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Diagnosis for all



FIND WOMEN'S
HEALTH PROGRAMME

HPV SCREENING AND CERVICAL CANCER

Cervical cancer is a major global health challenge, disproportionately affecting women in low-income countries and poor women within countries – a disparity all the more unacceptable as it is a preventable disease.

Cervical cancer is a leading cause of cancer-related mortality among women worldwide, **responsible for 342 000 deaths in 2020** [1]. **The burden of cervical cancer is highly inequitable**, disproportionately affecting women living in poverty, those living in lower-income countries, and women living with HIV [1, 3]. The highest incidence of cervical cancer and associated mortality is found in Africa, with mortality rates in some countries up to 18 times higher than in other regions [3, 4]. Almost all cases of cervical cancer are associated with persistent, high-risk human papillomavirus (HPV) infection, a highly prevalent viral disease spread by sexual contact [5]. Globally, one woman dies every two minutes from cervical cancer [6].

It is important to note, however, **that cervical cancer is one of the most preventable cancers**, and early diagnosis of cases via HPV screening has been proven to be a highly cost-effective intervention that saves women's lives [19]. The World Health Organization (WHO) asserts that most cases of cervical cancer can be prevented via a three-pillar approach: i) high coverage of HPV vaccination, ii) intensified screening, with prompt treatment of any pre-cancerous lesions detected, with a minimum of two life-time screens between the ages of 30 and 49 years, and iii) prompt, high-quality treatment of and palliative care for any cancers identified [5]. In 2020, in light of the growing burden and inequity of cervical cancer, WHO launched a global strategy to eliminate this disease as a public health problem [7]. WHO estimates that reaching the 90-70-90 targets (shown in Figure 1) by 2030, in 78 low- and middle-income countries (LMICs), has the potential to save 15 million lives by 2030 and would prevent more than 62 million deaths from cervical cancer by 2120.

WHO TARGETS TO ELIMINATE CERVICAL CANCER BY 2030

90%

OF GIRLS **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** (90% OF WOMEN WITH PRECANCER TREATED, AND 90% OF WOMEN WITH INVASIVE CANCER MANAGED)



Figure 1. The WHO global strategy to eliminate cervical cancer proposes the 90-70-90 targets, which countries have committed to meet by 2030 to be on the path towards cervical cancer elimination.

The measures that we know work are contributing to dramatic decreases in the incidence of cervical cancer in high-income countries, but these measures are currently not reaching the regions with the highest burden of disease and thus the greatest need for these services.

Pillar 2 of the WHO strategy calls for at least 70% of women to be screened for cervical cancer using a high-performance HPV test by the time they are 35 years old and again by age 45 [6]. The current generation of adult women have already been exposed to high-risk HPV strains (HPV 16 and 18); therefore, prophylactic HPV vaccination will not benefit them. Despite this strong imperative for screening, just 44% of women in LMICs overall have ever been screened for cervical cancer, compared with screening rates of more than 60% in high-income countries [1]. It is for this reason that, while approaches are being established for universal vaccination of the younger generation of vulnerable girls, the need for improved screening and the introduction of high-performance diagnostic tools is critical now and will remain critical until high-burden countries have routine vaccination, with high coverage levels [8], and these populations reach the age for screening. In addition, an achievable impact, i.e. a 30% reduction in mortality by 2030, is specifically driven by screening outcomes: lives will be saved by combining intensive screening and HPV vaccination prevention programmes, enabling countries with the highest burden of cervical cancer to feasibly achieve the elimination threshold [19].

Two screening-specific factors that will enable the acceleration towards elimination should also not be underestimated:

HPV screening not only increases access to prevention services but also increases the impact of early detection at a population level. Cervical cancer, which is detected and diagnosed at stage I, II or IIIa, can be cured by surgery or surgery plus radiation and systemic therapies, whereas with advanced cases of the disease (most stage IIIb and all stage IV cases) quality of life and palliative care are the focus.

