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Cervical Cancer Brief #4 for Global Fund programs  
February 2020

## Treatment for Cervical Precancer

*This brief is the fourth 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.”*

Screening followed by treatment is a proven strategy for secondary prevention of cervical cancer and reducing cervical cancer morbidity and mortality, especially among women living with HIV. Integrating cervical cancer prevention services into routine health services, including HIV-related services, is an example of a human-centered approach to health care that reflects women’s needs and preferences.

Appropriate follow-up and treatment of a woman who screens positive for cervical precancer (or suspected cancer) varies depending on the screening test used and the available resources for triage, diagnosis, referral, and treatment. The World Health Organization (WHO) recommends a same-day “screen-and-treat” approach to prevent losing patients to follow-up, wherever possible. If appropriate care cannot be offered during the same visit as screening, a robust referral and tracking system is essential.

In the case of a positive HPV test, the cervix should be examined to identify any visible lesion, and to determine whether the cervix can be safely ablated. Visual examination of the cervix can be done using VIA/VILI, but is more effective with digital imaging tools (see Brief #3 on screening). [WHO acknowledges](#) that providers may either 1) treat the cervix following any positive HPV test, even absent a visible lesion, or 2) wait one year and rescreen after a positive HPV test and a negative VIA test. The main risks of waiting are that a patient’s lesion could progress to cancer

TogetHER thanks the following partners for their assistance on this series of briefs:

- Basic Health International (BHI)
- FHI360
- Global Good
- Jhpiego
- PATH
- Pathfinder International
- Population Services International (PSI)
- Project Concern International (PCI)

before it is visible, and patient tracking and follow-up may be limited. Reflecting these risks, [WHO's latest guidance](#) (2019) recommends immediate treatment for all HPV-positive cases.

## Treatment Methods

WHO has published [recommendations](#) (2013) to guide decisions about which method of treatment to provide, including for women of HIV-positive status or unknown HIV status in areas with high endemic HIV infection. Additionally, the American Society of Clinical Oncology has published [resource-stratified screening guidelines](#) to help low- and middle-income countries identify optimal strategies for treating screen-positive cases.

After any treatment, [WHO recommends](#) that women receive post-treatment follow-up at one year to ensure effectiveness of the treatment.

Ablative treatments destroy precancerous cervical tissue with heat or cold.

- **Thermal ablation** uses a probe heated via an electrical outlet or battery, and applied by a trained health professional to destroy cervical tissue. It has gained popularity because, compared to cryotherapy, it costs less per treatment performed, presents fewer logistical challenges, and it takes less time to perform (~one minute compared to ~15 minutes). A [2012 meta-analysis](#) indicated 85%–92% cure rates for advanced-stage precancerous lesions. WHO issued [guidelines on thermal ablation](#) in 2019.
  - Examples of required resources: machine (approximately US\$1,300–\$1,500), plus some thermal ablation devices require purchase of component parts separately such as probes, carrying case, and extra batteries.
- **Cryotherapy** uses a probe that is chilled to a freezing temperature using nitrous oxide or carbon dioxide gas. The cold probe is applied by a trained health professional to freeze and destroy cervical tissue. A [2014 meta-analysis](#) indicated 85%–95% cure rates for advanced-stage precancerous lesions.
  - Examples of required resources: cryotherapy unit/device with trigger, etc. (US\$500–\$3,500 per Cremer et al), gas canister (per Castle et al, a 60-pound tank with enough nitrous oxide to treat up to 40 patients with a standard device can cost US\$200–\$400; carbon dioxide tanks tend to be cheaper). While affording the gas is a challenge, many countries have also struggled with obtaining and transporting the gas tanks.

In addition to the necessary resources identified above, programs using either thermal ablation or cryotherapy should budget for speculums, cleaning and high-level disinfection solutions, and supplies and tools to visualize the cervix.

Some lesions are not eligible for ablative treatment and must be excised. Excisional treatments remove all or part of the cervix, and produce tissue specimens that can be

biopsied for diagnosis where laboratory services exist. Excisions are performed in surgical or semi-surgical settings on lesions that are too large for ablation, or extend into the endocervical canal or into the vagina.

**Large loop excision of the transformation zone** (LLETZ; also known as loop electrosurgical excision procedure or LEEP) removes tissue with a thin, electrically heated wire. Patients receive local anesthesia.

- Examples of required resources: LLETZ unit; electrocautery system with electrodes, grounding pad, loops, and other accessories; analgesia medication; needles/syringes for analgesia application; gauze or cotton swabs; acetic acid and/or Lugol's solution, Monsel's solution to control bleeding. There are new devices on the market for about \$1800 with all parts; older models may cost considerably more.

WHO has a [2012 publication](#) to assist with the procurement, management and effective use of cryosurgical equipment. UNITAID published an [overview of procedure and product options](#) in 2019 that includes precancer treatment methods, 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 are sometimes added 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. PATH offers a [treatment module](#) as part of its Cervical Precancer Treatment and Planning Tool that may help countries budget.

In addition to the required resources identified for each method above, countries should budget for training, supportive supervision, community mobilization, counseling and educational materials (including counseling to avoid sexual intercourse, if possible, after treatment until the cervix is healed, to avoid increased risk of HIV transmission), health information systems that enable tracing of screen-positive women, diagnostic and treatment services, staff time per patient, and quality assurance (QA) and monitoring and evaluation (M&E) programs.

## Cervical Cancer

Invariably, some women who are screened will present with suspected cancer and will need referrals for advanced treatments, which could include surgery, chemotherapy, and/or radiation. Such treatments cannot be covered with Global Fund resources, presenting a challenge for countries with limited means to treat women with cancer. Screening and precancer treatment programs prevent cancer, but comprehensive cervical cancer programs incorporate treatment for women with cancer, including pain management and palliative care, for which there is a large unmet need in many countries. Country programs are encouraged to increase access to comprehensive cancer care.

## Further Reading

### Guidance

- [Comprehensive cervical cancer control: a guide to essential practice](#). WHO (2014)
- [Cryosurgical equipment for the treatment of precancerous cervical lesions and prevention of cervical cancer](#). WHO (2012)
- [Technology Landscape: Screening and treatment of pre-cancerous lesions for secondary prevention of cervical cancer](#). Unitaid (2019)
- [WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention](#). (2013)
- [WHO guidelines for the use of thermal ablation for cervical pre-cancer lesions](#) (2019)
- [WHO guidelines for treatment of cervical intraepithelial neoplasia 2–3 and adenocarcinoma in situ: cryotherapy, large loop excision of the transformation zone, and cold knife conization](#) (2014)
- [WHO list of priority medical devices for cancer management](#) (2017)

### Research

- Castle, Philip E. et al. [Treatment of cervical intraepithelial lesions](#). Int j Gynecol Obstet 138, Suppl. 1 (2017)
- Cremer, Miriam L. et al. [Ablative Therapies for Cervical Intraepithelial Neoplasia in Low-Resource Settings: Findings and Key Questions](#). Journal of Global Oncology 3 (2018)
- Jeronimo J et al. [Secondary Prevention of Cervical Cancer: ASCO Resource-Stratified Clinical Practice Guideline](#). Journal of Global Oncology 3:5 (2017)