# HPV self-sampling devices and tests – how far are we on regulations?

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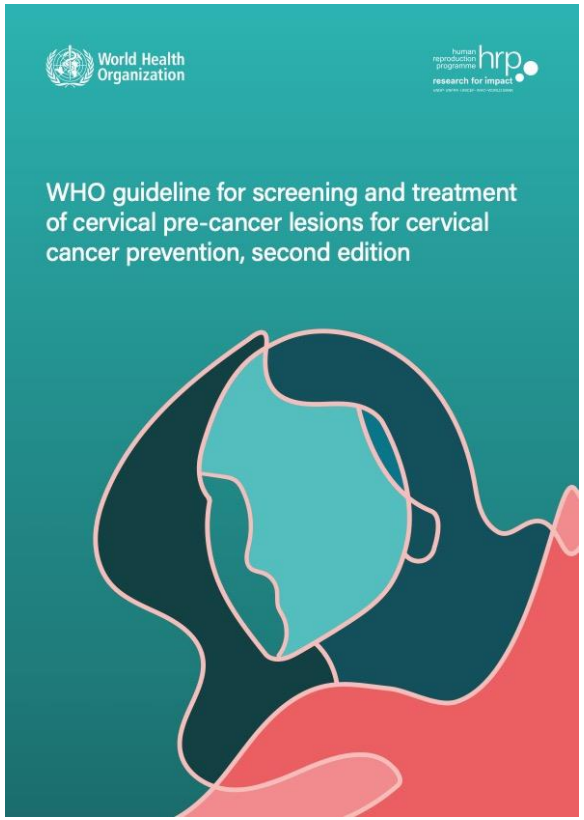
# Meeting the 70-90 goals by 2030: Review of algorithms to screening and treatment to prevent cervical cancer

**2021**




**Guideline objective:**

**To improve national strategies for screening and treatment to prevent cervical cancer in all women, including women living with HIV**

# 2022 Updated Recommendations

## WHO suggests using the following screening & treatment strategies:

## For the general population of women

- **Screen-and-Treat or Screen, Triage and Treat**

  **For primary screening:**

  ✓ HPV DNA using either provider or self-collected samples or

  ✓ HPV mRNA but only on provider-collected samples

  **For triage:**

  ✓ Partial genotyping, colposcopy, VIA, cytology or

  ✓ dual stain only on provider-collected samples

- **Screening every 5-10y if HPV DNA; 5y if HPV mRNA**

- **Retesting at 24m after a positive screen & after treatment**

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# 2022 Updated Recommendations

## WHO suggests using the following screening & treatment strategies:

## For women living with HIV

- **Screen, Triage and Treat ~~×No screen-and-treat~~**

  **For primary screening:**

  ✓ HPV DNA using either provider or self-collected samples

  × No HPV mRNA

  **For triage:**

  ✓ Partial genotyping, colposcopy, VIA, cytology

  × No dual stain

- **Screening every 3 to 5y**
- **Retesting at 12m after a positive screen & after treatment**

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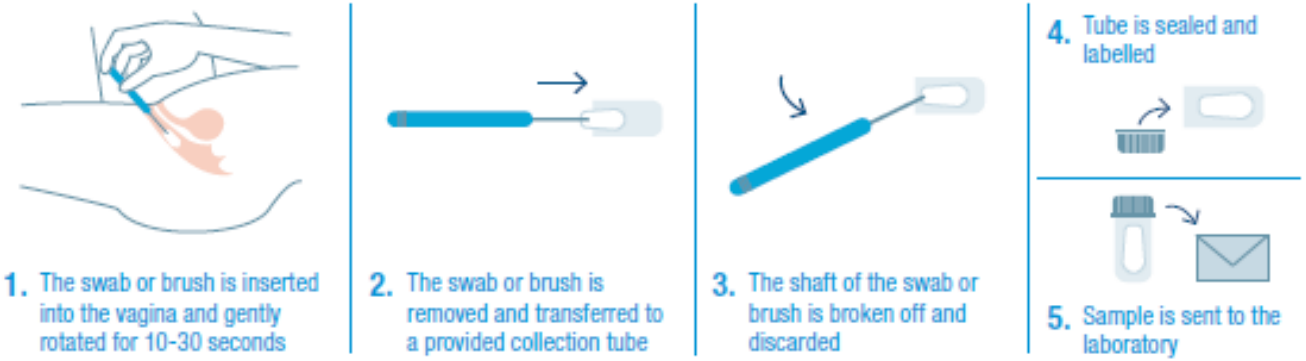
# WHO recommendations on self-care interventions

