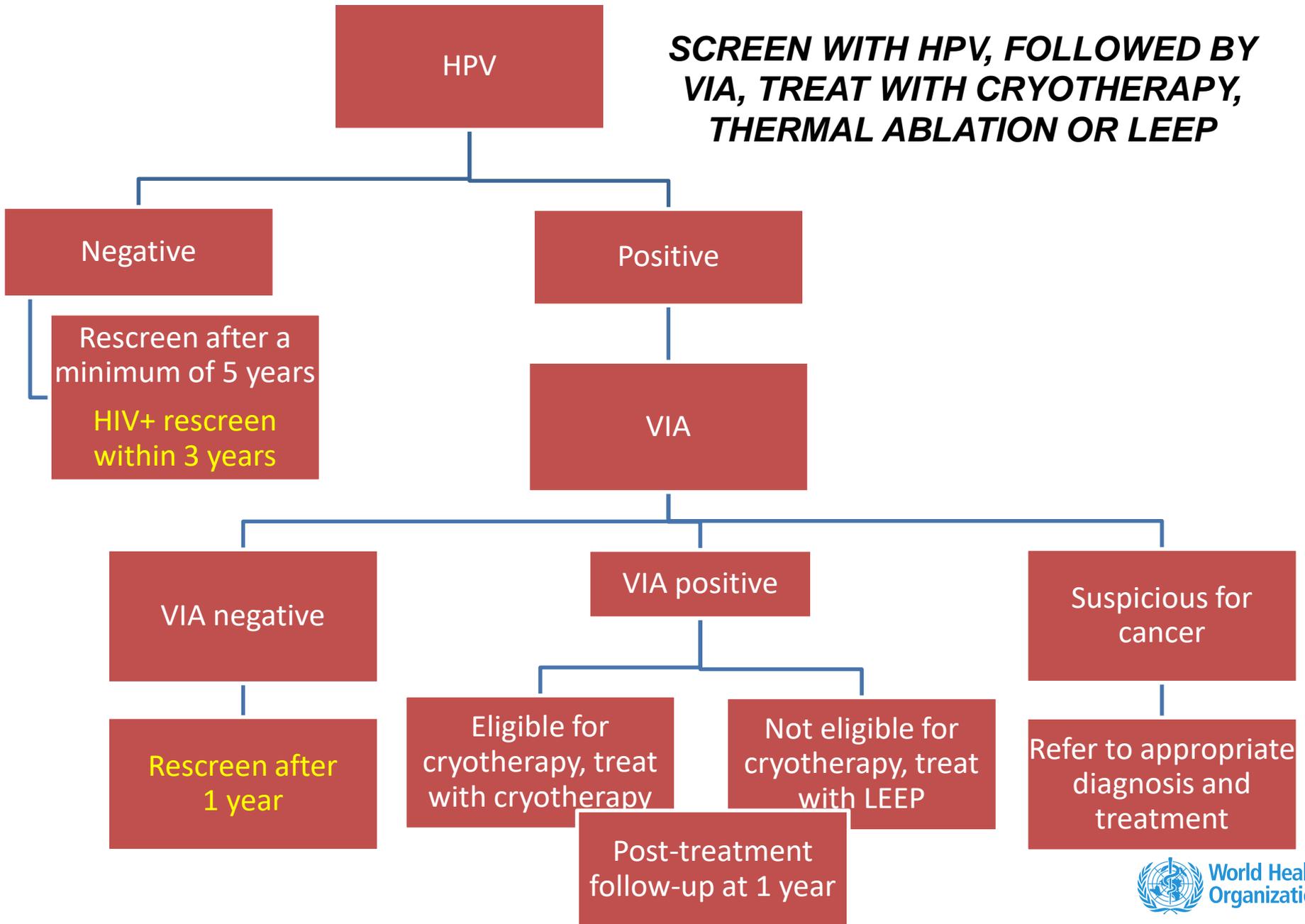


**No changes in the
Algorithms**

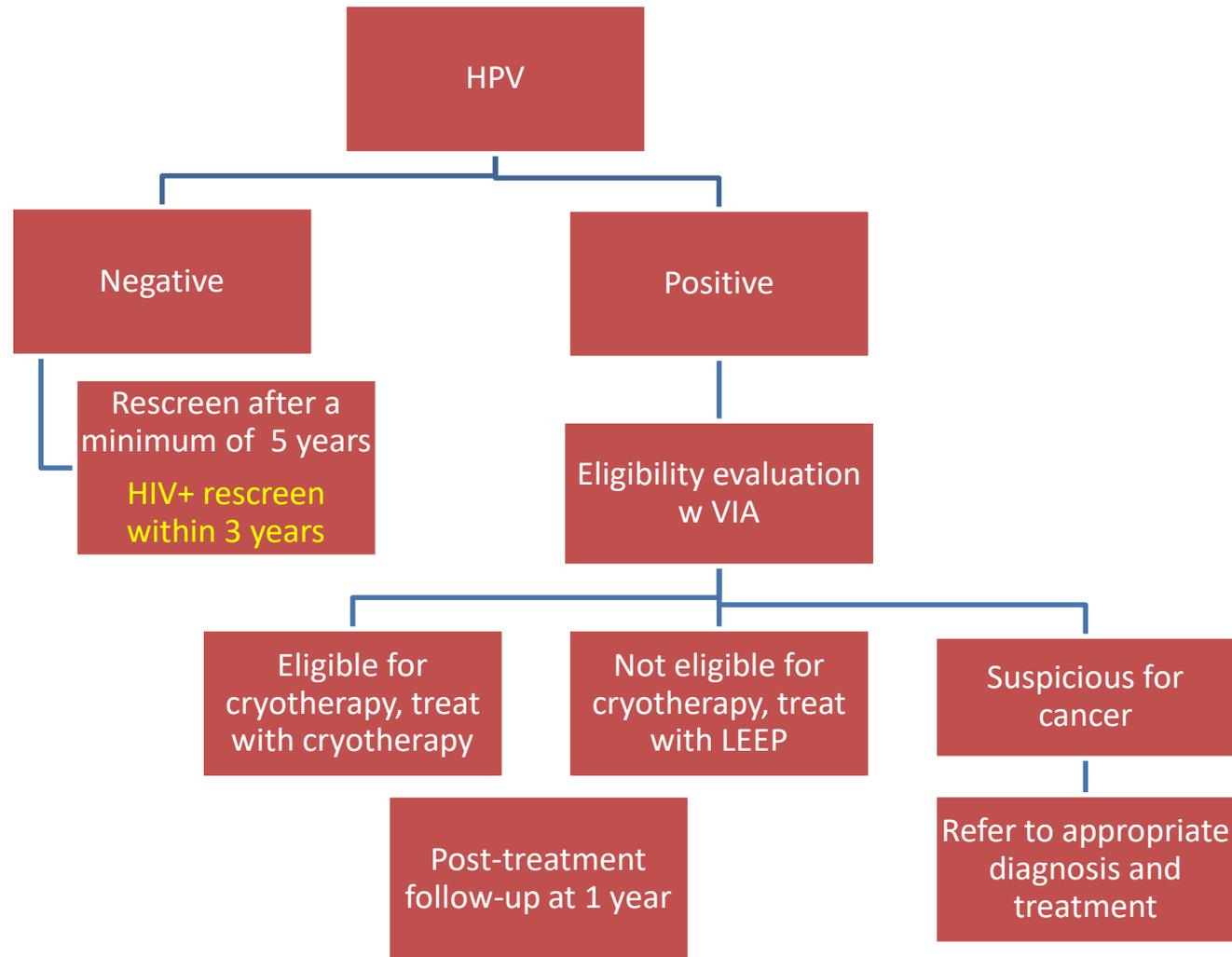
