

Eliminating Deaths From Cervical Cancer—Report of a Panel at the 7th Annual Symposium on Global Cancer Research, a Satellite Meeting at the Consortium of Universities for Global Health 10th Annual Meeting

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abstract

This is a summary of the presentations addressing approaches and achievements to reach the goal of eliminating cervical cancer as a global public health problem that were delivered at the 7th Annual Symposium on Global Cancer Research at the 10th Annual Consortium of Universities for Global Health Meeting in March 2019. Dr Princess Nothemba Simelela, Assistant Director-General for Family, Women, Children and Adolescents, World Health Organization, gave an introduction to the World Health Organization–led Cervical Cancer Elimination Initiative and the emerging conceptual framework and targets that will shape the global 2020 to 2030 strategy. Subsequent presentations shared experiences from national programs in Rwanda (Agnes Binagwaho), Latin America (Patricia J. Garcia), and Senegal (Babacar Gueye and J. Andrew Dykens). Successes in intensified human papillomavirus vaccination and screening with follow-up treatment of early and advanced lesions detected are highlighted as well as the challenges and obstacles in achieving and maintaining high coverage in Africa and Latin America. With strong political leadership, commitment of national stakeholders, and the use of proven and cost-effective approaches to human papillomavirus vaccination, screening, and treatment, the vision of a world free of cervical cancer and saving women’s lives every year by preventing deaths from cervical cancer will be achievable in the next generation in all countries.

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INTRODUCTION

Cervical cancer kills > 300,000 women worldwide annually and > 570,000 new cases are diagnosed each year. This is unacceptable because cervical cancer is highly preventable and, if detected early, treatable. Vaccination against infection with human papillomavirus (HPV) is available, safe, and highly efficacious, and there are effective approaches to screening and treatment of early lesions, as well as cancer. These highly cost-effective preventive measures formed the basis for a global call for action by the director-general of the World Health Organization (WHO), Dr Tedros Adhanom Ghebreyesus,¹ to eliminate this malignancy and were highlighted at the 6th Annual Symposium on Global Cancer Research at the 9th Annual Meeting of the Consortium of Universities for Global Health in 2018. The WHO-led Cervical Cancer Elimination Initiative resulted in a decision receiving overwhelming support from WHO Member

States mandating that WHO develop a global strategy to accelerate global cervical cancer elimination. A draft global strategy for the period 2020 to 2030 was released in May 2019 for online consultation and formal Member State consultations with the intent to submit a finalized strategy to the 172rd World Health Assembly in 2020.

Current efforts to address cervical cancer are having little impact in the face of the consistently rising global burden. Vaccination alone will result in an impact delay and not enable reaching the threshold for elimination as rapidly as the WHO’s 90:70:90 strategy would: 90% of girls vaccinated by age 15 years and screening of 70% of women at age 35 year and again at age 45 years at a minimum, with 90% follow-up treatment of precancerous lesions and invasive cancers. This approach will bend the curve toward an anticipated reduction in mortality of 30% by 2030 and cervical cancer incidence to a threshold of four per

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CONTEXT

Key Objective

Approaches to the goal of elimination of deaths from cervical cancer are presented by representatives of WHO, two African countries, and Latin America.

Knowledge Generated

Successful nationwide HPV vaccination in Rwanda and planning for countrywide screening, vaccination, and treatment in Senegal demonstrate this goal is achievable. Many hurdles to reach this goal exist in Latin America, Africa, and elsewhere, and need to be overcome, including lack of cervical cancer awareness, shortage of human and technological resources, fear of vaccination, lack of women's empowerment, and push-back from entrenched interests.

Relevance

Innovations in screening for cervical cancer (eg, HPV testing and self-sampling) and HPV vaccine development, vaccination strategies, and coverage will contribute to WHO's goal of reducing deaths from cervical cancer as a public health problem to less than four per 100,000 woman-years before the end of the current millennium.

100,000 woman-years (ie, the levels considered no longer a public health problem) before the end of the current millennium.

Here, we summarize three presentations addressing approaches and achievements to reach this goal in East and West Africa and Latin America that were delivered at the 7th Annual Symposium on Global Cancer Research at the 10th Annual Consortium of Universities for Global Health Meeting in March 2019.

