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Cervical Cancer Brief #3 for Global Fund programs
February 2020

Screening for HPV and Cervical Cancer

This brief is the third part of a five-part guide for countries seeking Global Fund funding to address cervical cancer. For an explanation of the value of cervical cancer prevention among women living with and vulnerable to HIV, please see “Brief #1: Overview.”

Almost all cases of cervical cancer are caused by human papillomavirus (HPV). Persistent HPV infection can cause cervical cell abnormalities (precancers) that may lead to invasive cervical cancer if untreated.

Screening is a proven strategy for enabling secondary prevention of cervical cancer by detecting and addressing HPV and/or precancerous cervical cells. Screening also enables detection of invasive cervical cancer.

Use of Global Fund resources to improve access to high-quality screening and treatment of precancers will reduce cervical cancer morbidity and mortality, especially among women living with HIV. Cervical cancer screening should be integrated into routine treatment services for women living with HIV.

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Target population

Every woman ages 30 to 49 should receive cervical cancer screening at least once, but women living with HIV are 5-6 times more likely to develop cervical cancer, and progress more quickly from HPV infection to cervical cancer. For those reasons, the [World Health Organization](#) recommends that women and girls who have initiated sexual activity be screened upon HIV diagnosis, and re-screened every three years.

The American Society of Clinical Oncology has published [resource-stratified screening guidelines](#) to help low- and middle-income countries identify optimal screening strategies.

Screening methods

HPV testing, cytology, and visual inspection are all acceptable screening methods.

- **HPV testing** is performed on a sample of cervical or vaginal cells, collected by a health care professional or self-collected by the woman herself. HPV DNA tests are highly sensitive and detect the HPV genotypes most likely to cause cervical cancer. WHO has [pre-qualified three HPV DNA tests](#); some additional tests have approval by other stringent regulatory authorities and may also be considered. HPV testing is increasingly seen as the best initial method for screening. Costs for HPV tests may be perceived as high, from \$5 to quite a bit higher, and there is a lack of expert consensus around the approach to women who test positive for HPV but have no lab- or visually confirmed precancer.
 - Potential costs: speculum, brush, collection container, preservative solution, assay reagents, assay device and computer, lab technician, transportation of samples where needed
- **Cytology** (liquid-based or Pap test) requires laboratory analysis of collected cervical cells by highly trained technicians. Per WHO, many countries have struggled to develop an effective cytology program. The WHO recommends that countries that do not currently have an effective cytology program do not begin one.
 - Potential costs: speculum, brush, collection container, preservative solution, laboratory services including pathological analysis, transportation of samples where needed
- **Visual inspection with acetic acid (VIA) or Lugol's Iodine (VILI)** involves trained health care providers visually examining a cervix that has been brushed with vinegar or iodine to identify precancerous areas that change color. VIA/VILI alone has low sensitivity, and it takes time and experience to build provider capacity in this technique, but it provides an immediate, low-cost result. Detection rates may improve when VIA/VILI is performed in conjunction with HPV testing and/or digital imaging. It is also useful to visualize the cervix following a positive HPV test to rule out invasive cancer and determine whether the cervix is treatable by ablation.
 - **Digital imaging** tools may increase VIA/VILI's effectiveness by 1) providing better visualization, 2) enabling machine-aided assessment of digital cervical images (Automated Visual Evaluation or AVE, with promising preliminary findings in field studies), and/or 3) enabling image review by offsite experts.
 - Potential costs: cotton and vinegar, colposcope or digital imaging device (for enhanced accuracy), access to offsite experts and/or computer algorithm to interpret digital images (for enhanced accuracy).

UNITAID published an [overview of procedure and product options](#) in 2019, and WHO's [list of priority medical devices for cancer management](#) (2017) includes products for cervical cancer prevention. These lists are very helpful, but new technologies occasionally become available and it is possible that a new approved technology will not be on these lists.

WHO has a [Cervical Cancer Prevention and Control Costing Tool](#) with a screening and treatment module available upon request. In addition to the costs identified for each method above, countries should budget for training, supportive supervision, community mobilization, counseling and educational materials, health information systems that enable tracing of screen-positive women, diagnostic and treatment services, staff time per patient, and quality assurance and M&E.

Funding for updating country-level screening and treatment guidelines, if needed, may be included within a Global Fund proposal.

Further Reading

Guidance

- [Comprehensive cervical cancer control: a guide to essential practice](#). WHO (2014)
- [Improving data for decision-making: a toolkit for cervical cancer prevention and control programmes](#). WHO (2018)
- [Integrating HPV testing in cervical cancer screening program: a manual for program managers](#). Pan American Health Organization (2016)
- [Public reports of WHO prequalified IVDs](#)
- [Technology Landscape: Screening and treatment of pre-cancerous lesions for secondary prevention of cervical cancer](#). Unitaid (2019)
- [WHO list of priority medical devices for cancer management](#) (2017)

Research

- Campos NJ et al. [Cost-Effectiveness of Cervical Cancer Screening in Women Living With HIV in South Africa: A Mathematical Modeling Study](#). *J Acquir Immune Defic Syndr* 79:2 (2018)
- [Cervical cancer screening and treatment in low-resource settings: practical experience from PATH](#). PATH (2013)
- Holme et al. [Scaling up proven innovative cervical cancer screening strategies: Challenges and opportunities in implementation at the population level in low- and lower-middle-income countries](#). *Int J Gynaecol Obstet*. 138 Suppl 1:63-68. doi: 10.1002/ijgo.12185 (2017)

- Hu L et al. [An Observational Study of Deep Learning and Automated Evaluation of Cervical Images for Cancer Screening](#). JNCI J Natl Cancer Inst 11:9 (2019)
- Jeronimo J et al. [Secondary Prevention of Cervical Cancer: ASCO Resource-Stratified Clinical Practice Guideline](#). Journal of Global Oncology 3:5 (2017)
- Krivacsy S et al. [Affordable human papillomavirus screening needed to eradicate cervical cancer for all](#). The Lancet Global Health 7:12 (2019)
- Ogilvie G et al. [Optimizing secondary prevention of cervical cancer: Recent advances and future challenges](#). Int J Gynecol Obstet, 138 (2017)
- Shah SS et al. [Current Technologies and Recent Developments for Screening of HPV-Associated Cervical and Oropharyngeal Cancers](#). Cancers 8 (2016)
- Tota JE et al. [Approaches for triaging women who test positive for human papillomavirus in cervical cancer screening](#). Preventive Medicine 98 (2017)
- Wentzensen N et al. [Triage of HPV positive women in cervical cancer screening](#). J Clin Virol 76:Suppl 1 (2016)