SCREEN WITH VIA, TREAT WITH CRYOTHERAPY, THERMAL ABLATION OR LEEP



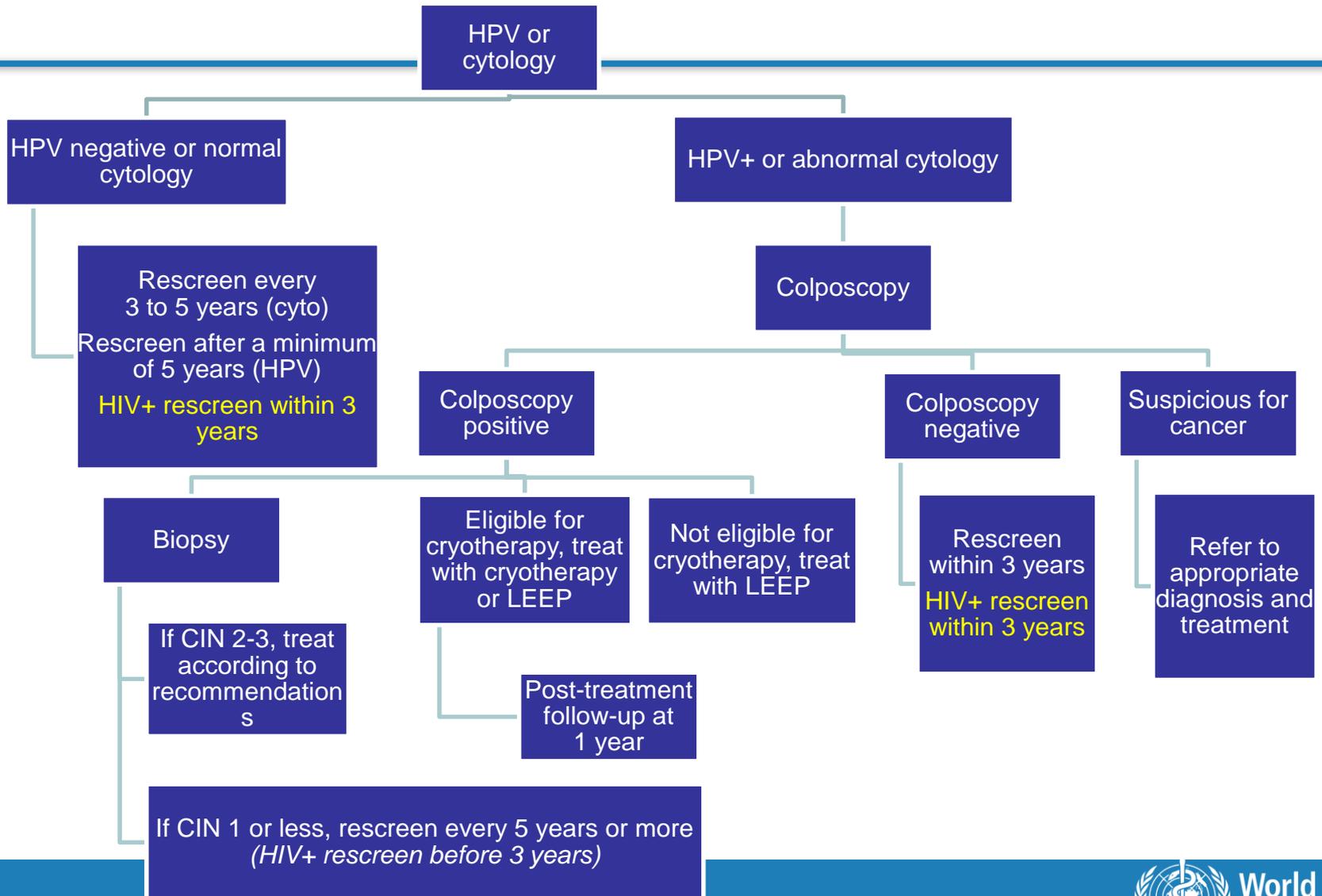
**SCREEN WITH HPV, FOLLOWED BY
VIA, TREAT WITH CRYOTHERAPY,
THERMAL ABLATION OR LEEP**