Human papillomavirus (HPV) self-sampling as part of cervical cancer screening

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

- The option to self-sample is generally associated with increased uptake of cervical cancer screening services: self-sampling nearly doubled use of cervical cancer screening services.
- Self-sampling is seen as highly acceptable for its privacy, convenience, time and effort saved, cost- effectiveness, ease, comfort (including decreased embarrassment, pain and anxiety), speed, safety and user-friendliness.
- **Linkages to follow-up testing and treatment after self-sampling and after regular screening remains limited.**

**Self-collection of a sample for cervical cancer screening by swabbing the vagina[1]**

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# New and rapidly evolving screening and treatment strategies

- **Many new or rapidly evolving evidence-based strategies for cervical cancer screening and treatment**

- **Stakeholders should not have to wait 3 to 5 years for an update of a guideline to know what should be implemented or removed from practice**

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# Living Guidelines

- Some recommendations become ‘living’ within the 3 to 5 year updating process

- More efficient ongoing process of reviewing evidence (all sources) and making recommendations

| Full guideline published | Living recommendations identified | Living recommendation process | Publish living recommendations | UPDATE full guideline with multiple recommendations | Full guideline published |
|---|---|---|---|---|---|
| Year 1 | Year 1 - 3 | | | Year 3 | Year 5 |

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# 6-7 December 2022 meeting
# Living GDG Experts, Reviewers & Observers