Dr Princess Nothemba Simelela, Assistant Director-General for Family, Women, Children and Adolescents, WHO, gave a strong introductory address outlining the call to action by Dr Tedros and the steps taken by WHO and partners to develop a strategy to achieve the goal of eliminating cervical cancer before the end of the current millennium. She emphasized the need for high-intensity vaccination and screening and treatment of early cervical lesions. She reported that several countries, including a number of low- and middle-income countries, already providing services at the coverage rates targeted by 2030. Dr Simelela also mentioned examples of new WHO materials the Cervical Cancer Elimination Initiative is generating to support acceleration of national action on cervical cancer: HPV DNA testing has been put on the WHO Essential Diagnostics List, a toolkit has been released for improving data management of screening programs, and guidelines for thermocoagulation of early lesions have been developed and will have been released by the time this article is in press. She finished by listing a set of guiding principles all stakeholders should embrace as they join the elimination ambition: integration and action across the life course and engagement of young people, not only to improve health literacy of the next generation but also to engage them as future champions for elimination. Dr Simelela reinforced a public health approach, emphasizing social justice, equity of access to care, and integrated, people-centered universal health services. She ended by stating, "To combat the scourge of

cervical cancer, an avoidable noncommunicable disease with huge inequities in prevalence and mortality between and within countries, we will require all public health specialists and health care providers to unite behind this vision and work together with national governments and the WHO to empower girls and women and engage our communities to join us on the pathway to elimination."

APPROACH TO CERVICAL CANCER ELIMINATION IN RWANDA (AGNES BINAGWAHO)

Rwanda, a country of 12 million people in sub-Saharan Africa, is a helpful example of a low-income country that strategically introduced the HPV vaccine and demonstrates that universal access to the HPV vaccine is not simply a matter of resources or advanced economic development but rather the result of the political and technical will to achieve this important objective.² Think of the millions of lives saved if the entire world were to embrace this challenge.

To appreciate Rwanda's experience with the rollout of the HPV vaccine, it is important to first understand key aspects of its history, because this informs the systems-level approaches the country takes to health care. In 1994, the country faced the horrific 1994 genocide against the Tutsi, which left 1 million dead. The health sector was devastated and nonfunctional. As the country started to recover and embraced a true sense of ownership, the nation's leadership aimed to rebuild the health sector on the basis of the principles that health is a human right and services must be provided equitably: no one should be left out, and services must be provided with transparency, honesty, and accountability. Motivated by these principles, Rwanda achieved unprecedented gains in life expectancy and universal access to HIV treatment, reduced infant mortality by 75%, curtailed maternal mortality by 80%, and promoted a transformation in care delivery so > 91% of expectant mothers gave birth in health facilities. These achievements were the result of concerted, multisectoral

national efforts embedded in the economic development of the country, and were based on human development. Rwanda also benefited from thoughtful and committed international partners who shared the vision of the country.

In early 2000, as Rwanda made steady progress toward the health-related Millennium Development Goals, rigorous assessments of population health demonstrated that noncommunicable diseases (NCDs) were becoming an increasingly important contributor to morbidity and mortality in Rwanda. For the continent overall, NCDs are projected to exceed deaths in Africa due to communicable, maternal, perinatal, and nutritional diseases combined by 2030.³ Though NCDs are a vast domain, Rwanda made a compelling case to take a closer look at what could lead to a real-time intervention. After carefully considering the effectiveness of the newly developed HPV vaccine, working with partners, Rwanda seized the opportunity to make the vaccine available to its people. In 2011, less than two decades after the country's almost complete destruction, Rwanda successfully introduced the HPV vaccine nationwide, achieving near-universal access to it through a strategic, collaborative, and multisectoral campaign. Specific steps that aided this successful rollout are highlighted here, and more detailed information is presented in the article by Binagwaho et al.²

Preparations for introducing the vaccine campaign began with advocacy and negotiation, including seeking advantageous pricing schemes with pharmaceutical companies that manufacture the vaccine. The Rwanda Ministry of Health led the formation of a technical working group that included representatives from private industry, communities, development agencies, and health-professional associations. In addition, microplanning committees were formed for specific aspects of the vaccine rollout (eg, supply chain, community outreach, data collection). After discussions with other governmental agencies and partners, the Ministry of Health worked with the Ministry of Education to develop a plan to deliver the vaccine in schools. This was felt to be the most streamlined and effective way to reach the majority of girls throughout the country, with follow-up strategies that included logistics and community health workers to reach out to girls who happened to miss school on the day of vaccination.

Once an implementation plan was finalized in coordination with community representatives and partners, a broader engagement effort was formed to educate the entire population about this important public health measure. This involved a continuous cascade of trainings that included teachers and health care providers. The effectiveness of the community engagement campaign, which included collaborations with churches, media (newspapers and radio), and local and national leaders, was demonstrated by the high acceptability of the vaccine and its subsequent high uptake, which was voluntary—girls or their parents may refuse vaccination. Since the beginning,

the HPV vaccine was offered freely and, once again, voluntarily to all girls of age 12 years. As a result of this campaign, today more than 93% of girls between 12 and 22 years old are fully vaccinated against HPV in Rwanda. Besides high coverage vaccination, Rwanda launched access to treatment in its cervical cancer elimination program.