The increasing numbers of women who are diagnosed with precancer or invasive cancer but who then receive optimal treatment and go on to experience a high quality of life as cancer survivors will, over time, shift the mindset in communities, from attitudes that include a fear of the disease and death, to attitudes favourable to active participation in prevention services.

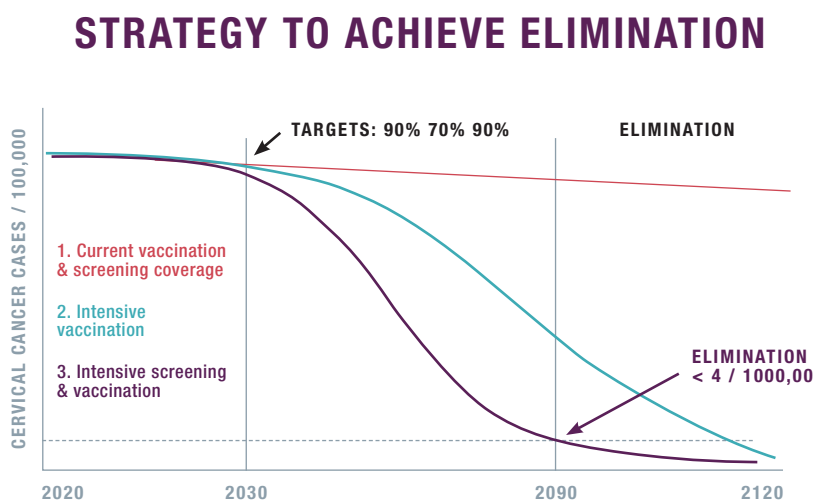


Figure 2. The pathway to elimination in 78 low- and middle-income countries harnessing the WHO global strategy to eliminate cervical cancer



The case for urgent action to reduce the burden of cervical cancer in LMICs, including high-performance HPV screening, has been made, and success here will be the driver for building momentum towards elimination in the coming decades.

Economic, infrastructural and cultural barriers limit access to services relating to all three pillars of the WHO global strategy, and these barriers have been exacerbated by the COVID-19 pandemic. The pandemic has had a major impact on many health services and a disproportionate toll on women in particular (including increased domestic violence towards women and diminished access to time-sensitive healthcare needs, including sexual and reproductive health). The pandemic has therefore also increased the disparities seen in cervical cancer prevention and screening in particular [9, 16]. In contrast, self-collection tools have demonstrated their worth during the COVID-19 pandemic. For example, the use of a stool test for colorectal cancer screening and kits for self-collection of samples for HPV testing for cervical cancer screening have permitted the continuation of critical early detection services for cancer despite disruptive pandemic control measures [20].

A silver lining of the pandemic is therefore an increase in the readiness of policymakers and service providers to accelerate the uptake of these more convenient tools and leapfrog older methodologies. **High-performance HPV tests, coupled with self-collection, are amenable to community-based care models** that have continued despite pandemic measures [20]. This is supported by a body of evidence showing that self-collection of samples for HPV testing is equally effective in terms of the quality of the sampling compared with healthcare provider collection of samples.

Furthermore, studies of women's preferences have shown that self-collection is both acceptable and indeed preferable to pelvic examinations conducted by a healthcare provider [13, 17]. This additional choice for women adds flexibility to the design of cervical cancer screening programmes, increasing health service resilience and permitting, where necessary, targeted approaches based on risk, in line with the WHO guidance for screening, which differentiates for example the screening interval for the general population versus women living with HIV [17].

In addition, in response to the pandemic, many LMICs have invested in COVID-19 testing platforms, which also support high-performance HPV testing.

Both of these factors have created a new window of opportunity to mobilize support for the rapid uptake of HPV-based screening for cervical cancer. Importantly, 'building back better' through a structured planning process for elimination services, with early and broad stakeholder engagement, including views from vulnerable and under-screened communities, will reveal inequities in access and ensure that the resulting implementation of these stakeholders' shared decisions is appropriately aligned with the culture, values and resource realities of each setting [21].