## GDG PRIORITIZATION

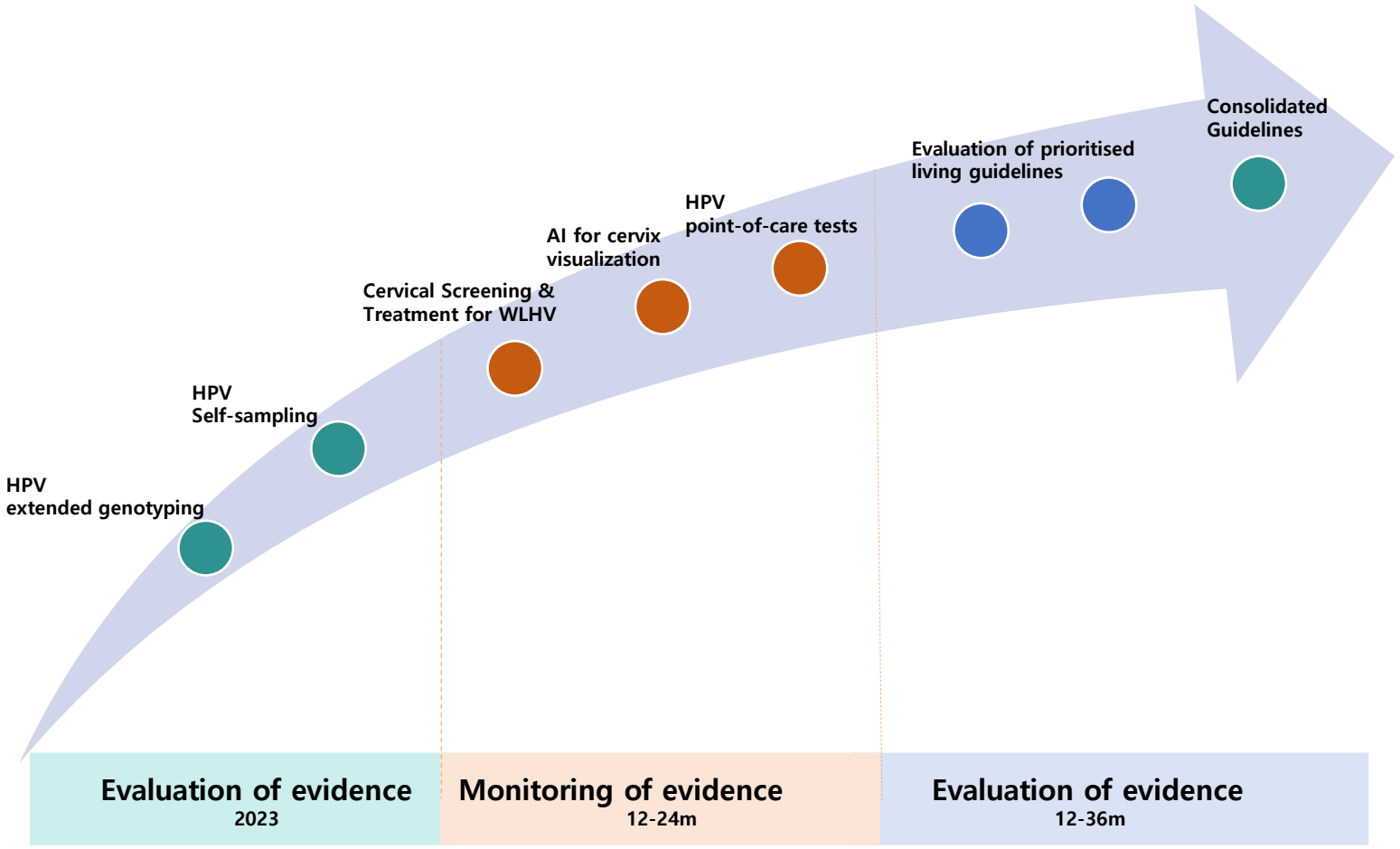
1. Extended genotyping

2. HPV self-sampling
   a. Optimize resources: standard sampling management protocol
   b. Longitudinal data
   c. Uptake & retention

3. Screening and Treatment techniques and approaches for WLHIV

4. AI for cervix visualization
   - Standardization of validation protocols

5. HPV point-of-care tests
   - Update of HPV TPPs

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**TSS-4 2018** In vitro diagnostic medical devices (IVDs) used for the detection of high-risk human papillomavirus (HPV) genotypes in cervical cancer screening

# Performance principles for WHO Prequalification

## 1. Intended use:

- *function of the IVD (DNA testing, individual genotyping)*
- *testing population for which IVD is intended and ages for which the test has clinical relevance,*
- *intended optional setting and user,*
- ***intended specimen types, collection media and collection device/method, can the specimen be self-collected?,***
- *indication for use (?primary screening)*

## 2. Diversity of specimen types, users and testing environments and impact on required studies

- *According to instructions for use (IFU) claimed*
- ***PQ IVDs in LMIC mostly used by lab tech in centralised testing labs or at POC or by providers trained in the test at POC, either self- or provider collected***
- *Complexity of the test clearly defined in IFU and reflected in risk analysis, and accordingly diverse operational settings should be considered*

## 3. Applicability of supporting evidence to IVD under review

- Analytical and clinical studies shall be undertaken using the specific final version of the IVD intended to be submitted to WHO
- *"The use of well-characterised repository specimens may be acceptable if they are relevant to the IVD considering:*
  - ***the collection device, collection media, storage conditions (age of specimen)***
  - ***nucleic-acid target and its stability, and/o***
  - ***any requirements for testing in fresh specimens only"***

**The collection device can be a swab, a brush or a different one, whether provider- or self-collected**

World Health Organization https://www.who.int/publications/i/item/9789241513814

**TSS-4 2018** In vitro diagnostic medical devices (IVDs) used for the detection of high-risk human papillomavirus (HPV) genotypes in cervical cancer screening

# Specific requirements for analytical and clinical performance

## For establishing analytical performance characteristics

1. *Specimen type and collection*
   - *Demonstration of equivalence between contrived and clinical specimens*
   - *Demonstration of equivalence between specimen collection methods*
2. *Specimen collection, storage and transport*
3. *Precision of measurement*
4. *Performance panels*
5. *Carry-over contamination*
6. *Analytical sensitivity*
   - *Analytical sensitivity: shall be estimated by determining the lowest concentration for which the rate of detection is 95%*
   - *Validation of assay cut-off*
7. *High dose hook effect*
8. *Analytical specificity*
9. *Metrological traceability of calibrators and control material values*
10. *Stability*
11. *Flex studies*

