World Health Organization

New WHO recommendations on screening and treatment to prevent cervical cancer among women living with HIV

Policy brief

Background

Women living with HIV have a six-fold increased risk of cervical cancer compared with women without HIV.[1] This elevated risk is manifested throughout the life course, beginning with an increased risk of acquiring human papillomavirus (HPV) infection, which is responsible for the majority of cervical cancer cases. Women living with HIV have more rapid progression of high-risk HPV infection to pre-cancer lesions and subsequently to cervical cancer, and also reduced likelihood of regression of pre-cancer lesions, and higher rates of recurrence following treatment.

Cervical cancer is the fourth most common cancer in women. In 2020, an estimated 604 000 women were diagnosed with cervical cancer worldwide and about 342 000 women died from the disease.[2] Globally, an estimated 5% of all cervical cancer cases are attributable to HIV.[1] However, these statistics vary enormously by region. In nine countries with high HIV prevalence, the proportion of cervical cancer attributable to HIV is 40% or higher, whereas it is less than 5% in 122 countries with much lower HIV prevalence. Thus, HIV contributes substantially to the stark geographic disparities seen in cervical cancer burden.

Since the countries with high HIV burden have some of the highest cervical cancer rates, a greater effort will be needed to achieve cervical cancer elimination in these settings. Focusing on the prevention and treatment of both cervical cancer and HIV can help maximize benefits in countries hardest hit by both cervical cancer and HIV.

In November 2020, the World Health Organization (WHO) Director-General Dr Tedros Adhanom Ghebreyesus launched the Global strategy to accelerate the elimination of cervical cancer as a public health problem,[3] including the **following global targets for 2030**:

- 90% of girls are fully vaccinated with HPV vaccine by age 15 years.
- 70% of women are screened with a high-performance test by 35 years of age and again by 45 years of age.
- 90% of women identified with cervical disease receive treatment.

[1] Stelzle D, Tanaka LF, Lee KK, Ibrahim Khalil A, Baussano I, Shah ASV, et al. Estimates of the global burden of cervical cancer associated with HIV. Lancet Glob Health 2020. doi:S2214-109X(20)30459-9.
[2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021:71:209–49. doi:10.3322/caac.21660.
[3] Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization; 2020 (https://www.who.int/publications/i/item/9789240014107).

Recommendations

As part of the efforts to achieve these targets for elimination of cervical cancer, WHO has published a new edition of its guideline on screening and treatment to prevent cervical cancer,[4] which **includes 16 new and updated recommendations and good practice statements for women living with HIV (Table 1)**. The guidance was developed to update the existing WHO recommendations on screening and treatment, including guidance on diagnostic tests, and to simplify the algorithms, while ensuring that the recommendations are feasible and acceptable for both the health workers providing screening and treatment services, and for women, the users of those services.[5]

Two approaches to screening and treatment are distinguished in the guidance:

- In the **"screen-and-treat approach"**, the decision to treat is based on a positive primary screening test only.
- In the **"screen, triage and treat approach"**, the decision to treat is based on a positive primary screening test followed by a positive second test (a "triage" test), with or without histologically confirmed diagnosis.

Key features of the new and updated recommendations

WHO suggests using the following strategy for cervical cancer prevention among women living with HIV: HPV DNA detection in a screen, triage and treat approach starting at the age of 25 years with regular screening every 3 to 5 years.

While countries are transitioning to HPV DNA testing for primary screening, cytology or visual inspection with acetic acid (VIA) screening tests should be continued until HPV DNA testing is operational. The choice of triage test to be used on women who screen positive will be dependent on feasibility, training, programme quality assurance and resources.

> Providing at least two screens over a woman's lifetime will reduce cervical cancer mortality.

