3. Important considerations for the recommendations

The WHO recommendations presented in this guideline are intended to support countries to improve the coverage and outcomes of cervical cancer screening. Additionally, they are designed to set standards and targets to improve the quality of services and reduce cervical cancer deaths. In many settings, bridging strategies will be needed to move from any existing screening infrastructure to the infrastructure needed to achieve implementation of the recommendations. This transition may take time and, as a first step, providing at least one or two screens over a woman's lifetime will have an important impact on cervical cancer mortality in settings without a routine screening programme. In the near future, WHO will develop and publish stepwise implementation guidelines to support the selection of algorithms, adaptation and scale-up of the recommendations.

3.1 Programme considerations

It is appropriate that a multidisciplinary health ministry team, which can consider different factors and make informed decisions, chooses which algorithm (or algorithms) to include in a national programme. The choice will vary by country – and in different settings within country programmes – and will depend on available resources, feasibility and acceptability.

Decisions are also needed about when and who to contact for follow-up care. This guideline makes recommendations that distinguish between three clinical scenarios in routine screening programmes:

- **Regular screening intervals: This applies to women who either had negative screening results or have completed the recommended additional follow-up after treatment and who are thus eligible to return to regular screening intervals.**
- **Follow-up of women with a positive primary screening test but a negative triage test.**
- **Follow-up of women after treatment.**

A key requirement for any programme for screening and treatment to prevent cervical cancer is that the screening approach and the tests used should be of the highest quality and standards to produce accurate and reliable results and beneficial outcomes. Only screening tests approved by regulatory agencies *(34)* should be considered for introduction.

To prevent and treat cervical cancer and reduce mortality, programmes are encouraged to implement population-based screening and treatment strategies. All programmes should ensure that women who have screened positive are treated or managed adequately. Screening registries

and call-and-recall efforts are important aspects of appropriate management to ensure that women are coming back to the service for treatment and follow-up. For the continuity and completeness of care, strong links need to be established between the multiple levels of the health service (primary and secondary care) and individual patients. A further description of quality assurance and more detailed programmatic guidance can be found in *Annex 6* and in other published documents *(5,35,36)*.

Cervical cancer screening and treatment should be provided to transgender men, and non-binary and intersex individuals who have a cervix. More data on cervical cancer screening and treatment are needed for these populations, including people living with HIV. WHO recognizes the need for health-care systems, including screening and treatment services for cervical pre-cancer and cancer, to be more inclusive of transgender, intersex and non-binary people, which may require additional training and sensitization of health workers. Public health authorities should also prioritize these groups of people for better awareness of and access to cervical cancer screening and treatment.

3.2 Screening and triage tests considered in this guideline

High-risk HPV DNA tests: These tests identify a group of high-risk carcinogenic HPV genotypes, typically including up to 14 types (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59, which are Group 1 carcinogens, and HPV66 and 68) *(37)*. HPV16 and 18 are the highest-risk genotypes and are the most common in cancers. Some of the tests on the market provide information about specific HPV genotypes, such as HPV16 and 18. We refer to HPV tests with partial genotyping when they report HPV16 and 18 (including HPV45 in some cases) and other carcinogenic types separately. Other HPV tests may provide extended genotyping, when they report additional types, or groups of types, such as HPV31, 33, 35, 45, 52 and 56. This guideline specifically refers to partial genotyping (i.e. the detection of HPV16 and 18 versus other carcinogenic types) to identify women at the highest risk of cervical cancer among those testing positive for HPV (*Annex 4*). Self-sampling or provider sampling can be used for HPV DNA testing. In this guideline, an HPV DNA test means a high-risk HPV DNA test, which is a nucleic acid amplification test (NAAT).

Cytology: Cytology tests (including the Papanicolaou smear test and liquid-based cytology [LBC]) identify atypical cells on the cervix through the preparation and interpretation of slides using microscopy by a trained expert. LBC requires sophisticated processing to create slides from liquid specimens. The threshold used in this guideline to identify the need for further evaluation or treatment is a cytological result of atypical squamous cells of undetermined significance (ASCUS) combined with the presence of high-risk HPV.