## For establishing clinical performance characteristics

1. *Diagnostic sensitivity and specificity*
   - *Diagnostic sensitivity:* ***testing at least 60 well characterised, clinically confirmed CIN2+ specimens***
   - *Diagnostic specificity:* ***testing at least 100 well characterised, clinically confirmed non-CIN2+ specimens***
2. *Qualification of usability of self-collection and/or POC testing*
   - *Label comprehension (including IFU)*
   - *Results interpretation*

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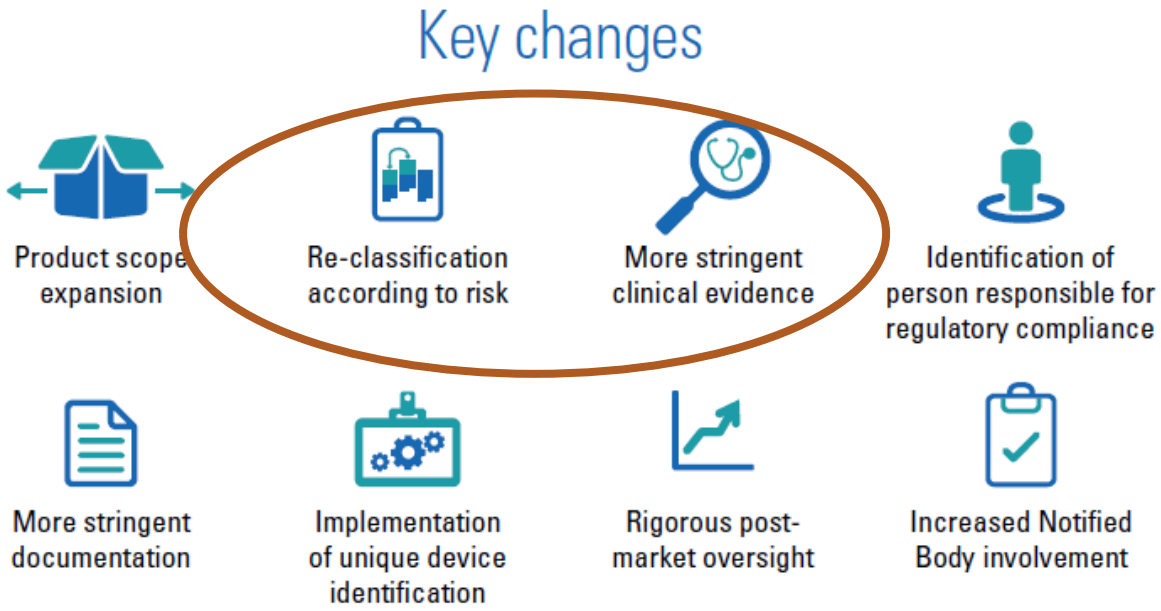
https://www.who.int/publications/i/item/9789241513814

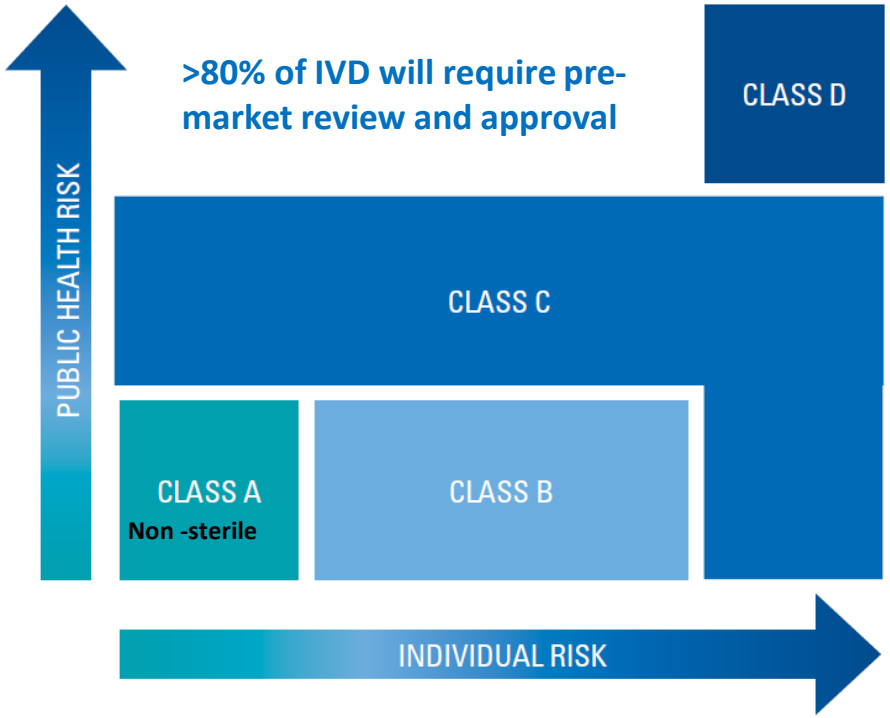
# The European In Vitro Diagnostic Medical Device Regulation (IVDR)

