WHITE PAPER

Deploying thermal ablation devices to expand access to treatment for cervical precancer: Experience from a multi-country Unitaid-supported project

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Date: May 2022

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In May 2018, in response to the World Health Organization (WHO) call for the elimination of cervical cancer, Unitaid announced a US$60 million investment with the clear goal of making life-changing improvements in the screening and treatment of women with cervical cancer in low- and middle-income countries (LMICs). In July 2019, the Clinton Health Access Initiative (CHAI), with funding from Unitaid, launched a multi-country project to increase access to screening and treatment for cervical precancer. This paper documents the project's experience with rolling out thermal ablation (TA) devices with accompanying training and support in partnership with the governments of India, Kenya, Malawi, Nigeria, Rwanda, Senegal, Uganda, Zambia, and Zimbabwe to increase access to precancer treatment. Unitaid is also funding related interventions under the SUCCESS[2] project, a consortium led by Expertise France and delivered in partnership with Jhpiego and Union for International Cancer Control (UICC), which has introduced thermal ablation in Guatemala, the Philippines, Burkina Faso, and Ivory Coast.

Highlights

- TA is a critical tool in the global effort to screen and treat women for cervical precancer and has potential to substantially expand treatment access beyond the current method of cryotherapy.
- TA devices are easy to use and maintain and can be run on battery power, allowing them to be used at primary health facilities and in outreach settings.
- Following training, these devices can be operated by a broad range of health care workers, expanding the pool of staff who can safely offer treatment.
- TA is less expensive than cryotherapy, allowing countries to affordably expand treatment access.
- The technology enables more women to access treatment following a positive screening result, saving lives, and helping countries to reach the goal of cervical cancer elimination.
- All these factors above together reduce barriers to access for clients, making treatment possible for women across LMICs and in hard-to-reach, rural areas.

Background: Scaling up screening and treatment for cervical cancer elimination

Although cervical cancer is a preventable and curable disease, it continues to be a leading cause of cancer-related deaths for women globally. Women in LMICs are more likely to experience cervical cancer due to a lack of access to affordable and high-quality services for primary prevention, screening, and treatment. Of the 300,000 deaths from cervical cancer reported in 2018, almost 90 percent occurred in LMICs.[3] Women living with HIV are particularly at risk of illness and death due to cervical cancer.

In August 2020, the WHO launched its first-ever Global Strategy for Cervical Cancer Elimination to combat this public health challenge. Elimination of cervical cancer will be achieved when all countries reach and maintain an incidence rate of four per 100,000 women. As of 2018, incidence rates ranged from 10 to 75 per 100,000 women in LMICs.[4] Figure 1 highlights the three key pillars (vaccination, screening, and treatment) to help countries achieve elimination along with the targets that must be met by 2030.

Figure 1: *WHO Global Strategy for Cervical Cancer Elimination 90-70-90 targets that must be met by 2030 for countries to be on the path to cervical cancer elimination.*

Access to cryotherapy, which has been the standard of care for treatment of precancerous cervical lesions, has been limited in LMICs due to challenges with costs and logistics associated with the technology. Cryotherapy devices operate using nitrous oxide or high-quality carbon dioxide which can be difficult to procure in LMICs. Transporting the heavy tanks in uncertain conditions can be arduous.[5] Cryotherapy machines can also be expensive, around $2,000 plus the cost of the gas required to operate the machine (which can range from $13 - $38 per treatment). This does not include the cost to transport the gas (Maza et al., 2017).

In 2019, WHO endorsed the use of TA devices for the treatment of precancerous cervical lesions eligible for ablation, issuing the *WHO Guidelines for the use of thermal ablation for cervical precancer lesions,*[6] and changing the treatment landscape by expanding the secondary prevention toolkit for cervical cancer. The WHO recommendation takes into consideration that TA devices:

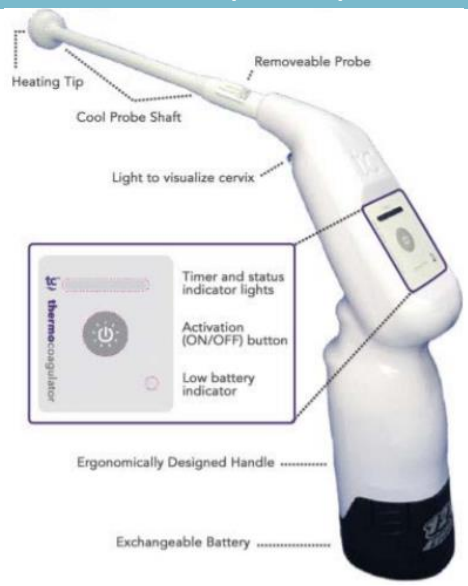
- show equivalent clinical outcomes to cryotherapy ablative treatment7, and
- can help LMICs overcome current supply chain and access barriers faced with cryotherapy.

