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## Accelerating action on cervical screening in lower- and middle-income countries (LMICs) post COVID-19 era

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### ABSTRACT

Cervical cancer remains the fourth most common cancer in women, with 85% of deaths occurring in LMICs. Despite the existence of effective vaccine and screening tools, efforts to reduce the burden of cervical cancer must be considered in the context of the social structures within the health systems of LMICs. Compounding this existing challenge is the global COVID-19 pandemic, declared in March 2020. While it is too soon to tell how health systems priorities will change as a result of COVID-19 and its impact on the cervical cancer elimination agenda, there are opportunities to strengthen cervical screening by leveraging on several trends. Many LMICs maximized the strengths of their long established community-based primary care and public health systems with expansion of surveillance systems which incorporated mobile technologies. LMICs can harness the momentum of the measures taken against COVID-19 to consolidate the efforts against cervical cancer. Self-sampling, molecular human papillomavirus (HPV) testing and digital health will shift health systems towards stronger public health and primary care networks and away from expensive hospital-based care investments. While COVID-19 will change health systems priorities in LMICs in ways that may de-prioritize cervical cancer screening, there are significant opportunities for integration into longer-term trends towards universal health coverage, self-care and digital health.

### 1. Introduction and background

The significant progress made in the last few decades has resulted in the existence of effective vaccines and screening tools against cervical cancer. Despite being a largely preventable disease, cervical cancer remains the fourth most common cancer in women with 311,000 women dying from it in 2018 (Bray et al., 2018). With limited health delivery infrastructure and financial resources, it is not surprising that 85% of these deaths occurred in low- and middle- income countries (LMIC). Moreover, by 2030, WHO predicts a 27% rise in cervical cancer mortality in low-income countries compared to just 1% increase in high income countries (Krivacsy et al., 2019). It is also estimated that deaths from cervical cancer will rise by almost 50% if no action is taken today (IARC, 2018). In the wider context, deaths from cervical cancer in LMICs is but one of the many ‘symptoms’ of countries that have ‘ailing’ social structures whether it be economical, political, religious, cultural or within the health systems (Abeler et al., 2020; Agampodi et al., 2015; Obrist et al., 2007). While solutions are complex, the efforts to reduce the burden of cervical cancer must be considered in the context of what appears to be competing demands. For example, LMICs also bear the largest burden of HIV infections which results in the double burden of

cervical cancer among women living with HIV (Ghebre et al., 2017). The health system reforms that are taking place in the light of the pandemic must and should be leveraged to address the growing burden of both communicable and non-communicable diseases (Amatya and Khan, 2020; Bornstein et al., 2020; Gates, 2020).

A global call to action on eliminating cervical cancer through intensified vaccination against human papillomavirus (HPV), screening and treatment was announced by the Director General of the World Health Organization (WHO) in May 2018. This was followed by a broad consultative process led by the WHO to draft a global strategy for a comprehensive, population-based approach to put all countries on the path to eliminate cervical cancer. The strategy proposed key interventions to cover the decade leading to 2030. In February 2020, the WHO Executive Board recommended to the 73rd World Health Assembly (WHA) the adoption and implementation of the draft Global Strategy to accelerate the elimination of cervical cancer as a public health priority. The draft resolution, which is in alignment with the principles of Universal Health Coverage (UHC), was presented in May 2020 during the virtual abridged version of the WHA underscored the need to address the disproportional impact of cervical cancer on the most vulnerable. In August 2020, the World Health Assembly adopted the proposed strategy

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outlined by WHO.

As of 15th of October 2020, there have been more than 38 million confirmed cases and more than 1 million deaths as a result of COVID-19 with no signs of slowing down (Dong et al., 2020). The final case and death tally will only be known months after this pandemic officially ends. While SARS-CoV2 rages and economies reel, the global political order is also described to be undergoing a 'seismic shift', bringing countries to their knees. The full extent of the pandemic is yet to be seen, with the adverse effects expected to reverberate long after the health crisis has passed. The chronic problem of disparate access to healthcare facilities and existing inequalities have suffered an acute exacerbation. The phenomenon was not just experienced by LMIC but also in high-income economies.