- New European IVDR regulation entered into force on May 2017
- Date of Application of IVDR is 26 May 2022, transitional provisions of the IVDR have been modified based on Regulation 2022/112 (Jan 25,2022)
- **As an EU regulation, the IVDR has the force of law throughout the EU and eliminates country-by-country interpretations of the requirements permitted under directives.**



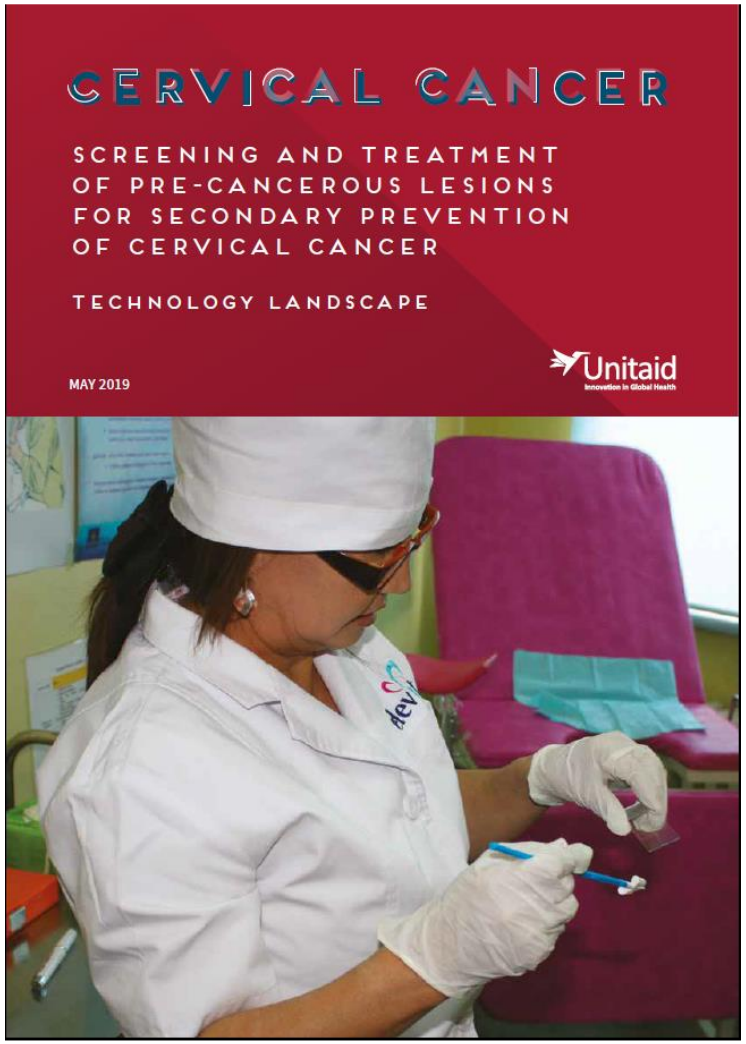

## Devices, products covered

- ✓ All sort of reagents, products, calibrators, control materials, kits, instruments, apparatus, pieces of equipment, software or systems, whether used alone or in combination, and intended to be used for the examination of specimens derived from the human body (blood, urine, tissue, etc.) to diagnose diseases, to monitor a person's state of health, to monitor therapeutic measures, to determine predisposition to a medical condition or a disease, or to provide information about susceptibility for a medical treatment.
- ✓ **Devices for self-testing – e.g. pregnancy tests or DNA genetic testing.**
- ✓ **Devices for near-patient testing: devices not intended for self-testing but intended to perform testing outside a laboratory environment, generally near to or at the side of the patient by a health professional**
- ✓ Companion diagnostic devices: essential for the safe and effective use of a product to identify, before and/or during treatment, patients most likely to benefit or at increased risk of serious adverse reactions
- ✓ Accessories: items not IVD by which are intended by the manufacturer to be used together

