WHO treatment guidelines update
– HPV screening and treatment

Hugo De Vuyst – WHO/IARC
Ricky Lu – JHPIEGO
Mauricio Maza – Basic Health International
Katherine Hencher – UNITAID

Joint UNICEF, UNFPA and WHO meeting with manufacturers and suppliers

Copenhagen, 25 September 2018
WHO treatment guidelines update – HPV screening and treatment

- Upcoming changes to HPV screening and treatment guidelines within the context of global goal of elimination
  - Dr Hugo De Vuyst (WHO/IARC)

- Cervical Cancer Prevention – Better Tools, Greater Coverage, Towards Elimination, Issues and Opportunities
  - Dr Ricky Lu (JHPIEGO)

- Implementation of HPV testing in limited resource settings
  - Dr Mauricio Maza (BHI)

- UNITAID: Call for proposals to accelerate access and scale use of optimal tools for cervical cancer secondary prevention in low- and middle-income countries
  - Dr Katherine Hencher (UNITAID)
Cervical cancer – an avoidable NCD with gross inequities

- An estimated 266,000 women died of cervical cancer in 2012*
  ➔ equivalent of 1 woman dying every 2 minutes.

*GLOBOCAN 2012
Cervical cancer – an avoidable NCD with gross inequities

- An estimated 266,000 women died of cervical cancer in 2012*
  ➔ 86% of these deaths in LMIC.

*GLOBOCAN 2012
WHO life course approach to cervical cancer control

**Primary Prevention**
- **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

**Secondary Prevention**
- **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

**Tertiary Prevention**
- **All women as needed**
  - Treatment of invasive cancer at any age and palliative care
    - Ablative surgery
    - Radiotherapy
    - Chemotherapy
    - Palliative Care
May 2018: WHO Director General’s Call to Action to Eliminate Cervical Cancer as a Public Health Problem
OVERALL CONCEPTUAL FRAMEWORK

Cervical cancer cases/100,000

- Current vaccination and screening
- Intensive vaccination
- Very intensive screening and vaccination

Elimination goal 1
Elimination goal 2
Example of scenario with elimination by 2060-2070: targets for 2030

**Vision:** A world without cervical cancer

**Goal:** below 4 cases of cervical cancer per 100,000 woman-years

### 2030 TARGETS

- **90%**
  - of girls fully vaccinated with HPV vaccine by 15 years of age

- **70%**
  - of women screened with an HPV test at 35 and 45 years of age and all managed appropriately

- **30%**
  - reduction in mortality from cervical cancer

The 2030 targets and elimination threshold are subject to revision depending on the outcomes of the modeling.
WHO Guidelines related to cervical cancer prevention and control

- Comprehensive Cervical Cancer Control; guide to essential practice (C4-GEP) (update 2014)
  A guide for programme managers and health care providers.
  - Primary prevention (HPV vaccination)
  - Secondary prevention (cervical cancers screening and treatment)
  - Tertiary prevention (diagnostic; treatment invasive disease and palliative care)
Secondary prevention: Screen-and-treat algorithms

- Do you have a screening programme in place?
  - Yes
    - Do you have enough resources to provide an HPV test?
      - Yes
        - Do you have enough resources to provide a sequence of tests (i.e. HPV test followed by another test)?
          - Yes
            - HPV test followed by VIA
          - No
            - HPV test alone
      - No
        - VIA alone
  - No
    - Yes, cytology followed by colposcopy
    - No
      - Does the programme meet quality indicators (e.g. training, coverage, and follow-up)?
        - Yes
          - Cytology or HPV test followed by colposcopy
        - No
          - Cryotherapy and/or LEEP must be part of a screen-and-treat programme
Secondary prevention: Screen-and-treat algorithms

1. Do you have a screening programme in place?
   - Yes,
     - Do you have enough resources to provide an HPV test?
       - Yes
         - Do you have enough resources to provide a sequence of tests (i.e. HPV test followed by another test)?
           - Yes
             - HPV test followed by VIA
           - No
             - HPV test alone
     - No
     - Does the programme meet quality indicators (e.g. training, coverage, and follow-up)?
       - Yes, cytology followed by colposcopy
       - No
         - VIA alone
         - Cytology or HPV test followed by colposcopy

2. Cryotherapy and/or LEEP must be part of a screen-and-treat programme
Primary HPV screening for secondary prevention

- Challenge to screen 70% of women >30yrs by 2030 with HPV testing:
  - simple, feasible, affordable test
  - sensitive and specific, that can be used in a screen-and-treat algorithm, avoiding as much as possible overtreatments
  - near Point-of-Care (POC) use

- Currently pre-qualified:
  - Genexpert HPV (Cepheid)
  - CareHPV (Qiagen)

- Challenge of supply
Decision-making flowchart for programme managers

Do you have a screening programme in place?

Yes,

Do you have enough resources to provide an HPV test?

Yes, cytology followed by colposcopy

No

Does the programme meet quality indicators (e.g. training, coverage, and follow-up)?