Often quoted, 'Unprecedented times call for extraordinary measures' - the COVID-19 crisis can serve as a wake-up call and afford us the opportunity to rethink, reinvent and reform strategies to get back on track with the cervical cancer elimination goals. This however must be woven into the bigger picture of how we repair the structural inequities that exist within our healthcare system. With the elimination strategy's adoption by WHA, it is said that the resolution presents an opportunity for leaders and advocates "to end the inequity and restore women's dignity".

## 2. New tools that can accelerate cervical screening uptake in LMIC settings

### 2.1. Primary HPV testing replacing conventional cytology

The understanding that cervical cancer is almost always caused by one of 14 types of Human papillomavirus (HPV) has led to the development of HPV tests as an effective and recommended primary cervical screening modality. Evidence has comprehensively shown that HPV tests are more sensitive and provide better cancer prevention effectiveness than conventional cytology or visual inspection with acetic acid (VIA) (Koliopoulos et al., 2017; Ogilvie et al., 2018; Ronco et al., 2010). The significantly lower sensitivity of cytology compared to HPV testing necessitates more frequent and regular screening which is not practical in any LMIC setting. HPV testing is a real breakthrough as it bypasses the human and infrastructural constraints against organized cytology programs.

HPV testing is less dependent on operator expertise than cytology or VIA, and so is less challenging to establish in LMICs. A randomized control trial in India showed that even a single HPV test can reduce advanced cervical cancer and mortality compared to those screened by VIA which did not show any benefit (Sankaranarayanan et al., 2009). The automated molecular platforms are multipurpose and are easier to maintain and to assure ongoing quality.

A unique opportunity to accelerate HPV testing as a of the COVID-19 pandemic is the acquisition of molecular testing capabilities in major diagnostic laboratories for SARS-CoV2 testing. This would have introduced the principles and protocols for molecular diagnostic or more specifically, polymerase chain reaction (PCR), capabilities in conventional LMIC laboratories which can be capitalized on for HPV testing (World Health Organization, 2020a). Depending on the demand/uptake of screening tests, expansion of services and upscaling of the quantity of tests performed per day can be introduced by simply upgrading the machines. This is an example of how a rising tide can lift all boats.

While currently available HPV tests may still be expensive for most LMICs, a large body of research has shown that using HPV DNA testing is effective, cost-effective and feasible in low income settings. Cost-effectiveness studies done in LMICs including India, Kenya, Peru, South Africa and Thailand confirm the efficacy of HPV DNA screening and suggest a financial obligation to implement it (Krivacsy et al., 2019).

The investment into national HPV screening programs is money well spent. Screening allows disease in a woman to be detected early. Often this is at a stage in which treatment can be carried out using less

expensive and less invasive means, an important consideration in resource poor LMICs. It has been predicted that high HPV vaccination coverage can reduce cervical cancer burdens to the elimination threshold of 4 or less than 4 cases per 100,000 women-years in many LMICs by the end of the 21st century. However, inclusion of twice-lifetime screening will allow most LMICs, including countries with the highest cancer burdens, to reach this elimination threshold much sooner (Brisson et al., 2020).

While the cost of HPV testing have been perceived as a major barrier to primary HPV testing, modelling studies have already demonstrated the benefits of even just one high precision screen in a lifetime (Canfell et al., 2020). As part of the global cervical cancer elimination strategy, WHO will be working with manufacturers of HPV tests, providing pre-qualification and also innovative market shaping strategies. It is anticipated that on-going reduction in the cost of validated PCR-based HPV will continue. For example, in 2019, Roche announced their Global Access Program (GAP) to HPV tests (ROCHE, 2019), while two other companies were making progress towards a validated, affordable point-of-care HPV test: 1. AmpFiree HPV assay (Fujirebio) and 2. QuantumDx Q-POC™ multiplexed HPV assay (QuantuMDx Group).

