ELIMINATION OF CERVICAL CANCER AS A GLOBAL PUBLIC HEALTH PROBLEM AND THERMAL ABLATION GUIDELINES

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World Health Organization

MAY 2018: WHO DIRECTOR-GENERAL'S CALL TO ACTION TO ELIMINATE CERVICAL CANCER

World Health Organization · UN Women · unicef · UNFPA · UNAIDS · IAEA International Atomic Energy Agency

International Agency for Research on Cancer
World Health Organization

UNODC United Nations Office on Drugs and Crime · Unitaid Innovation in Global Health · The Global Fund · Gavi The Vaccine Alliance

Clinton Health Access Initiative · uicc global cancer control · GHO Global Health Observatory · unfm Université Numérique Francophone Mondiale · NYU Langone Health

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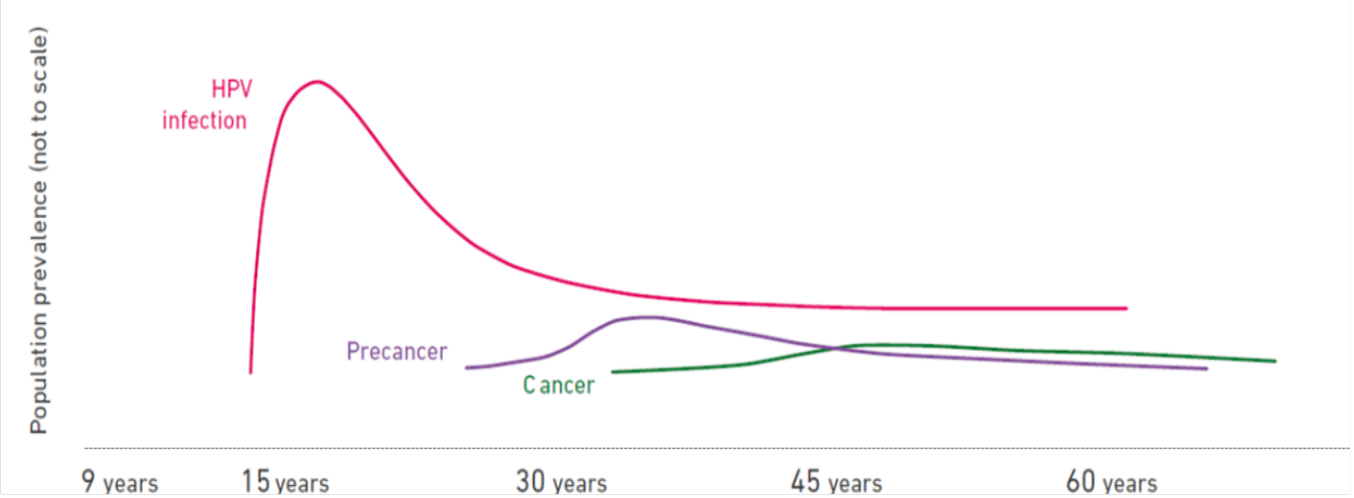
WHO LIFE COURSE APPROACH TO CERVICAL CANCER CONTROL



Primary Prevention	Secondary Prevention	Tertiary Prevention and Palliative Care

Girls 9-14 years
• HPV vaccination
Girls and boys, as appropriate
•Health information and warnings about tobacco use
•Sexuality education tailored to age & culture
•Condom promotion/provision for those engaged in sexual activity
•Male circumcision
	Women > 30 years of age
	"Screen and treat" – single visit approach
	• Point-of-care rapid HPV testing for high risk HPV types
	• Followed by immediate treatment
	• On site treatment
		All women as needed at any age
		• Treatment of invasive cancer:
		  • Surgery
		  • Radiotherapy
		  • Chemotherapy
		• Palliative care

