

# SECTION 1: SCIENTIFIC EVIDENCE ON HPV TESTING FOR CERVICAL CANCER SCREENING

## KEY MESSAGES

- Evidence shows that HPV tests are an effective screening test for cervical cancer prevention.
- At a minimum, screening all women aged 30 to 49 years, at least once in their life, is recommended. Screening may be extended to younger or older women, depending on the available resources and women's risk of cervical cancer.
- Regardless of the screening test used, an organized screening program must include high coverage in the group of high-risk women (aged 30-49 years) and prompt follow-up and treatment for all women with abnormal results.

## NATURAL HISTORY OF CERVICAL CANCER

The main cause of cervical cancer is persistent infection with high-risk types of human papillomavirus (HPV). HPV 16 and HPV 18 are among the most common high-risk HPV types and are found in approximately 70% of all cervical cancer cases. Low-risk HPV types, such as HPV 6 and HPV 11 are not associated with cancer, but cause genital warts (WHO, 2014).

HPV is primarily sexually transmitted. It is a very common infection and most people are infected shortly after they become sexually active. The risk factors for HPV infection, in both men and women, are related to sexual behavior and include sexual debut at an early age and a high number of sexual partners. A small proportion of women with persistent HPV infection will develop cervical cancer, which can take decades to develop (WHO, 2014).

HPV vaccination in girls aged 9 to 13 years, combined with screening women aged 30 years and older, followed by appropriate treatment are key strategies to prevent cervical cancer (WHO, 2014). HPV vaccination does not replace screening for cervical cancer.

## SUMMARY OF WHO RECOMMENDATIONS FOR CERVICAL CANCER SCREENING AND PRECANCER TREATMENT

WHO issued a cervical cancer prevention and control guideline, in 2014, following an extensive review of the scientific evidence. The highlights of the guideline are as follows (WHO, 2014):

- Cervical cancer screening tests include: HPV tests, conventional or liquid based cytology (Pap smear), and visual inspection with acetic acid (VIA).
- Evidence shows that HPV tests are much more sensitive and more effective in identifying women at higher risk of developing precancerous cervical lesions.
- Women aged 30 to 49 years need to be screened at least once in their lifetime, at a minimum. Screening could be extended to younger and/or older age groups, according to available resources.
- For women at average risk -who are HIV negative, not otherwise immunocompromised, and women with no prior abnormal cervical screening test- with negative HPV test results, a minimum of five years is recommended for re-screening.
- Regardless of the test used, an organized screening program needs to assure high screening coverage in the target group (aged 30-49 years), linked to prompt follow-up and treatment for all women with abnormal test results.

The WHO cervical cancer guideline also includes recommendations for screening and precancer treatment strategies. These were developed based on an extensive review of evidence by subject matter experts, as well as modeling where gaps in evidence existed, to compare different service delivery strategies. The highlights of the WHO recommendation for screening and precancer treatment strategies are as follows (WHO, 2013):

1. Use a strategy of screen with an HPV test and treat, over a strategy of screen with VIA and treat. In resource-constrained settings, where screening with an HPV test is not feasible, the panel suggests a strategy of screen with VIA and treatment of precancerous lesions in the same visit, if possible.
2. Use a strategy of screen with an HPV test and treat, over a strategy of screen with cytology followed by colposcopy (with or without biopsy) and treat. However, in countries where an appropriate, high-quality screening strategy with cytology followed by colposcopy already exists, an HPV test or cytology followed by colposcopy could be used.
3. Use a strategy of VIA screening and treatment, over a strategy of cytology followed by colposcopy (with or without biopsy) and treatment. The recommendation for VIA over cytology followed by colposcopy can be applied in countries that are currently considering establishing a screening program.
4. Use a strategy of HPV testing followed by VIA and treatment, over a strategy of VIA screening and treatment.
5. Use a strategy of HPV testing followed by VIA and treatment, over a strategy of cytology screening followed by colposcopy (with or without biopsy) and treatment.

Due to practical reasons and because the WHO subject matter experts prioritized the screen and treat strategy, the option of using HPV testing as the primary screening test, followed by cytology (Pap smear) as a triage test was not included in the revision of evidence nor in the comparison between different strategies. However,

this is a strategy used in several countries where Pap smear programs already exist, and a reason why it can be considered as an option:

- HPV test followed by cytology (Pap smear) and referral of those women with abnormal test results on both tests to colposcopy, biopsy, and treatment, according to biopsy result.

**Options for screening strategies using HPV tests**

STRATEGY	ADVANTAGES	DISADVANTAGES
<b>HPV, and cytology triage in HPV+ women</b>	<ul style="list-style-type: none"> <li>• Identifies women at greater risk of precancerous lesions.</li> </ul>	<ul style="list-style-type: none"> <li>• More resources are required for cytology.</li> <li>• Multiple visits required by women and greater risk of loss to follow-up.</li> </ul>
<b>HPV, and VIA triage in HPV+ women</b>	<ul style="list-style-type: none"> <li>• Identifies women at greater risk of precancerous lesions.</li> </ul>	<ul style="list-style-type: none"> <li>• Quality control for VIA is required.</li> <li>• High-grade lesions that are not visible with VIA could be missed.</li> </ul>
<b>HPV and treatment (without triage)</b>	<ul style="list-style-type: none"> <li>• Simplifies the process for completing treatment.</li> <li>• Reduces the number of visits required by the woman.</li> <li>• May lead to more women being treated, and less women being lost to follow-up care.</li> </ul>	<ul style="list-style-type: none"> <li>• Over-treatment may occur.</li> <li>• Treatment costs may be higher.</li> </ul>