Although most have accepted the need to transition to HPV testing in the elimination of cervical cancer, there are still some who are still debating over the choice of primary screening modality. This is a false choice. The performance of a high-precision test such as HPV DNA testing far outweighs that of conventional cytology but the transition will, as in all change, result in some degree of disruption in the work-force priorities.

In short, the argument that HPV tests are too expensive cannot hold water. Innovative financial models and increasing global demand for these tests will allow for further access in the near future. In the meantime, it is critical to continue to evaluate other aspects of proposed screening programs to ensure high acceptability and coverage of screening, together with systems and processes to facilitate follow-up of women in whom HPV is detected.

### 2.2. Self-sampling with low vaginal swabs for HPV testing

The advantage of HPV testing is that it can be performed on low vaginal swabs acquired by the women themselves. What's even more important is that HPV tests are as accurate when performed on a self-acquired sample collected from the vagina as they are when a doctor of nurse collects a sample from the cervix, as is required for cytology, provided PCR based tests are used (El-Zein et al., 2019). In multiple pilot studies, where women collected their own vaginal sample, self-sampling was found to be highly acceptable, across a range of cultural settings (Yeh et al., 2019).

Self-sampling using a low-cost flocked swab can be offered in a clinic setting or in the community. It can also be offered at home, either through home delivery or by mobile health workers. Within the context of the pandemic, this offers the opportunity to screen women without requiring them to attend a healthcare facility and without requiring an intimate clinical examination. Another advantage of a flocked swab is that it can be stored at room temperature and is stable for up to two weeks before it is processed. This allows time for collection and transport of the swabs to a central HPV testing facility without cold-chains or complicated logistic requirements.

The contact points for women in the community must be mapped out at grassroots levels and this will vary between countries and within each country. For example, screening women in the rural setting within a country may be completely different from that in an urban setting in the same country. Women in these remote rural settings may well require "see and treat" approaches, necessitating point of care HPV tests. Conversely, in urban settings the use of less expensive laboratory based tests is feasible provided there are strong systems linking women in whom HPV is detected to appropriate follow-up care.

This ability to perform self-sampling for HPV testing will strengthen

community-based approaches focusing on education, outreach and awareness to ensure feasible, sustainable and socio-culturally acceptable screening programs.

As stakeholders weigh the evidence for self-sampling, healthcare workers in particular will have to make important and honest choices as they adopt the change in acquiring cervical samples. Perhaps, the training of healthcare professionals should be channelled to colposcopy and treatment (modified see and treat) in order to achieve the 90% treatment target for those who have abnormal screening test.

### 2.3. Digital and mobile technology in cervical screening

While we use mobile phones for communication, they are increasingly being used to assist in the delivery of healthcare in the developing world (Beratarrechea et al., 2014). The advent of secure cloud computing offers the opportunity to establish population health IT platforms (with all data kept “in-country”) to record the details of screened women, their test results and to make this information available to health care workers in a way that facilitates follow-up. The rapid adoption of ‘contact tracing’ apps and solutions that were developed over the COVID-19 pandemic (Abeler et al., 2020) can be seen as an accelerator in the adoption of screening registries.

For the longest time, one of the major barriers for organized cervical cancer screening in LMICs is the lack of formal screening registry as used in high-income countries (HICs) such as England, Scotland, Wales, the Nordic countries, Australia and New Zealand. The extensive contact tracing exercise during the pandemic should have led policy makers and stakeholders to appreciate the value of such ‘screen and follow up’ platforms.

Attending healthcare facilities particularly in the rural setting of LMICs can be a real challenge. For many women, it is not a priority to carve out hours for the purpose of screening when they are well. However, in LMICs, the extensive mobile telephone utility can be the primary mode of contact and communication for screening. This is particularly relevant with self-sampling HPV testing. Otherwise, geolocation of the woman’s home might enable healthcare workers to find her when follow up is required, with appropriate privacy safeguards in place.