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

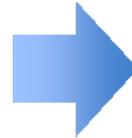
Complex or Low-Sensitivity

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

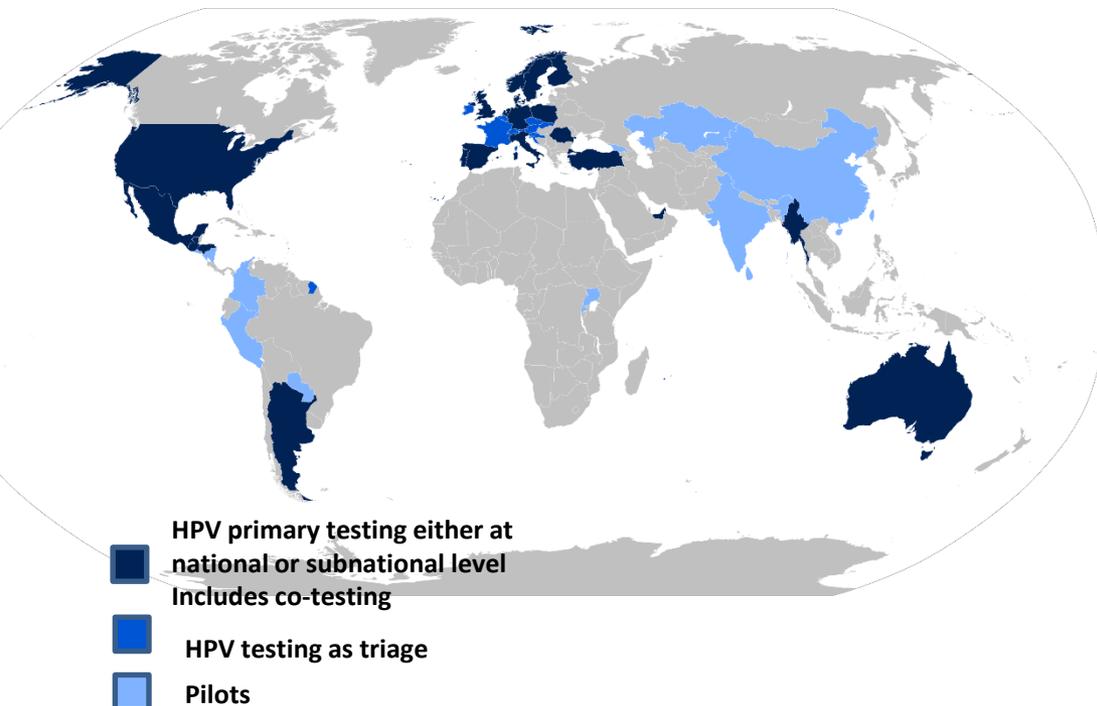
- **For women with HIV (by mid 2020):**
 - Age at first screening
 - Frequency of screening