This opportunity to shape cancer health literacy in the community and drive the ambition of elimination through activities focused on the screening pillar of the WHO global strategy is timely and conducive to leveraging FIND's strategy and expertise.



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AFYA YA




FIND'S STRATEGY TO
**INCREASE ACCESS TO HPV
SCREENING AND MEET THE
WORLD HEALTH ORGANIZATION'S
ELIMINATION GOALS**



Cervical cancer is a priority disease area for FIND, the global alliance for diagnostics, as part of our newly consolidated Women's Health programme. FIND connects countries, funders, decision-makers, healthcare providers and diagnostic developers to spur innovation in diagnostics and make testing an integral part of sustainable, resilient health systems. We are committed to transforming diagnostic challenges into simple and holistic solutions for diseases of poverty, working to address the lack of diagnostics for major global health challenges, including cervical cancer. We have considerable experience in implementing programmes that expand access to diagnostics, build capacity within health systems and provide education and awareness.

“Scientists and researchers have developed novel tools for both prevention and treatment of cervical cancer. Furthermore, high-grade precancerous and early-stage cervical cancer can be treated effectively. Consequently, cervical cancer should be considered the most preventable cancer in our lifetime.” [2]



We are experiencing a paradigm shift in screening and have an expanded landscape of testing technologies, which calls for a consolidated approach.

For half a century, screening for cervical cancer has predominantly involved cytology-based testing (the ‘pap smear’) or, in the absence of high-quality cytology, visual inspection with acetic acid (VIA). Now, however, HPV testing as a means of cervical cancer screening has been thoroughly researched, proven to be cost-effective for health systems [10], and shown to be highly effective [11]. In addition, methods of self-collection of samples for HPV testing have proven to be effective both in terms of performance and acceptability. This current situation, in essence a disruptor of the long-held ‘gold standard’, means that the landscape of screening for cervical cancer, including healthcare service delivery, public health actors, vertical disease programmes (e.g. HIV and TB), and donors (e.g. PEPFAR, The U.S. President’s Emergency Plan for AIDS Relief), as well as diagnostics innovators, is undergoing a paradigm shift, in which an approach that can have a ‘consolidating’ and ‘coherence augmenting’ effect may help to move the needle on the elimination of cervical cancer [12].

Following the launch of its global strategy to eliminate cervical cancer, WHO has already issued guidance on cervical cancer screening and treatment and will continue to update this guidance via a living expert review process. Recommendations at the highest level of government are therefore in place, although challenges to local implementation remain, including i) concerns around the cost of the commodities (reagents, swabs, equipment) and cost-barriers to scaling to national level services and ii) concerns about demand creation and sustaining that demand to enable the shift to routine, high-coverage services.

Screening is a key service for women:

The majority get the good news of a negative HPV test and the sense of wellbeing that this brings.

Some have a positive HPV test and are found to have a pre-cancer, which can be treated simply, with low-cost thermal ablation or cryotherapy, even on the same day, which prevents cancer occurring.

A few will have suspicion of cancer, but early detection can save lives: treatment at early stage can lead to cure and the health system costs are lower than those for late stage disease. Palliative care started promptly can manage pain and side effects.

WHY IS THIS A PRIORITY FOR FIND?

Through our response to the COVID-19 pandemic, FIND has further strengthened relationships with global and regional policymakers, such as WHO, the Pan American Health Organization (PAHO), and the Africa Centres for Disease Control and Prevention (Africa CDC), by supporting evidence generation and providing strategic guidance for diagnostics and testing strategies. We have played a key role in the response to the pandemic through the Access to COVID-19 Tools Accelerator (ACT-A) framework of partnerships, in our capacity as co-lead, together with The Global Fund, of the diagnostics pillar [22]. A pivotal success has been securing early investments in high-quality rapid diagnostic tools, both for professional and home use. FIND has a long-standing track record of working with diagnostics developers and manufacturers to ensure innovations in field-adapted, point-of-care diagnostics, negotiating equitable access, and promoting the decentralization of manufacturing for more sustainable supply.