TA, which is also called cold coagulation or thermocoagulation, is an ablative treatment for cervical intraepithelial neoplasia (CIN). TA has been around since the 1960s and provides treatment for precancerous lesions more efficiently and economically than cryotherapy without compromising the effectiveness in terms treatment outcomes.[8] Examples of quality-assured, portable TA devices include Liger Medical LLC (Liger) and Wisap Medical Technologies GmbH (Wisap); see Table 1. TA devices employ a reusable metallic probe that is electrically heated to 100˚C to treat the precancerous lesion for 20 to 40 seconds and can be reapplied quickly for additional areas of treatment as necessary. The equipment is portable, lightweight, simple to operate, and can be used by a variety of health care professionals including trained physicians or nurses, midwives, or other health care workers. The cost for these devices can range from US$925 to US$995 per handheld unit under access pricing agreed to through the Unitaid-CHAI project. Market prices are significantly higher; interested buyers are encouraged to check the latest access pricing information available on the WHO website.[9]

Unlike cryotherapy, TA devices can be battery operated and do not require the use of refrigerant gas— a consumable that comes in containers separate to the device. These various benefits of TA reduce the logistical barriers, supply chain challenges, and operating costs of secondary prevention for LMICs as compared with cryotherapy while providing equivalent clinical outcomes.[10,11] Despite

being a relatively newer secondary prevention option for cervical cancer, TA devices will be critical for countries to achieve their global strategy elimination targets.

Table 1: *Liger and Wisap Thermal Ablation Devices*

Liger HTU-110 (FDA / CE)	Wisap C3 Thermo-Coagulator (CE)
	

Source: Communication from manufacturers and manufacturer websites (www.ligermedical.com and www.wisap.de/en)

CHAI, with funding from Unitaid, has been working with partner governments to deploy high-quality, low-cost precancer screening and treatment technologies that can enable broad scale-up of secondary prevention. One of the key components of the partnership is the introduction of TA devices alongside supportive training and mentoring for health workers. The WHO's cervical cancer elimination strategy renewed focus on the wide gap in prevention, treatment, and deaths from cervical cancer between high-income and low- and middle-income countries. The initiative also showed that scaling up cervical cancer services and programs in LMICs can have a significant impact on reducing incidence and deaths. Since there is currently limited experience with TA device use in LMICs, the experience gained through this project will provide insight about its introduction and use so that more treatment options can be made available for women with cervical precancer.

Global pricing agreements supported deployment of TA devices in partner countries

In May 2019, CHAI and Unitaid announced a partnership to help eliminate cervical cancer by investing in the use of innovative secondary prevention screening and portable treatment tools. This three and a half-year project kicked off in July 2019 with the goal of generating evidence about the use of effective delivery models with available tools such as HPV tests, visual inspection with acetic acid (VIA), and portable treatment devices to lay the groundwork for scale-up. The countries where the project is being implemented intentionally represent a diverse range of settings so that the lessons learned may be applied across LMICs.

CHAI worked closely with government officials in the partner countries to understand the cervical cancer treatment landscape and create country-specific TA deployment plans. These implementation plans highlighted the following areas for each country:

- Goals and key program indicators.
- Budget and TA device selection options.
- Team members and stakeholders.
- Roll out plans and locations.
- Treatment guidelines, clinical approaches, and training requirements.
- Mentorship and Quality Improvement/Quality Assurance
- Program evaluation processes and data to be captured.

To help expand the use of portable TA devices, CHAI and Unitaid negotiated global price agreements with Liger Medical LLC (Liger) and Wisap Medical Technologies GmbH (Wisap). These two global suppliers of quality-assured, portable TA devices were identified from a detailed product analysis conducted by CHAI. Liger and Wisap are now respectively offering prices at least 38 percent (US$925/unit) and 54 percent (Euro 904/unit) lower, respectively, than the current market prices.

The access pricing is available to public sector buyers such as ministries of health and parastatal procurement agencies of LMICs specified in the pricing agreements and international donors such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria, President's Emergency Plan for AIDS Relief (PEPFAR), United States Agency for International Development (USAID) and United Nations organizations. TA devices from these suppliers are now also included in the UNICEF-SD catalogue and interested buyers have the flexibility of procuring them directly through the suppliers or through UNICEF-SD.