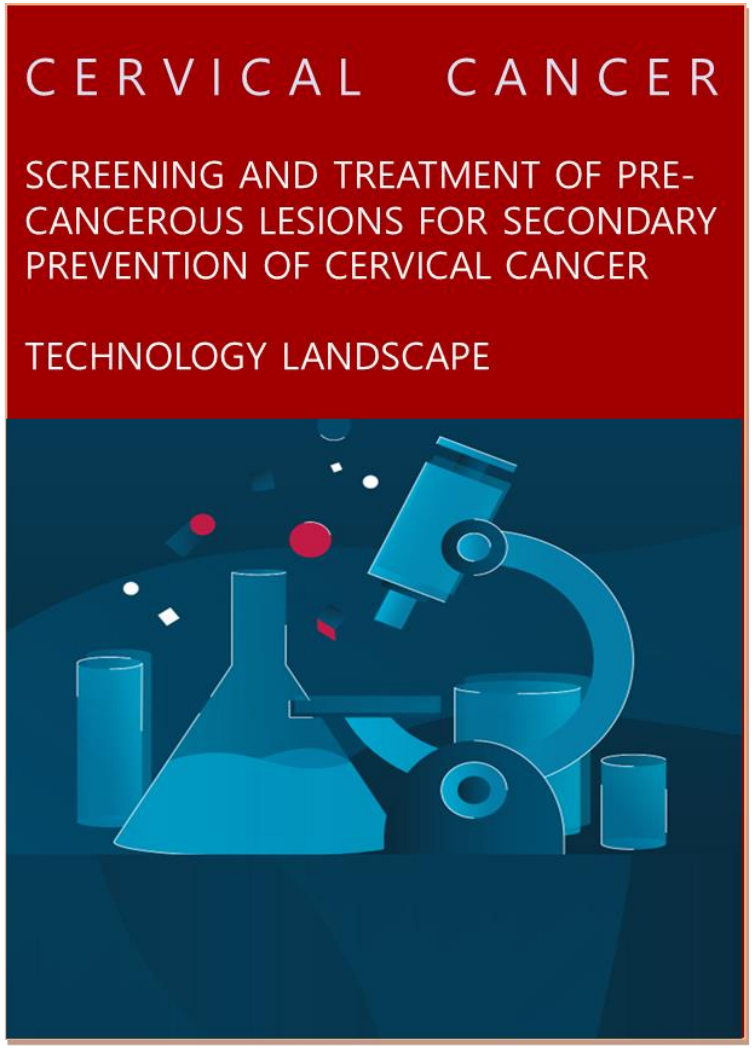


# Technology landscape of cervical cancer screening and treatment

**2019**




**2023**

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# Technology Landscape

**Examples of sampling devices 2019**


© Aprovix, AB


© Copan Flock Technologies


© Rover Medical Devices


© Hologic/Ilex

| | | |
|---|---|---|
| Collection Product | Collection Type | - Swab vs. Brush<br>- Cervical (HCW collection) vs. vaginal (self-sampling) |
| | Self/HCW Regulatory Approval | CE IVD / FDA / WHO PQ product approval for self vs. HCW collection |
| | Dry / Wet Transport | Sample transported dry vs. requiring transfer to a transport media |
| | Stability/Transport | Stability for dry-sample; wet-sample stability dependent on media |
| Collection Media | Regulatory Approval | CE IVD / FDA / WHO PQ |
| | Recommendation by Test Supplier | On-label use of media with respective HPV NAT assays |
| Other | Product Use | - Proprietary product for HPV assay supplier only<br>- Non-proprietary, able to be paired across various media / assays |
| | Costs | Individual product and kit-specific costs |