The new and updated WHO recommendations are intended to support countries to scale up access to and uptake of cervical cancer screening and treatment with quality modern technologies and thereby improve coverage of both screening and treatment and reduce cervical cancer disease and deaths. In many settings, bridging strategies will be needed to transition to the infrastructure needed to achieve implementation of the recommendations. This may take time. As a first step, providing at least two screens over a woman's lifetime will reduce cervical cancer morbidity and mortality.

Integration of cervical cancer screening and HIV care for women living with HIV is a priority.
R. Awori, Uganda Network of Young People Living with HIV & AIDS ©WHO

[4] WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. Geneva: World Health Organization; 2021.
[5] To be concise and facilitate readability, we use the term "women" in this brief, although we recognize that all gender diverse people with a female reproductive system are at risk for cervical cancer. Most of the available evidence on cervical cancer is based on study populations of cisgender women. All individuals have the right to equality and non-discrimination in sexual and reproductive health care.

Table 1. Screening and treatment recommendations and good practice statements to prevent cervical cancer among women living with HIV

Recommendations and good practice statements for women living with HIV	*Strength of recommendation and level of evidence*
21.[a] WHO recommends using HPV DNA detection as the primary screening test rather than VIA or cytology in screening and treatment approaches among both the general population of women and women living with HIV. *Remarks: Existing programmes with quality-assured cytology as the primary screening test should be continued until HPV DNA testing is operational; existing programmes using VIA as the primary screening test should transition rapidly because of the inherent challenges with quality assurance.*	*Strong recommendation, moderate-certainty evidence*
22. WHO suggests using an HPV DNA primary screening test **with triage rather than without triage** to prevent cervical cancer among women living with HIV.	*Conditional recommendation, moderate-certainty evidence*
23. **In a screen, triage and treat approach** using HPV DNA detection as the primary screening test among women living with HIV, WHO suggests using partial genotyping, colposcopy, VIA or cytology to triage women after a positive HPV DNA test. *Remarks: The benefits, harms and programmatic costs of the triage options are similar; therefore, the choice of triage method will be dependent on feasibility, training, programme quality assurance and resources in countries. HPV16/18 genotyping could be integrated into the HPV DNA test.*	*Conditional recommendation, moderate-certainty evidence*
24. When providing HPV DNA testing, WHO suggests using either samples taken by a health-care provider or self-collected samples among both the general population of women and women living with HIV.	*Conditional recommendation, low-certainty evidence*
25. WHO suggests starting regular cervical cancer screening at the **age of 25 years** among women living with HIV. *Remarks: Low-certainty evidence found that there are likely to be small numbers of women living with HIV with cervical cancer who are below the age of 25. This recommendation applies to women living with HIV regardless of when they first tested positive for HIV.*	*Conditional recommendation, low-certainty evidence*
26. After the age of 50 years, WHO suggests screening is stopped after two consecutive negative screening results consistent with the recommended regular screening intervals among both the general population of women and women living with HIV. *Remarks: Neither VIA nor ablative treatment are suitable for screening or treatment of women in whom the transformation zone is not visible. Inadequate visualization is typical after the menopause.*	*Conditional recommendation, very low-certainty evidence*
27. Priority should be given to screening women living with HIV **aged 25–49 years**. When tools are available to manage women living with HIV aged 50–65 years, those in that age bracket who have never been screened should also be prioritized.	*Good practice statement*
28. WHO suggests a regular screening interval of **every 3 to 5 years** when using HPV DNA detection as the primary screening test among women living with HIV.	*Conditional recommendation, low-certainty evidence*
29. Where HPV DNA testing is not yet operational, WHO suggests a regular screening interval of every 3 years when using VIA or cytology as the primary screening test, among both the general population of women and women living with HIV.	*Conditional recommendation, low-certainty evidence*