Visual inspection with acetic acid (VIA): VIA testing uses dilute acetic acid (vinegar) on the cervix without magnification to identify aceto-white lesions that need treatment (e.g. ablation or excision) or further evaluation. VIA is not appropriate for use in women when the transformation zone is no longer visible or after menopause. This guideline

makes a distinction between using VIA as a screening or triage test, and assessing eligibility for treatment (after positive screening) using acetic acid and visual evaluation (see *Box 3.1* below; for further information, refer to *Annex 5, section 5.1*).

Colposcopy: Colposcopy is used to assess the epithelium of the transformation zone to determine its type (*Annex 5, section 5.4*), whether or not there is evidence of abnormality, and, where indicated, to facilitate a biopsy or treatment. It is not commonly used as a screening tool. Colposcopy may also be used after a primary positive screening test, to assess whether ablative or excisional therapy is appropriate.

Triage tests: The triage tests considered in this guideline include high-risk HPV DNA partial genotyping, cytology, VIA and colposcopy that may or may not include a biopsy for histological diagnosis. Some of these triage tests may be conducted sequentially (e.g. cytology followed by colposcopy with biopsy). Other triage tests are currently undergoing clinical evaluation and may be added to this guideline later as part of the "living guidelines" process.

Further information on these tests is available in *Annex 6*.

Box 3.1: Visual evaluation to assess eligibility for treatment versus visual inspection with acetic acid (VIA) as a screening test

There is a distinction in these recommendations between (a) using visual evaluation to assess eligibility for ablative treatment (*Annex 5, section 5.1*), and (b) using VIA as a screening test as part of an algorithm to determine whether or not to treat (*Annex 4*). This distinction is illustrated in the following scenarios:

a. In the HPV test screen-and-treat strategy (i.e. algorithm 2 in *Table 2.2*), women who are HPV-negative are not treated, nor evaluated further. Women who are HPV-positive should all be treated but first eligibility for ablative treatment must be assessed with application of acetic acid and visual evaluation using the naked eye or with a colposcope. Those who are ineligible for ablative treatment should be referred for excisional treatment or further evaluation.

b. In the HPV test screen, triage and treat strategy (i.e. algorithms 4 to 7 in *Table 2.2*), women who are HPV negative are not treated, nor evaluated further. Women who are HPV-positive undergo VIA as a triage test (i.e. algorithm 5 in *Table 2.2*) to determine whether they should be treated. Women who are HPV-positive and VIA-positive will be treated with ablation if adequate, or referred for excisional treatment or further evaluation, while women who are HPV-positive and VIA-negative will not be treated but followed-up as indicated in the algorithm.

3.3 Treatment considerations

In a screen-and-treat approach, women who screen positive are treated without histological diagnosis. The treatment aims to destroy or remove the transformation zone of the cervix, or remove areas of the cervix that have been identified as abnormal by screening.

The methods of treatment may be ablative (destroying abnormal tissue by heating it with thermal coagulation or freezing it with cryotherapy) or excisional (surgically removing abnormal tissue with LLETZ or CKC) (*Annex 5, section 5.4*). Ablative treatments do not result in a tissue specimen for histological evaluation.

In this guideline, the term LLETZ is used to refer to excision of the transformation zone. LLETZ uses local anaesthesia, is done in an outpatient setting and yields a tissue specimen for pathology. In some countries, this terminology was changed to LEEP (loop electrosurgical excision procedure), and the two terms are often used interchangeably (*Annex 5, section 5.4*).

WHO has published technical specifications for ablative therapy and LLETZ *(36)*. For further summary comparisons of the treatment methods, refer to the WHO *Comprehensive cervical cancer control: a guide to essential practice* *(5)* and the thermal ablation treatment guidance *(15)*.

Before treatment, all women who have screened positive with any test other than VIA should be visually inspected with acetic acid by a trained health worker to determine the transformation zone type (*Annex 5, section 5.4*), rule out suspected cervical cancer and determine eligibility for ablative therapy.

Refer to *Annex 5* for the definition of eligibility for ablative treatment (section *5.1 of the annex*) and for further description of the transformation zone (section *5.4 of the annex*).