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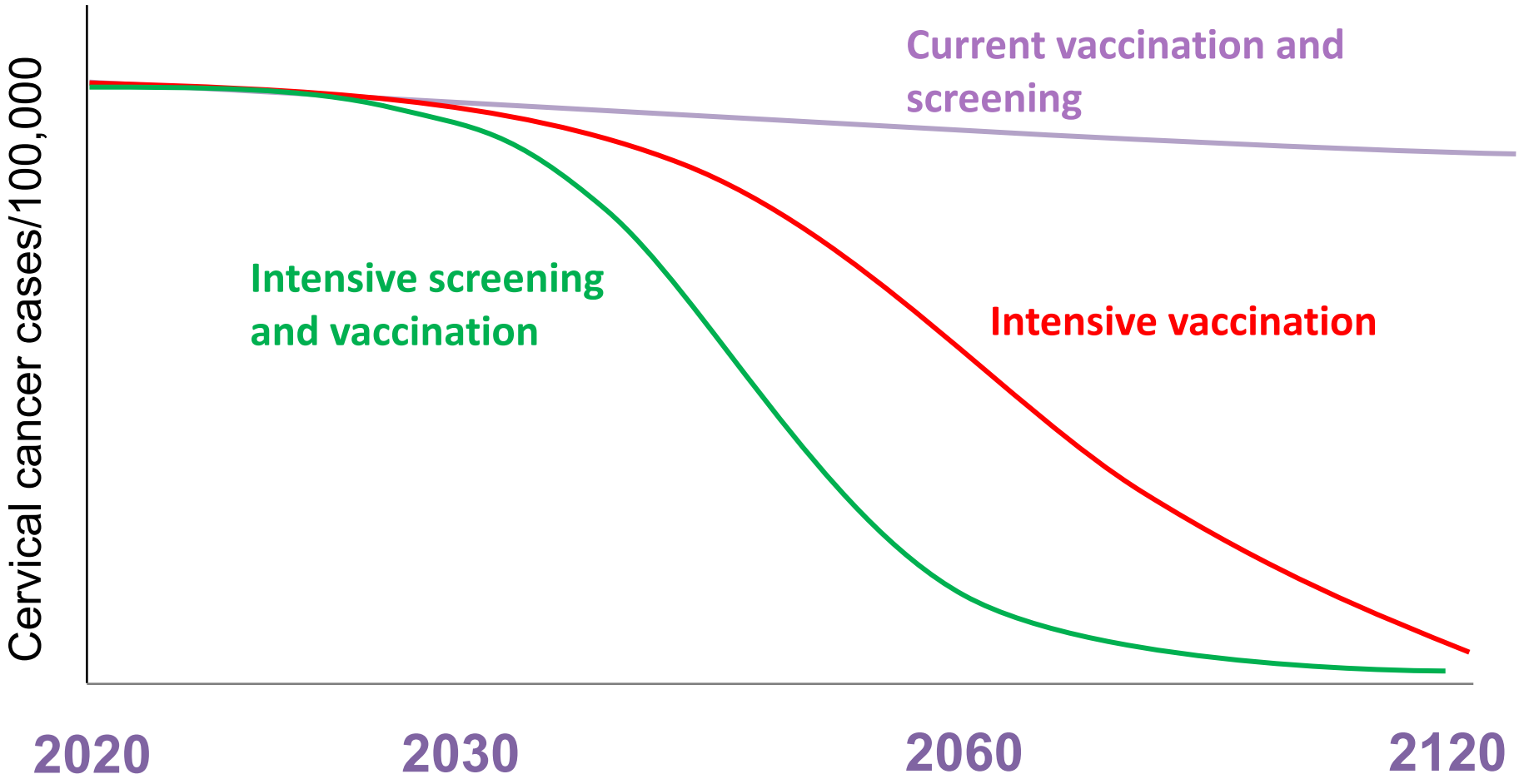
CERVICAL CANCER ELIMINATION: CONCEPTUAL FRAMEWORK



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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

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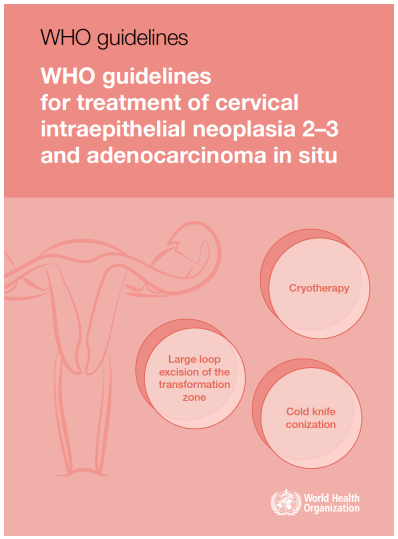
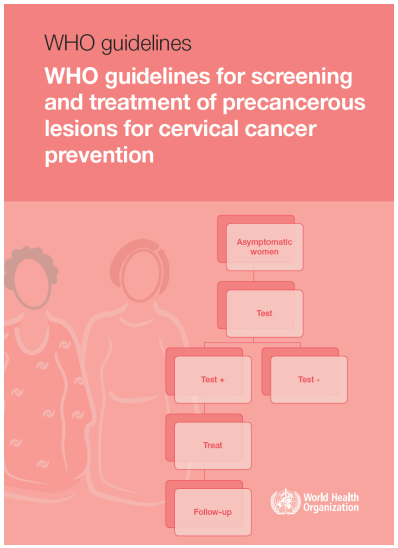
WHO guidelines