Furthermore, if appropriately established, these platforms can make use of the data at program level, enabling evaluation of indicators such as screening coverage and rates of follow-up of screen positive participants. Progress towards the WHO targets can be monitored and strategies to improve the reach of screening and effectiveness of follow-up can be evaluated and adjusted to continuously improve the allocation of resources and ultimately the performance of the program.

### 3. Re-organising health-systems to support cervical screening in LMIC

Most healthcare systems in LMIC struggle to meet basic standards of care where systemwide barriers exist. Conventionally, most healthcare systems in LMIC consist of care provided by health workers within a network of primary, secondary and tertiary care facilities which may not even be accessible geographically. Unfortunately, the most disadvantaged populations will fail to access let alone navigate existing complex healthcare systems. An effective cervical screening program must have wide coverage, accurately identify persons at risk of developing or having early cervical cancer and most importantly, must be able to provide linkage to treatment if required. To execute such a screening program in LMICs, health inequities and complexities within the health systems will need to be addressed systematically. Fewer than 50% of countries with a cervical screening policy have an operation plan that is fully funded.

Coherent programs across all governmental ministries spanning health, education, transport, housing and finance will be critical for improving health equity. This requires political will, time and financial investments. Furthermore, it is estimated that by 2030, there will be an

estimated shortage of 14.5 million healthcare workers (WHO, 2016) with at least 400 million people worldwide lacking the most essential health services. The brain drain of healthcare workers from LMICs to high-income countries (HICs) is another confounder.

Therefore, an alternative to strengthening a three-tiered healthcare structure dependent on hospital-based specialist care is to invest in community and primary care. One such strategy is to promote self-care in sexual and reproductive health as advocated by WHO. Self-care is defined as ‘the ability of individuals, families and communities to promote health, prevent disease, maintain health, and to cope with illness and disabilities with or without the support of a healthcare provider (World Health Organization, 2019). The ability to undertake self-sampling is aligned with the concept of shifting screening from acute care hospitals and healthcare facilities; only women who test positive need to be seen within a healthcare setting (and if necessary, they could be screened for SARS-CoV-2, prior to being seen). Self-sampling outside of the hospital and clinics, with adequate support and education will be one of the major enablers to achieve higher uptake of cervical screening in LMICs.

As LMICs navigate through the current crisis, the ability to encourage self-sampling within the community as part of the wider self-care strategy promoted by WHO can be used as a springboard to a paradigm shift in cervical screening. In addition, innovative human capital solutions have been pioneered in LMICs to meet human capital gaps. For example, Eritrea has recently trained nurse assistants under their Community-based Healthcare Program, or more popularly known as ‘barefoot doctors’ (UNICEF, 2019). These health professionals have the added advantages of existing trust and relationships in their communities, creating a ready talent pool for future up-skilling, and long-term sustainability in the health system.

WHO recommends that HPV self-sampling should be made available as an additional approach to sampling in cervical cancer screening services for women aged 30–60 years old (World Health Organization, 2020b). Self-sampling can help reach a global target of 70% coverage of screening by 2030 as set out by the WHO cervical cancer elimination strategic proposal.

An important caveat though is that no screening program can deliver the desired outcomes (reduced incidence and mortality due to the targeted cancer) without proper follow up. In order to achieve these outcomes, it is essential that participants whose screening test is positive receive appropriate evaluation and treatment as required. Traditionally records have been kept on paper or in siloed health service electronic records with many women falling through the cracks or lost to follow-up.