Expansion of clinical practice to include TA

Operating at the invitation of partner governments within their health sectors, CHAI helps to promote clinical skill attainment through public health system training and mentoring programs. Introduction of a new device and a new way to perform ablation of precancerous cervical lesions requires four basic implementation initiatives: 1) adoption of TA into clinical practice guidelines; 2) adaptation of training materials to include TA; 3) execution of trainings that include both didactics and clinical practicum for strategically selected health workers; and 4) ongoing clinical mentoring tailored to individual and continuous quality improvement in secondary prevention of cervical cancer. As a complementary initiative, countries strengthened their existing health information systems to enable collection of quality data on screening and treatment, track adverse events, and ensure screen-positive women were followed through the continuum of care to receive appropriate treatment and/or referral services.

Post-service training for health workers, even for a straightforward procedure such as TA, can become an operational and budgetary burden if the introduction and scale-up of the skill set is not optimized. CHAI and partner governments utilize a cascade model for trainings as one facet of a practical approach to make clinical skills building more efficient. In the cascade model, a group of Master Trainers that represent different regions of the country are given in-depth training and clinical practice and then become responsible for training and mentoring groups of health workers from their regions. Further cost effectiveness of scale-up of these new clinical skills can be achieved when the didactic portion of the training is delivered remotely, an approach that gained attention as the COVID-19 pandemic limited mobility and ability to gather. When the didactic

portion of training is delivered through virtual platforms, knowledge acquisition is verified through unit tests or other objective means before trainees can proceed with in-person training at the clinical practicum.

In secondary prevention of cervical cancer, as in other programs, CHAI, and partners champion continuous quality improvement through routine clinical mentorship. Because mentorship requires structured assessment of clinical skill and personalized attention, it plays a critical role in quality of care and building effective networks of care. Master Trainers who then serve as Clinical Mentors are often also the regional consultants for more complicated clinical cases. As such, clinical mentorship not only fosters communication among health workers and better-quality services, but often also buttresses the referral network for cervical cancer prevention and treatment.

Preparation for device management

Proper training, care, and maintenance is important to ensure devices remain functional in the field for as long as possible. Based on our experience with the initial roll out, the following elements have the greatest impact on extending the lifespan of the devices and ensuring functionality:

- Ensure sites have the proper cleaning and disinfecting solutions as the coatings on the probes require special care. Without proper solutions and following the appropriate procedures, coatings can be damaged which compromise device lifespan and functionality.
- Facilities should have access to extra batteries and a voltmeter in case a battery isn't charged or malfunctions at the time of procedure. The voltmeter can be used to troubleshoot when batteries aren't working to ensure they are holding a charge.
- Adequate training is very important to ensure the success of the procedure and longevity of the devices. Procedure preparation, device cleaning/disinfection, and processes for filing complaints are important steps to cover during the training.
    - It is valuable to have multiple types of training materials such as reference guides, instructions for use, videos, simulations, checklists, and/or live sessions with the suppliers.
    - It is also beneficial to have continued technical training for individuals who would be able to troubleshoot in case of device malfunction, such as a local biomedical engineer. These individuals would have more in-depth training on the devices and liaise with the suppliers as needed for support.
    - Additional training on initiating replacements and a centralized complaint handling team would facilitate quick device replacements, minimizing interruption of services.

Deployment of TA devices within screening and treatment programs

Planning for the roll out of TA devices across partner countries began in the second half of 2019, with roll out commencing in the first quarter of 2020 and continuing throughout 2021. In order to deploy TA devices, most partner countries had to work through in-country protocols to gain approval for the use of the new treatment and adapt treatment guidelines and information systems for their countries as needed. In addition to being pioneers in introducing TA in their countries,

partner countries showed resilience and perseverance by adapting roll out plans to accommodate the unexpected challenges of the COVID-19 pandemic.

While implementation is still underway, the project has gained hands-on experience with introduction and use of the TA devices in the field. This may be beneficial for other programs considering a similar approach. Highlights shared in the following sections have been generalized from the experiences of our partners in India, Kenya, Malawi, Nigeria, Rwanda, Senegal, Uganda, Zambia, and Zimbabwe. While most countries shared similar themes and comments, not all the experiences were common to every country. Comparisons to cryotherapy are shared as relevant.

Benefits of TA

The experience using TA devices in our partner countries has been overwhelmingly positive. The project has found that TA's benefits include: 1) ease of use; 2) ease of clinical deployment; 3) improved access; 4) improved health equity; 5) ease of procurement; and 6) cost.

Ease of use: Across countries, TA devices are considered user-friendly, particularly because they are portable and battery-operated. Specific benefits include:

- Easy operation with an automated procedure timer and visual and audible indicators which eliminate the need for a watch or clock.
- Lightweight equipment that is easy to carry and use in static facilities as well as in field clinics or mobile settings. In contrast, cryotherapy is mostly limited to static facilities since gas cylinders make transport challenging and additional infrastructure may be required.
- Battery operation helps address challenges with poor or no power supply.