Courtesy of UNITIAD, Daffodil Centre

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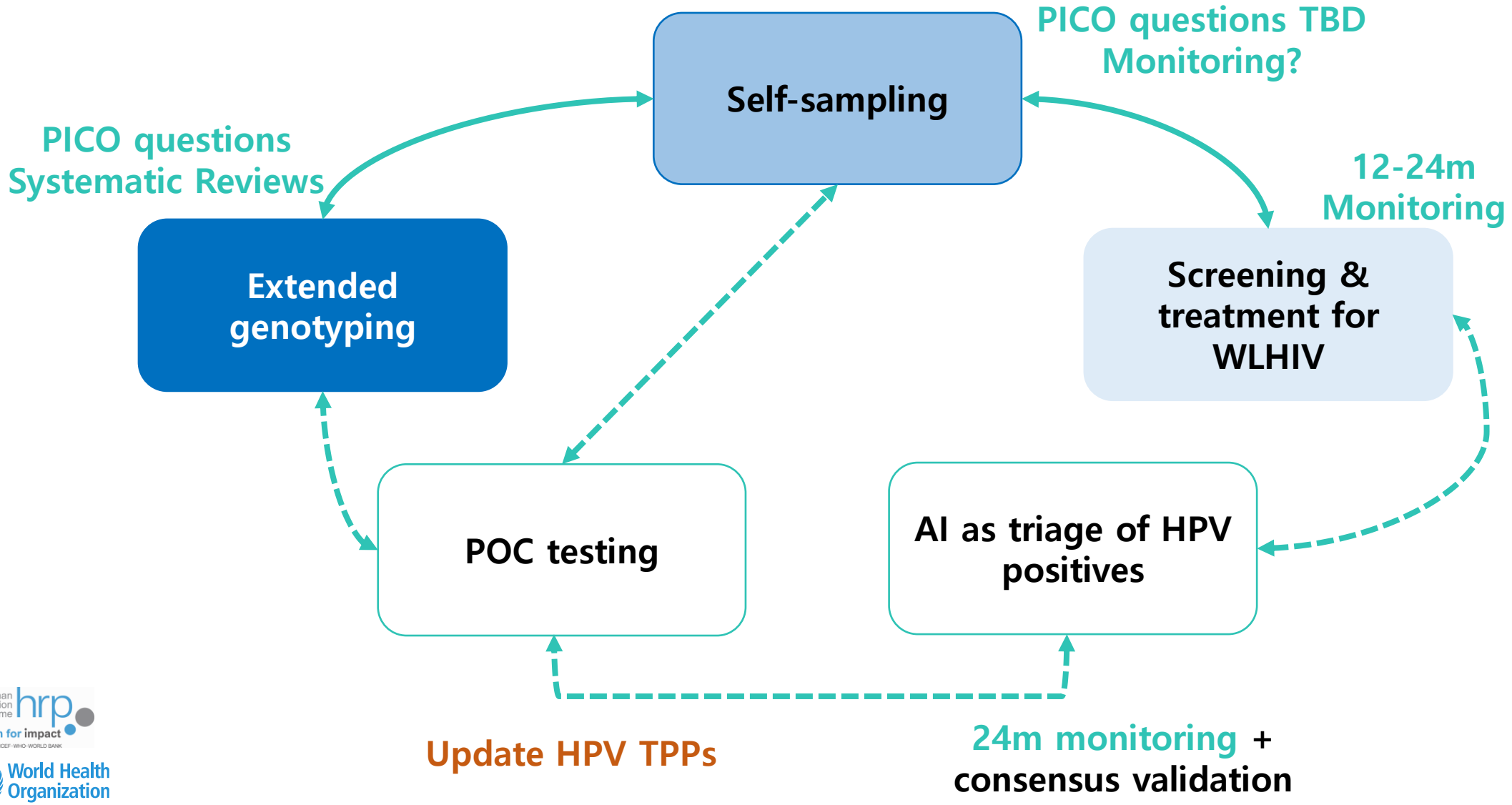