In our quest to democratize testing, FIND continues to empower women and communities to address their priorities within existing primary healthcare services (e.g. sexual and reproductive health programmes). Hence, FIND is now in a unique position to make considerable progress towards achieving the global target for cervical cancer screening with HPV testing. In this endeavour, FIND will build on the investments, work and expertise gained through our experience with COVID-19 and various other programmes, to save women's lives.

Aligning our cervical cancer screening programme with the WHO global strategy and emerging regional and national action plans, FIND proposes a three-pronged approach to help accelerate the countries with the highest burden of HPV towards achieving HPV screening for more than 70% of all eligible women with follow-up of 90% for all women with cervical lesions.

Building on FIND's expertise, we will work in a number of key countries to generate the evidence needed by decision-makers. Examples of locally adapted solutions with support from communities and demonstrated demand will be used to advocate for the scale-up of routine screening services. Outcomes in these key countries will resonate with policymakers in all settings with a high burden of HPV and thus help to build momentum towards achieving the 2030 targets.

We have identified three workstreams for acting in partnership with high-burden countries, notably in Africa, with a focus on community needs and preferences (see **Figure 3**).



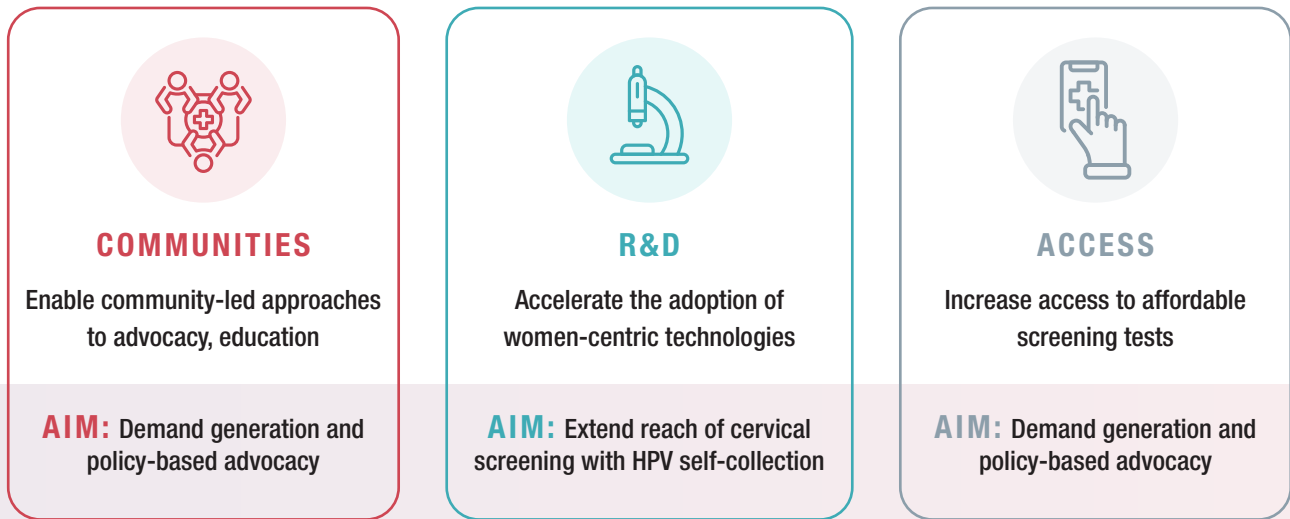


Figure 3. FIND's three-pronged approach to HPV screening

FIND's strategy focuses on community-led demand generation for high-performance HPV (hpHPV) screening using technologies and approaches that are more women-centric. It aims to develop affordable and acceptable self-collection tools with companion digital solutions that keep women engaged with the health system, reducing the loss to follow-up and increasing linkage to care.



FIND is seeking to understand the barriers to the uptake of HPV screening and resulting inequities in access and outcomes, by supporting civil society and community initiatives, notably in Africa. Our aim is to help increase the acceptability of a suite of approaches to HPV screening. These can be summarized in three main workstreams, as outlined below.