Ease of clinical roll-out: TA is straightforward to roll out to new sites because it is easy to use and maintain, requires a simple training, and allows for a broader range of health care workers to administer treatment compared to cryotherapy.

Improved access: Across countries, TA improves access because it is an immediate, fast, safe, and effective treatment option for precancerous lesions, reducing loss to follow up and increasing treatment coverage. TA allows for decentralization of precancerous cervical lesion treatment to more healthcare facilities (including Primary Health Centers and mobile clinics) due to its ease of use, portability, and minimal infrastructure needs. For clients who are hesitant to visit a central health facility for reasons including distance, time, and cost of transport, mobile clinics and outreach become a practical solution. Increased portability allows government partners to plan for screening and treatment sessions in camp settings and leverage community level health service platforms, thereby expanding access.

Improved health equity: The introduction of the TA program has improved equitable access to treatment across country settings. Roll-out of TA has delivered services to more people from hard-to-reach and rural areas. Women now have access to additional facilities (i.e., primary and secondary level facilities) as well as mobile clinics which offer TA, whereas before they could only receive cryotherapy at a limited number of more centralized facilities that had the necessary infrastructure.

Ease of Procurement: Partners on the ground find that TA is easier to procure than cryotherapy. Some of the key reasons include:

- TA procurement requires coordination only with the dedicated suppliers, whereas, for cryotherapy, logistics must be managed with device manufacturers and different suppliers to secure gas cylinders and regular gas supply.
- The price of TA is standardized, whereas prices for cryotherapy, specifically gas cylinders, fluctuate and are affected by changes in local currency exchange rates.
- The TA supply chain is dependable, whereas cryotherapy refrigerant gas regularly faces supply chain issues.

Cost

Partner countries expressed that TA can be rolled out for a fraction of the cost in comparison to cryotherapy. TA is cheaper than cryotherapy in terms of initial cost, does not require the ongoing purchase of gas cylinders, and is a shorter procedure than cryotherapy. Many countries highlighted that the procedure time for TA is 10 times shorter than for cryotherapy (under one minute for TA compared to over 10 minutes for cryotherapy). Therefore, the procedure cost is lower and utilizes less of health workers' valuable time.

Challenges with TA

CHAI and our in-country partners have experienced limited challenges with TA. Broadly speaking, the largest challenge moving forward is identifying resources to support scale-up of screening and treatment programs, including finding recurrent budget to procure additional devices and accessories.

Countries have not experienced challenges with adoption hesitancy by clinics or health workers. From the patient perspective, TA has generally been widely accepted. Patients have reported that the procedure is surprisingly quick and painless. Some patients express concern about the need for abstinence following treatment while the cervix heals, but this concern is common to TA and cryotherapy treatment and speaks to the need for adequate counseling and engagement of women's partners. As TA scales up, it will be important to create community awareness and mobilize women to participate in screening and subsequent treatment. In many partner countries, CHAI is actively working on demand generation activities to leverage the influence of community health workers, local leaders, and family members/partners.

For instance, in India greater in-country distributor presence was identified as a key opportunity to ensure that technical and maintenance support would be available in-country as needed. More broadly, through this project, CHAI and Unitaid are aiming to strengthen the supply of TA devices by working with both manufacturers and countries to ensure the TA market is accessible as well as sustainable.

TA is a key tool to help countries achieve cervical cancer elimination

With their endorsement of TA, the WHO provided a critical additional tool to help countries achieve their cervical cancer elimination targets. The experience from TA roll-out in this Unitaid-funded project supports the use of TA and highlights the many benefits and limited challenges experienced

with this new treatment technology. Field teams in partner countries have highlighted numerous advantages of TA over cryotherapy. Alongside being easy to use and maintain, the devices can be operated by a larger group of health care workers (with proper training) making treatment more accessible. Furthermore, TA is a fast, safe, and effective treatment alternative for precancerous lesions which can in turn result in higher coverage rates. These factors can also reduce logistical and travel related barriers for patients making treatment possible for many in hard-to-reach, rural areas of LMICs. Making treatment available at the same sites that conduct screening greatly reduces the risk that women are lost to follow-up during referral to a higher-level health facility.

Although our partner countries indicated TA is more economical than cryotherapy, recurrent costs associated with procuring additional devices and spare parts is seen as a barrier to scale-up. Further efforts to mobilize resources to support countries' screening and treatment scale-up plans will be key to expanding access to this lifesaving technology. TA devices can enable more women to have access to treatment, improving health outcomes and enabling more countries to ultimately achieve elimination of cervical cancer.

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