### 4. Challenges and opportunities for cervical cancer screening in the Post-COVID-19 Era

At the time of writing, it is too soon to tell how health system priorities in LMICs will change as a result of COVID-19, and its impact on cervical cancer screening. However, some general trends can already be ascertained. First, LMICs will increasingly consider health and health security to be an important determinant (not just a consequence) of national development and national security. Therefore, more political, financial and human capital will flow into the health and healthcare space, with positive effects for population health and the health system at large. Secondly, health systems of LMICs are likely to prioritize communicable diseases over non-communicable diseases. This reprioritisation is likely because of a recent and profoundly overt existential threat, coupled with public pressure for more health security. Therefore, the more invisible threat of non-communicable diseases, oncology and cervical cancer included, may be deprioritised in terms of funding, political will and public attention. Thirdly, there is emerging evidence that COVID-19 is accelerating health inequities (Okonkwo et al., 2020), in ethnic, socio-economic and gender terms. Cancer affecting women, especially in LMICs where gender is an obstacle to



accessing healthcare, may be disproportionately affected by the accelerating health inequities.

The post-COVID-19 healthcare world is not yet finalised. Therefore, there are still opportunities to strengthen cervical cancer screening by leveraging on several trends. The conversation surrounding UHC needs to include stakeholders in the cervical cancer community, the oncology community and the non-communicable disease community (in progressively larger terms). UHC is integral in fighting pandemics, and building cancer sentinel surveillance, monitoring and registry set-ups will also help fight pandemics due to their reasonably similar public health, data analytics and IT requirements (Abeler et al., 2020).

This pandemic will shift health systems towards stronger public health and primary care networks and away from expensive hospital-based care investments. Community health care workers who are trained adequately can undertake cervical cancer prevention along with other health promotion activities (Woldie et al., 2018). More importantly, they can service as liaisons to more skilled health care professionals. Mobile clinics supported by basic mobile communication technologies can significantly improve access (Roess, 2017). It is imperative that the cervical cancer community recognise these two trends and build stronger alliances and networks with the public health and primary care community. These could take the form of education, advocacy, integration with existing cancer screening and treatment pathways, and a smoother escalation/de-escalation of care across the primary-secondary-tertiary continuum. This integration with the public health and primary care networks in LMICs can help re-organise the system to quickly shift women from screening to treatment when needed.

The COVID-19 pandemic has also accelerated trends towards digital health and telemedicine, anchored by a greater willingness and comfort for public-private partnerships. Self-sampling, using mobile technology in screening programs and electronic health records are discussed elsewhere in this monograph, and should be integrated into a national push towards digital health and telemedicine. Building a digital health ecosystem is a multi-year and expensive proposition, and it will require changing relevant laws in LMICs, while also scrutinising procurement and privacy policies.

## 5. Experience from COVID-19 in accelerating action in cervical cancer elimination in LMICs

The COVID-19 pandemic has debunked the myth that health systems in LMICs are not able to tackle challenges to their integrity than systems in richer countries. Over the past few months since COVID-19 emerged from China, health systems of many LMICs, including many in the Asia Pacific region, have shown high levels of resilience while health systems in many richer countries have faltered. Many LMICs prioritised prevention of community spread by conducting intensive contact tracing and isolation of cases. They maximized the strengths of their long-established community-based primary care and public health systems to provide time to build up the capacity of hospitals to deal with influx of more severe cases. Surveillance systems were expanded to support public health measures, often incorporating readily available mobile technologies. Wide-spread use of such technologies in LMICs in the fight to contain the spread of COVID-19 reveals communities' acceptance to adopt new practices in their daily living. Communities were thus empowered, with knowledge and technology, to adopt preventive measures against COVID-19. A new norm has emerged – acceptance and practice of self-care. LMICs should now work towards harnessing this momentum and public spirit to ensure elimination of cervical cancer in all countries.

## 6. Summary

Deaths due to cervical cancers remains high in LMICs, although long-term trends show some progress. Currently, there are three tools that

appear appropriate and promising for LMICs: primary HPV testing, self-sampling with low-vaginal swabs and digital and mobile technologies. While COVID-19 will change the health systems priorities in LMICs in ways that may de-prioritize cervical cancer screening, there are significant opportunities for integration of cervical cancer screening into longer-term trends towards Universal Health Coverage, stronger public health and primary care networks, and digital health and telemedicine. It is hoped that COVID-19 can be used as a nation-changing event that can further strengthen health systems and health outcomes, including for cervical cancer screening.

## Author statement

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