No

Yes

Do you have enough resources to provide a sequence of tests (i.e. HPV test followed by another test)?

HPV test followed by VIA

HPV test alone

VIA alone

Cytology or HPV test followed by colposcopy

Cryotherapy and/or LEEP must be part of a screen-and-treat programme
WHO: Ongoing development of recommendations on novel ablative treatment methods:

**THERMAL ABLATION:**
- The equipment is fairly simple and treatment is based on a 20-40 seconds application of a reusable metallic probe that is electrically heated to 100-120°Celsius.
- Recently light weight hand held and battery operated models have been developed.
- Recommendations expected by end of 2018

**ELECTRICITY-POWERED CRYOTHERAPY DEVICES:**
- Hand-held devices that use electricity to cool the treatment probe to freezing temperatures, in order to overcome the need for cryo-gas (e.g. CryoPen™).
- It should be established if these devices comply to the WHO technical specifications for cryotherapy equipment [WHO 2012].
WHO Guidelines related to cervical cancer prevention and control

- HPV self-collection: systematic literature review
  - In context of self-initiated interventions; increase person’s autonomy to control their health and health care
    - self-collection
    - services, behaviours and information

- Update Comprehensive Cervical Cancer Control: screening algorithms specific to HIV-positive women:
  - Age at first screening
  - Frequency of screening
  - Which screening (and triage) test (VIA, HPV test)
  - Treatment; efficacy and potential harm of overtreatment
WHO prequalification: Full assessment

Pre-submission form

Priority product

Yes

No

Dossier screening

Dossier incomplete

Dossier complete

Dossier review

Site inspection

Laboratory evaluation

Prequalification decision

New pathway
Technical Specifications Series (TSS)

- Summarize minimum performance requirements for WHO prequalification, to establish:
  - appropriate performance evaluation and re-evaluation criteria
  - appropriate reference methods and reference materials

- Specific requirements tailored to types of infections, conditions, etc.
  - Requirements that address needs of Member States in LMIC
  - Requirements that relate to general performance characteristics

- Clarify requirements to Manufacturers and Assessors

- TSS 4: IVD used for the detection of high-risk HPV types in cervical cancer screening:
  - http://apps.who.int/iris/bitstream/handle/10665/272282/9789241513814-eng.pdf?ua=1
The Technical Guidance Series (TGS) is for manufacturers interested in WHO prequalification of their IVD.

The series is intended to help manufacturers in meeting prequalification requirements.
The ESTAMPA Study: primary HPV testing and triage (IARC/WHO)

RECRUITMENT
✓ 30,179 / 50,000 women 30-64y recruited in 12 centres in nine Latin American countries

RESEARCH NETWORK
✓ Over 300 Latin American collaborators
✓ 12 multidisciplinary research teams: 200 screening providers (nurses, midwives, GPs), 50 colposcopists, 25 pathologists, 35 laboratory technicians/scientists
✓ Other local professionals benefitted with up-to-date trainings and are part of specialised regional networks

Fig 1. Number of women recruited per country

Fig 2. Prevalence of high-risk HPV infection

Overall high-risk HPV prevalence: 14.3% (95% CI 13.9–14.8)
Cervical cancer Screen and Treat algorithms study using HPV testing in Africa (CESTA, WHO/IARC)

Pilot studies:
Senegal / South Africa

Pilot studies (Phase 1):
Durban, South-Africa: Sample size 5500 women (Jan 2018 – Dec 2023)
Dakar, Senegal: sample size 350 women (Nov 2018 – Feb 2019)

1 year FU: HPV + biopsy² (on HPV+); Treatment for colposcopy+ or biopsy CIN2+

¹ Only distinct VIA-positive lesions will be treated; ² Biopsies taken by a nurse on all HPV-pos women; ³ If not eligible for ablative treatment; ⁴ If suspicious for cancer; ⁵ Biopsies taken by a colposcopist; HPV: Human papillomavirus; LEEP: Loop electrosurgical excision procedure; VIA: Visual Inspection with acetic acid
UN Joint Global Programme (UNJGP) on Cervical Cancer Prevention and Control

End Cervical Cancer: Prevent, Treat, Care

Partners
- GAVI
- GFATM
- Unitaid
- UICC
- CHAI

UN Agencies
- WHO
- IAEA
- IARC
- UNAIDS
- UNFPA
- UNICEF
- UN Women
- UNODC

Participating Countries
- Bolivia
- Ghana
- Guinea
- Kenya
- Kyrgyzstan
- Madagascar
- Malawi
- Mongolia
- Morocco
- Myanmar
- Nigeria
- Senegal
- Sierra Leone
- Tanzania
- Uzbekistan
- Zambia
- Zimbabwe

UN Joint Global Programme on Cervical Cancer Prevention and Control
WHO, IAEA, IARC, UNAIDS, UNFPA, UNICEF, UN Women and UNODC
IARC – an influential publications programme