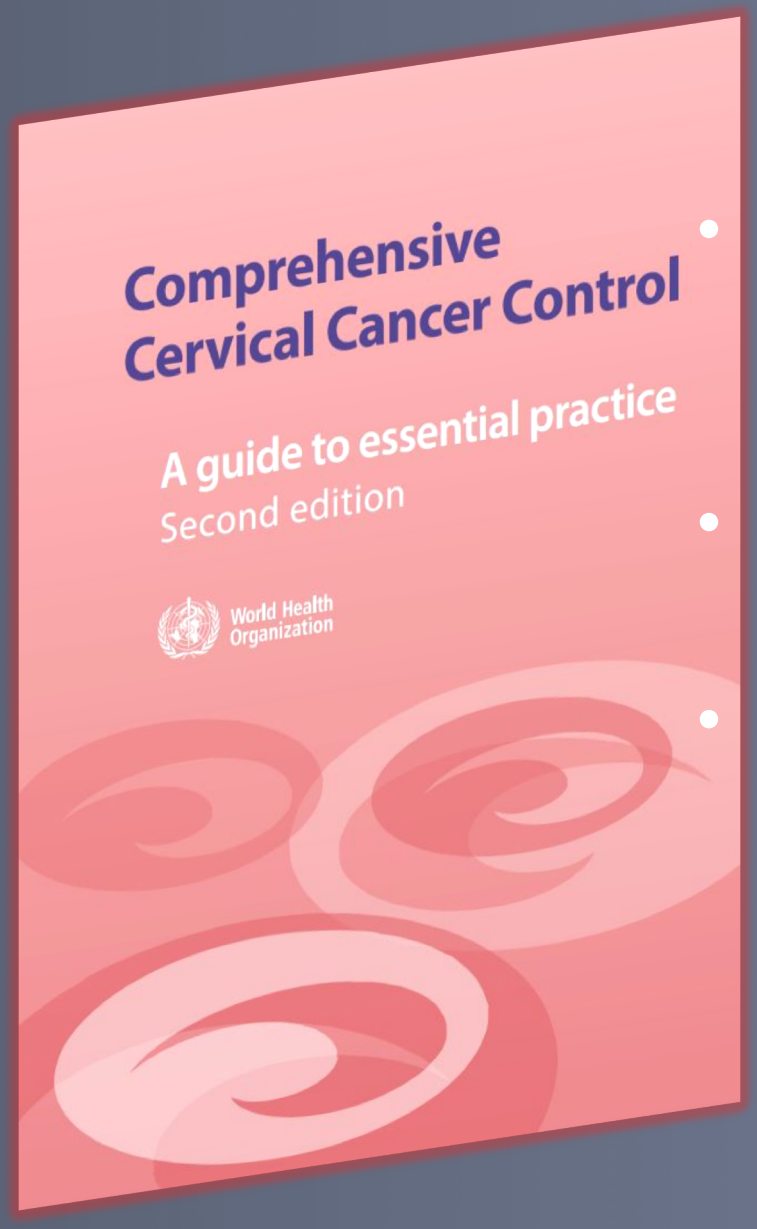




- published 2013
- treatments include cryotherapy, LLETZ/LEEP, cold knife conisation

- published 2014
- Screening/triage tests
- treatments include cryotherapy, LLETZ/LEEP, cold knife conisation

WHO recommendations for Screen Treat



- Screening should start at 30 years

  Although the magnitude of the net benefit will differ between age groups and may extend to younger and older women depending on their baseline risk.

