Removing global barriers to cervical cancer prevention and moving towards elimination

Karla Alfaro[1]✉, *Mauricio Maza*[1], *Miriam Cremer*[2,3], *Rachel Masch*[2] *and Montserrat Soler*[2,3]

Cervical cancer is a disease of inequality. The majority of cervical cancer cases can be prevented through vaccination against the human papillomavirus (HPV) (primary prevention) and screening and early treatment of precancerous lesions caused by HPV infections (secondary prevention), and it can be controlled if treated in early stages (tertiary prevention). However, significant gaps in access to care have shifted the burden of disease to resource-poor countries in Africa, Asia and Latin America. The recent World Health Organization's Call to Action to eliminate cervical cancer is a unique opportunity to galvanize change and remove barriers to prevention and care.

In 2018, over 570,000 women around the world were diagnosed with cervical cancer[1]. Of the 311,365 women who died from the disease[1], 90% lived in low- and middle-income countries (LMICs)[1,2]. In November 2020, the World Health Organization (WHO) launched a strategy to reduce the current worldwide incidence of 13.3 per 100,000 (age-adjusted)[2] to 4 per 100,000 women by 2030 as the first step towards elimination of cervical cancer[3]. As cervical cancer is caused by persistent infections of high-risk strains of the human papillomavirus (HPV), to accomplish this it will be necessary to 1) vaccinate 90% of girls by the age of 15 against HPV infection, 2) screen 70% of women with a high-performance test by the age of 35 and again at age 45, and 3) treat 90% of women identified with cervical pre-cancer and invasive cancer[3]. This call to action has created unprecedented momentum to make the elimination of a cancer within our lifetimes a real possibility. However, there are significant barriers that contribute to gaps in care for underserved populations in both high-income countries (HICs) and LMICs. In addition to the need to increase HPV vaccination coverage (primary prevention), secondary prevention (screening and early treatment of precancerous lesions) will remain an essential tool for non-vaccinated women. If the global community is to succeed in achieving elimination goals, the challenges in secondary prevention we discuss below must also be addressed.

Reliance on ineffective screening methods

Most cervical cancer prevention programmes in LMICs rely on cytology (pap smears) or visual inspection with acetic acid (VIA), but these strategies have significant limitations[4]. Although cytology programmes have been highly successful in HICs, lack of availability and limited access to health facilities and providers have blunted their impact in other settings. In LMICs, pathology services needed for a successful cytology programme are often limited, overburdened and of low quality, and the under-diagnosis of high-grade cervical precancer is widespread. In addition, cytology requires multiple visits to obtain test results and follow-up procedures (such as colposcopy and biopsy). For many women, wait times of several months are common owing to limited colposcopy services, and this results in high loss to follow-up.

While VIA is an appropriate approach to screen for cervical cancer in some settings, there are challenges to maintain quality and accuracy of screening, and to scale services to reach adequate coverage levels[5]. VIA programmes have not made the impact that advocates had hoped for in reducing cervical disease burden in the most affected areas.

Lack of viable screening alternatives

Screening tests that detect the presence of high-risk HPV afford the opportunity to identify nearly all cervical precancers, which can then be easily treated. Furthermore, there is good evidence that HPV has excellent negative predictive value, meaning that women who have a negative HPV test will be highly unlikely to develop cervical cancer in the next 10 years[6]. For over a decade, different companies have developed highly sensitive HPV tests, yet the price point is still too high for use in the national programmes of many countries. In addition to affordability, a test that is feasible for use in LMICs must have high sensitivity in self-collected samples, relatively simple processing and rapid result delivery. Currently, only a few HPV tests in the market are pre-qualified

[1]*Basic Health International, San Salvador, El Salvador.*

[2]*Basic Health International, Pittsburgh, PA, USA.*

[3]*Ob/Gyn and Women's Health Institute, Cleveland Clinic Lerner College of Medicine, Cleveland, OH, USA.*

✉*e-mail: kalfaro@basichealth.org*

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by the WHO, and not all have approval or adequate sensitivity for self-sampling. More alternatives are urgently needed.

While many LMICs do not have adequate laboratory infrastructure, the COVID-19 pandemic has resulted in unprecedented investments in molecular diagnostic testing. This can be leveraged to expand HPV testing into existing public health systems. Researchers and industry partners have an important role to play in meeting this demand, and funding agencies should encourage partnerships that promote innovative collaborations.

Need for effective implementation strategies

In addition to new screening technologies, strategies that increase accessibility to screening and training must be an integral part of cervical cancer control programmes that are effective and context appropriate. Patient awareness and educational programmes that target screening refusal, treatment non-adherence and vaccine hesitancy should be designed and delivered using evidence-based implementation approaches. Education and training of health-care providers are also key components to improving in-country capacity. This may include adding laboratory personnel or conducting training and refresher courses on screening techniques. For example, appropriate training of general practitioners and mid-level providers in visual assessment is a very cost-effective strategy.

Care delivery innovations can increase cervical cancer prevention coverage, but more data are needed on systematic implementation efforts in LMICs. For example, self-collection of samples for HPV testing can avoid the need for specialized providers and overcome barriers associated with gynecologic examinations, but may encounter other provider and patient acceptability issues. Recently, portable thermal ablation treatments for precancerous lesions have been endorsed by the WHO to treat most pre-cancer with lower implementation and logistical costs than cryotherapy, which remains the most widespread treatment in LMICs.[7] Channeling these innovations to create true point-of-care cervical cancer prevention strategies could significantly increase access for women in remote, rural and other hard-to-reach locations.

A roadmap to cervical cancer prevention in LMICs

In El Salvador, the national cervical cancer prevention programme was based on screening through cytology and colposcopy for several decades. Despite the presence of a formal screening programme, cervical cancer incidence in El Salvador was one of the highest in Latin America and, by 2009, an estimated 55.1% of women with abnormal cytology results were lost to follow up[8].

In 2012, we introduced a pilot programme comparing low-cost HPV testing to cytology in one of the five regions of the country. Most women received HPV test results within one month, and the majority of eligible women positive for HPV were treated with cryotherapy immediately after result delivery, while ineligible women were referred to colposcopy. The HPV testing programme decreased the number of steps required for treatment, and follow-up increased to 89% compared to 44.4% in the cytology screening group[9]. The model was scaled-up and has now been adopted as part of El Salvador's national programme[10]. While the challenges of current HPV testing have resulted in limited uptake in LMICs, this project has demonstrated that it is possible to use this method on a country-wide level, and we believe that this can serve as a blueprint that can be adapted and used in other LMICs.

Cervical cancer elimination depends on coordinated efforts between governments, civil society organizations, industry, researchers and international agencies. It is critical to ensure that the effective tools we have for immunization, screening and treatment can be made universally available. The call to action is an opportunity for cervical cancer elimination; it is our generation's responsibility to ensure that no woman dies of this preventable disease.

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Competing interests

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