1

SUPPORT COMMUNITY-LED APPROACHES TO ADVOCACY, EDUCATION, AND DEMAND GENERATION FOR hpHPV TOOLS, TO HELP SCALE-UP SCREENING

Advocacy and education at the community level can help to generate demand for cervical cancer screening with hpHPV diagnostic tools, including self-collection of samples (whether supervised by a community or primary healthcare worker or alone). While the term ‘context-specific’ is often used to explain the lack of publicly available and adaptable toolkits for communities to provide education and support in relation to screening, the need for coherence in community approaches has been expressed. FIND will thus take up this work to i) identify civil society and community-based organizations that are ready and willing to engage, ii) support these organizations in their own knowledge development with respect to the goal of elimination and the role of hpHPV testing, and iii) work with these organizations to develop a clear understanding of communities’ and women’s perspectives and preferences.

These same organizations will be critical partners in making the case to national decision-makers for the adoption and scale-up of innovative screening modalities and models of care. The organizations will be supported in developing a coalition-based approach to their advocacy messaging, including harnessing the survivor perspective and voice and working with research findings to make the case for action.



2**ACCELERATE THE ADOPTION OF WOMEN-CENTRIC TECHNOLOGY**

This workstream aims to galvanize the efforts of many actors in the diagnostics ecosystem. Point-of-care testing (POCT) in any setting is costly but knowing where the benefits outweigh the costs of a decentralized system (enabling access to hard-to-reach populations or to mitigate results not arriving on time or being lost) is essential. Applying lessons learned from the HIV experience, this implies models of care where potentially higher costs are acceptable if it means being able to test women near to locations where treatment is available. For example, while centralizing swab transport to a laboratory once per week reduces costs and may be feasible in urban settings, POCT may be required for more rural or isolated settings, as was found in a study conducted in Malaysia [18]. As the market for molecular diagnostics devices has grown considerably during the COVID-19 pandemic, this workstream aims to leverage this increasing infrastructure base (or ‘install base’ of diagnostic machines). In addition, laboratory information systems using mobile health (mHealth, i.e. the use of apps and mobile devices for healthcare purposes) have evolved substantially, and FIND’s work conducted with partner countries to implement digital diagnostic tools will be leveraged to ensure rapid delivery of test results and linkage to treatment where necessary. The data collected through trialling this workstream aims to help countries move from cytology and/or VIA to hpHPV testing.

We aim to extend the reach of cervical screening through the use of self-collection of samples for HPV testing. Self-collection methods present an opportunity to address many cultural barriers and sensitivities around HPV screening, particularly if existing technological advancements are leveraged. A meta-analysis led by WHO found that self-collection was associated with higher acceptance of HPV screening among women [13, 14]. Studies have also shown that self-collection methods for HPV screening can be cost-effective in LMICs [15].

3**INCREASING ACCESS TO AFFORDABLE SCREENING TESTS**

This workstream aims to catalyse projects through the uptake of pre-approved HPV screening tools. It will seek out non-traditional channels for HPV self-collection (provider, community or other health worker-facilitated, or alone), such as antiretroviral drug clinics, pharmacy chains, online outlets, existing PEPFAR mechanisms, or specific campaign-driven approaches. It will also explore private sector primary healthcare services in a public-private partnership model. Diagnostic network optimization activities, to improve efficiencies and reduce costs, will be explored. Linking to our community work described above, operational research trials will be designed and conducted to generate evidence (even with previously approved tests), which will help understand the role of self-collection in each country and incentivize uptake of HPV testing.

FIND's cervical cancer strategy supports countries to realize the pillar 2 screening target of the WHO global strategy to eliminate cervical cancer as a public health problem. It achieves this by mobilizing the rapid adoption of HPV-based cervical screening and increasing the understanding of women-centred screening models in LMICs, embedded in communities and integrated into primary healthcare services.

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