- Priority should be given to screening women 30 to 49.
- Women HIV + should be screened immediately when they know their status if they are sexually active

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

Screening tests

- HPV tests (DNA based)
- VIA
- Cytology

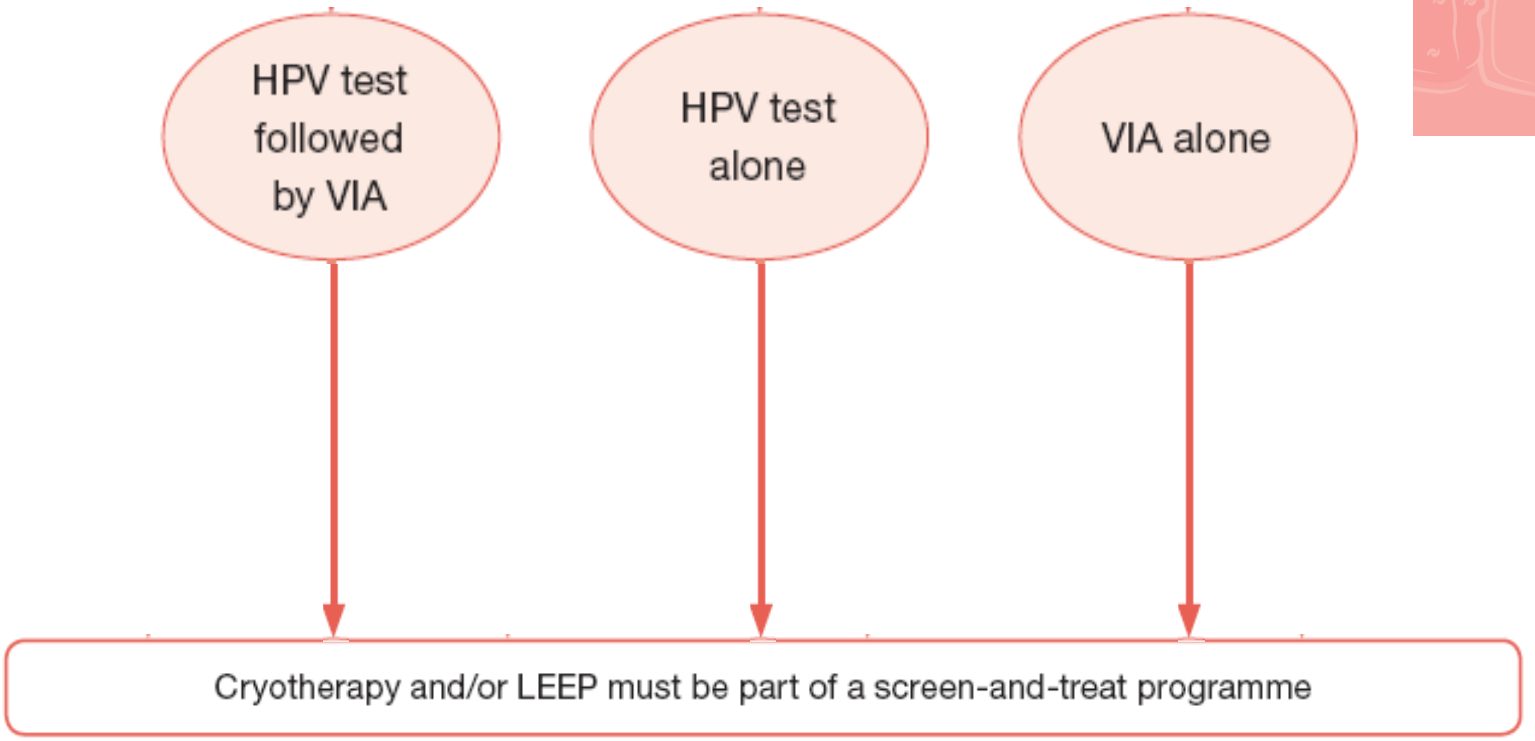
Ablative treatment (of women screened positive and eligible)

- 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

WHO recommended screen and treat algorithms



http://www.who.int/reproductivehealth/topics/cancers/en/

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Key recommendations:

For women with histologically confirmed CIN2+ disease, regardless of HIV status

Conditional recommendation

The expert panel suggests:

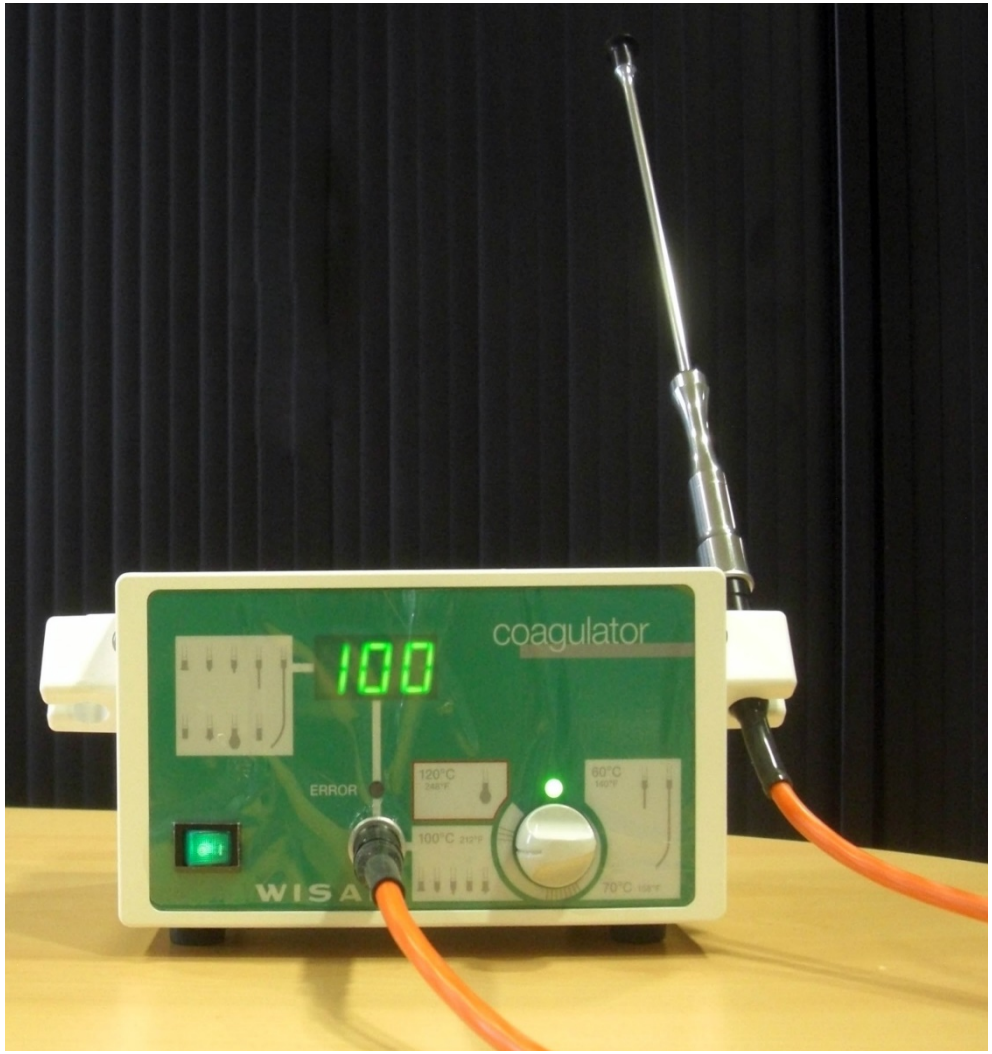
4. Use either cryotherapy or LEEP in women for whom either cryotherapy or LEEP is appropriate to use and available. ⊕⊖⊖⊖ evidenc

The expert panel[1] recommends against the use of CKC as a treatment in a screen-and-treat strategy. Therefore, all screen-and-treat strategies below involve treatment with cryotherapy, or LEEP when the patient is not eligible for cryotherapy.

In practice:

- Major disadvantage of cryotherapy is the need for a cryo-gas (N_2O or CO_2)
  - containers are bulky and heavy for transportation
  - gas is not always easily available in rural areas of low and middle-income countries
- Results in delays to treatment

Thermal ablation



- also called cold coagulation
- ablative method
- light weight
- electricity or battery operated
- used in the UK in the 1980s - early 1990s
- increasing research in low and middle-income countries

Update the WHO cervical pre-cancer treatment guidelines

- Include treatment with thermal ablation

- Follow methods of WHO Guidelines for Guidelines (2014)
  - establish Guideline Development Group (GDG) which includes clinical experts, researchers, representatives from member states, programme managers
  - conduct systematic reviews of the evidence for benefits and harms, resources, acceptability, equity and feasibility
  - meeting to make recommendations based on evidence
  - peer review process of the recommendations
  - publication

Key questions

In women with histologically confirmed CIN 2-3 or screened positive, should thermal ablation or cryotherapy, LLETZ, or cold knife conization be recommended?