Recommendations and good practice statements for women living with HIV	*Strength of recommendation and level of evidence*
30. While transitioning to a programme with a recommended regular screening interval, screening even just twice in a lifetime is beneficial among both the general population of women and women living with HIV.	*Good practice statement*
31. WHO suggests that women living with HIV who have screened positive on an HPV DNA primary screening test and then negative on a triage test, are retested with HPV DNA testing **at 12 months** and, if negative, move to the recommended regular screening interval.	*Conditional recommendation, low-certainty evidence*
32. WHO suggests that women from the general population and women living with HIV who have screened positive on a cytology primary screening test and then have normal results on colposcopy are retested with HPV DNA testing at 12 months and, if negative, move to the recommended regular screening interval.	*Conditional recommendation, low-certainty evidence*
33. WHO suggests that women living with HIV who have been treated for histologically confirmed CIN2/3 or adenocarcinoma in situ (AIS), or treated as a result of a positive screening test are retested at 12 months with HPV DNA testing when available, rather than with cytology or VIA or co-testing, and, if negative, **are retested again at 12 months and, if negative again**, move to the recommended regular screening interval.	*Conditional recommendation, low-certainty evidence*
34. As programmes introduce HPV DNA testing, use this test at the woman's next routine screening date regardless of the test that was used at prior screening. In existing programmes with cytology or VIA as the primary screening test, rescreening with the same test should be continued until HPV DNA testing is operational among both the general population of women and women living with HIV.	*Good practice statement*
41. Once a decision to treat a woman is made – whether from the general population of women or women living with HIV – it is good practice to treat as soon as possible within six months to reduce the risk of loss to follow-up. However, in women who are pregnant, good practice includes deferral until after pregnancy. In circumstances when treatment is not provided within this time frame, it is good practice to re-evaluate the woman before treatment.	*Good practice statement*
42. WHO suggests large-loop excision of the transformation zone (LLETZ) or cold knife conization (CKC) for women from the general population and women living with HIV who have histologically confirmed adenocarcinoma in situ (AIS). *Remarks: Loop excision may be preferred in women of reproductive age, in settings with greater availability of LLETZ and by providers with greater expertise performing LLETZ. CKC may be preferred when interpretation of the margins of the histological specimen is imperative.*	*Conditional recommendation, low-certainty evidence*

[a] The numbering corresponds to the numbers in the main guideline, which also includes guidance for the general population of women.[4]

Summary recommendation for the general population of women

WHO suggests using either of the following strategies for cervical cancer prevention among the general population of women:

- HPV DNA detection in a **screen-and-treat** approach starting at the **age of 30 years** with regular screening **every 5 to 10 years**.
- HPV DNA detection in a **screen, triage and treat** approach starting at the **age of 30 years** with regular screening **every 5 to 10 years**.

Summary recommendation for women living with HIV

WHO suggests using the following strategy for cervical cancer prevention among women living with HIV:

- HPV DNA detection in a **screen, triage and treat** approach starting at the **age of 25 years** with regular screening **every 3 to 5 years**.

Programme considerations

To prevent, treat and consequently reduce mortality from cervical cancer, countries and programmes are encouraged to implement population-based cervical cancer screening and treatment strategies. It is appropriate that a multidisciplinary health ministry team chooses which screening and treatment 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, acceptability and local context.

Service delivery

Policy-makers and programme managers will also need to make decisions about when and where individuals who have received cervical cancer services should go for follow-up care and support. The recommendations 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.

Cervical cancer screening and treatment should be provided to transgender men, non-binary,

All programmes should ensure that:

- Women living with HIV are offered cervical cancer screening as part of standard HIV care.
- Women who have screened positive for cervical pre-cancer or cancer are treated or managed adequately.
- Screening registries and call-and-recall efforts are made to encourage women to return for treatment and follow-up.
- Strong links are established at all levels of the health system between HIV and cervical cancer services for cross-referral.

managers. Public health authorities should also prioritize these groups of people for better awareness of, access to, and uptake of cervical cancer screening and treatment.

Service integration

Integrating HIV services more broadly with sexual and reproductive health (SRH) and cancer services, including cervical cancer screening and treatment, is feasible and has the potential for positive joint outcomes. In the 2021 edition of the *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations*

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