- **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



**₄₁ 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

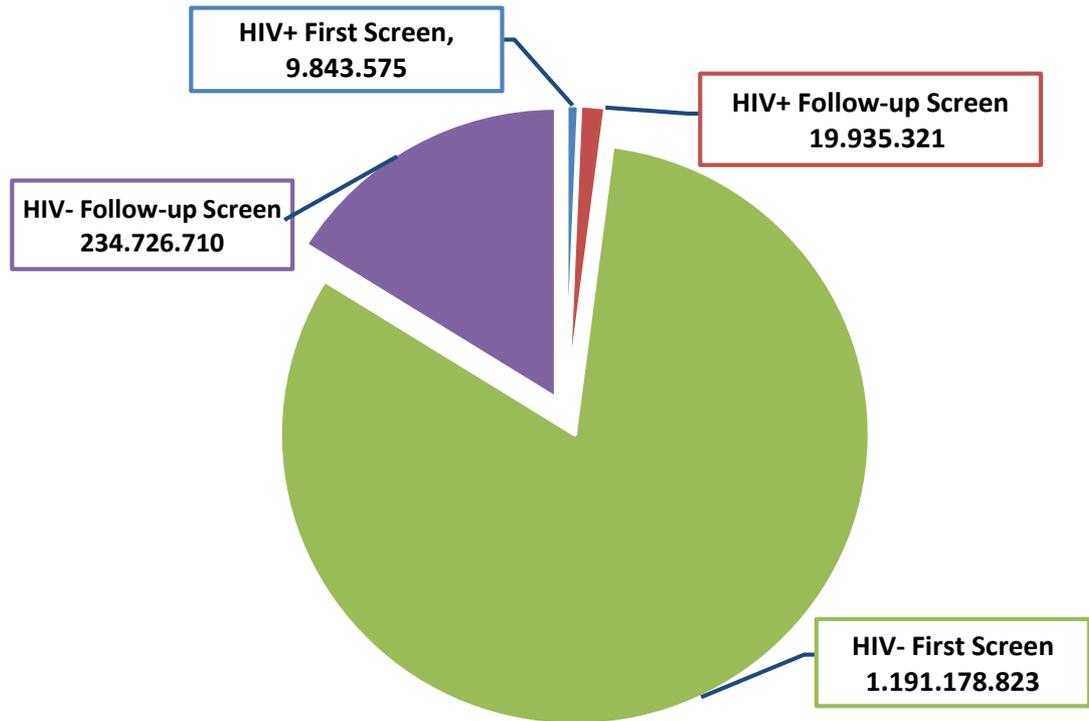
Each year's screening need includes:

- 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

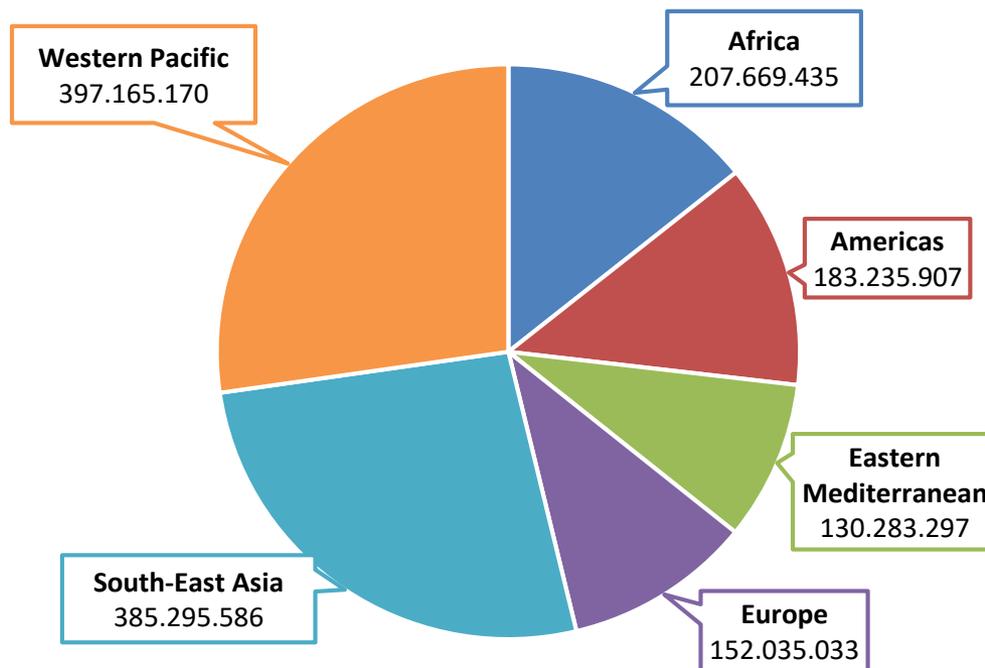
>1.4 billion tests



Summary			
	First Screen	Follow-up	Total Need
Patient Need			
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
Number of Total HPV Tests	1,201,022,398	254,662,031	1,455,684,429

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
Total HPV Screening Need	9,843,575	19,935,321	1,191,178,823	234,726,710	1,455,684,429

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/

... and one under evaluation

Abbott RealTime High Risk HPV

https://www.who.int/diagnostics_laboratory/hpv.pdf?ua=1

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