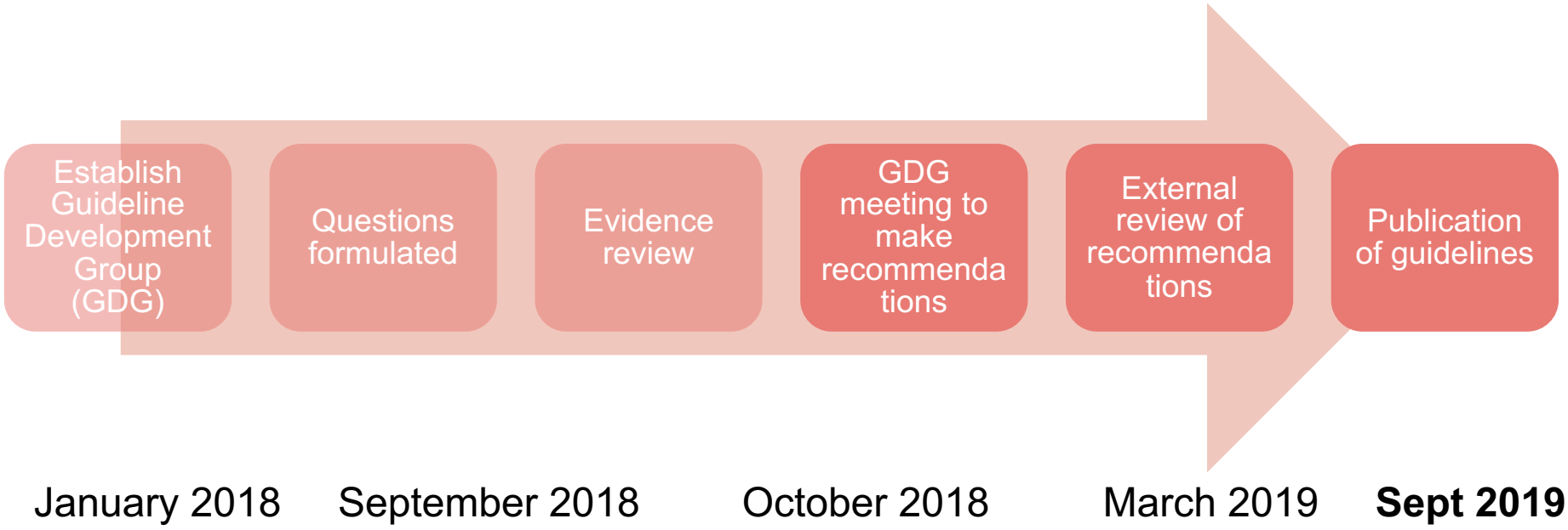
Considerations:

- HIV status, age of women, lesion size, endocervical involvement
- number of applications, duration, shape and size of probe
- use of antibiotics
- health care provider