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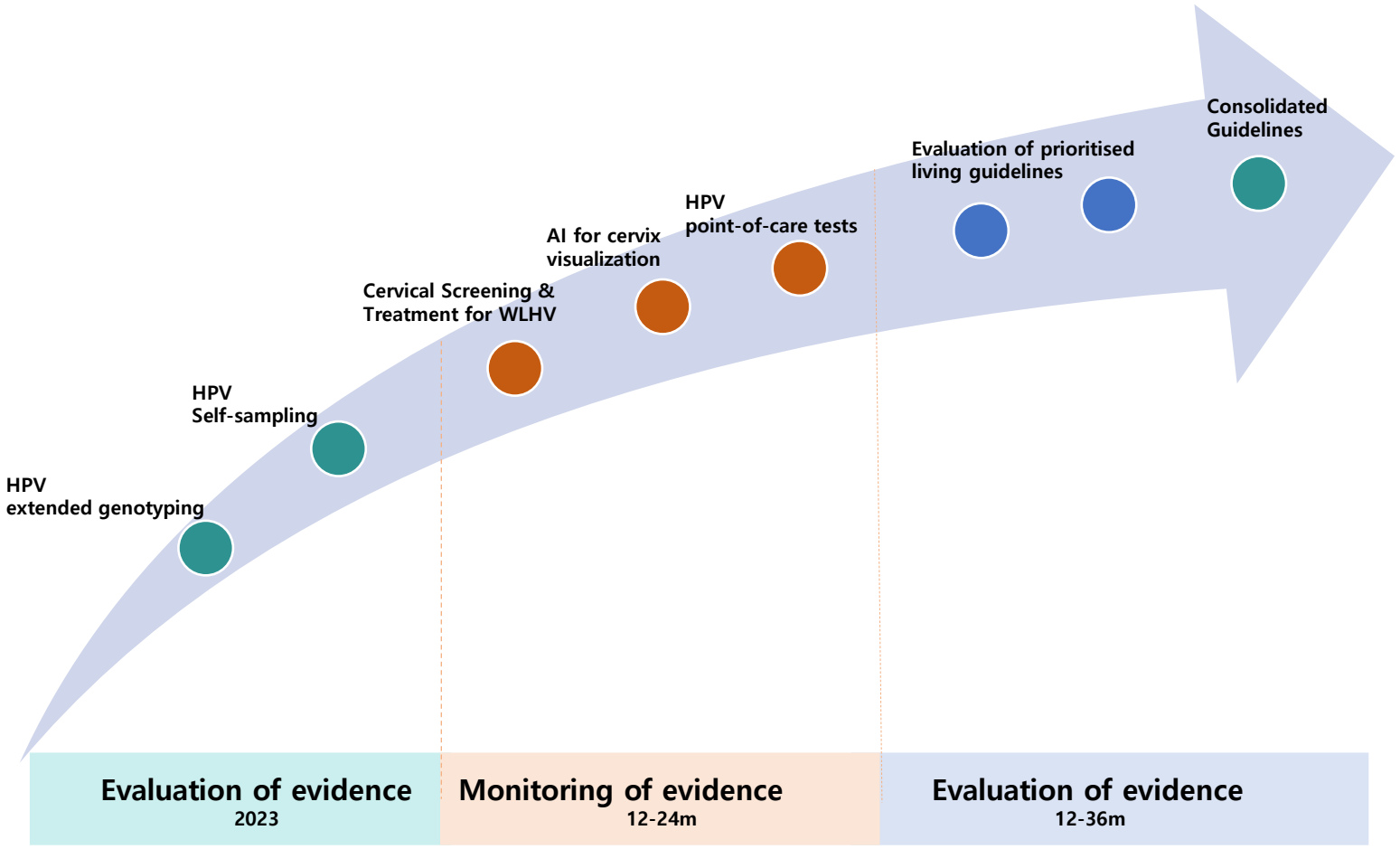


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# Next steps

(1) **Innovations** offering opportunity to accelerate elimination of cervical cancer

- **Living guidelines:**
  - Rapid evidence assessment of evolving technology

(2) Need to support countries implementing and scaling up cervical cancer screening

- **Standard management protocol of self-collected samples, from collection to testing**
- **Update of HPV TPPs**
- **Support to evaluation of different self-sampling approaches ensuring retention to treatment and follow-up**

THANKS