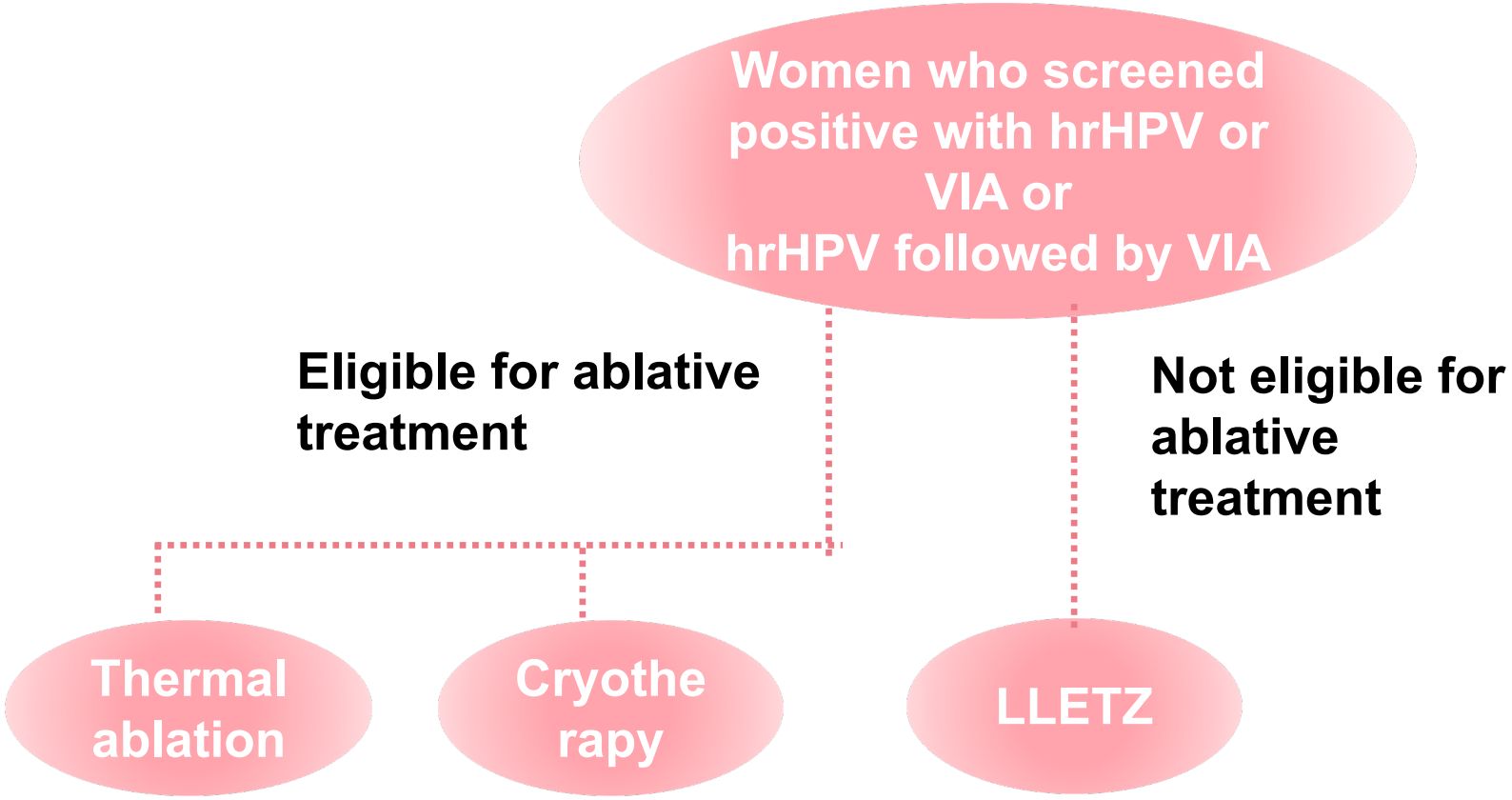
Guideline Development Group

- 35 members
- varied expertise in technical and societal aspects of screening and treatment of precancerous lesions
- from the African Region, Region of the Americas, South-East Asia Region, European Region, and the Western Pacific Region

WHO Handbook for Guideline Development



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.

- Few studies comparing different modalities for use of thermal ablation
- Future research should explore the use of a **2-probe method**, in which 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**

Future research

Few studies compared thermal ablation to other treatments for histologically confirmed pre-cancer cervical lesions or screen positive

- no studies in WHIV

Evidence based primarily on studies following one group of women receiving thermal ablation

- few outcomes measured (need for fertility and reproductive outcomes)
- few outcomes important outcomes in WHIV (need for HIV shedding or risk of transmission after treatment)

WHO CONSOLIDATED GUIDELINE ON SELF-CARE INTERVENTIONS FOR HEALTH
Sexual and reproductive health and rights

New recommendation on HPV self-sampling

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

STRENGTH OF RECOMMENDATION: Strong recommendation

CERTAINTY OF EVIDENCE: Moderate-certainty evidence

CERVICAL CANCER SCREENING AND TREATMENT: HOW TO INCREASE COVERAGE BY 2030

Complex or Low Sensitivity Techniques:

- Cytology: very successful in high resource countries, but implementing well performing cytology screening is very challenging in middle and low resource countries
- Naked eye visual inspection with 3-5% acetic acid (VIA)
- Visual inspection with Lugol's iodine (VILI)

Alternatives:

- **HPV testing plus triage with VIA -- followed by cryo or TA**
- **HPV testing, with no triage -- followed by cryo or TA**

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