At the time, researchers external to Rwanda questioned whether this initiative was in the best interest of the country's people, suggesting that implementing the HPV vaccine would threaten our ability to tackle other diseases. Other skeptics raised questions about the cost-effectiveness and sustainability of delivering this vaccine. These critics neglected to remember Rwanda's impressive track record of 93% of all children already fully vaccinated for 11 infectious diseases. To these doubters, Rwanda responded that it was our moral obligation to act for our women and girls when the opportunity to do so existed. Inaction, especially when we had the tools and support to do something about this real disease burden, would essentially be a violation of their human right to health.

Cervical cancer is only one of the many cancers facing Rwanda. For each of these cancers, Rwanda embraces a holistic effort and does not prioritize prevention over treatment or vice versa. It is a combined approach. It is this approach that Rwanda and many long-term partners, including Partners In Health, subscribed to when it opened its first cancer facility in 2012 at Butaro Hospital, enrolling nearly 10,000 patients with cancer and becoming a true center of excellence not just for the country but for the region.

Furthermore, Partners in Health has established in Rwanda the University of Global Health Equity (UGHE), a new, private, nonprofit university that has at its core teaching the approach to health with equity. UGHE has the mission to radically change the way health care is delivered around the world by training generations of global health professionals who strive to deliver more equitable, quality health services for all, in every corner of the globe. UGHE educates students to use implementation science approaches to harness existing best practices and to innovate for solutions, including those that guided the previous HPV rollout and those that will inform future policies to broaden the impact of this initiative.

ELIMINATING DEATHS FROM CERVICAL CANCER IN LATIN AMERICA: REALITIES, CHALLENGES, AND OPPORTUNITIES (PATRICIA J. GARCIA)

Latin America (LA) is characterized as “the most unequal region in the world,” despite significant improvements in past decades.⁴ Inequalities affect distribution of resources and social opportunities, causing high levels of poverty, deterioration of environment, blocking the development of human capital, and affecting health.⁵ Cervical cancer is closely associated with poverty and lack of access to

services for screening. Cervical cancer is still the leading cause of cancer mortality among women in at least 11 countries in LA.⁶ In LA, approximately 248 million women are at risk for cervical cancer, there are > 70,000 new cases each year, approximately one of two women with cervical cancer will die, and the mortality rate is still rising to a projected 45% in 2030 unless something is changed.⁷

Because the impact of women dying from cervical cancer is enormous, affecting individuals, families, and whole societies, immediate actions are required; this is the reality. Death from cervical cancer can be prevented by vaccination and effective screening, and there are significant opportunities to change the trends in LA and change the history of future generations of women. Scientists in LA have been involved since early on in the investigation of HPV and its association to cervical cancer globally, and they have been major contributors in vaccine trials and implementation trials in the region.⁸⁻¹⁰ LA also is pioneering the implementation of new models for cervical cancer screening, introducing HPV testing and self-sampling.¹¹⁻¹⁴ However, among the biggest challenges in HPV and cervical cancer research in LA are the scarce global funding opportunities directed toward the region and the relatively little research funding from national governments. In the global space, LA is not seen necessarily as a region in which to invest in research, denying not only the needs the region has but also the opportunities LA offers, because funding could be catalytic for meaningful research and result in excellent examples for other countries in the global south of what could be achieved and how to do it.

The landscape of the introduction and implementation of HPV vaccination in LA is quite interesting, especially because of the experience of LA in making significant advances against other vaccine-preventable diseases with the technical support of the Pan American Health Organization (PAHO).¹⁵ Approximately 55% of countries in the region (ie, ≥ 12) have introduced HPV vaccination; several are using the PAHO revolving fund, which allows countries to save significantly in the procurement of the vaccine. All the vaccination programs are based in public schools and directed to girls 9 to 13 years old, with schedules of two or three doses. Argentina, Brazil, Chile, and Colombia are already catching up and Panama, Puerto Rico, Argentina, and Brazil have already started gender-neutral vaccination.^{16,17} Nevertheless, there are several challenges. At least nine countries remain to introduce HPV vaccination nationally; vaccine coverage varies among countries and different years, with reports ranging from 30% to 87%; gender-neutral vaccination and catch-up strategies are still to be implemented. Finally, there is a need to establish a system for monitoring coverage, safety, and impact of HPV vaccines.

Many efforts in LA have been made to implement cytology-based (ie, Papanicolaou) screening programs; results have been variable but definitely not enough to control cervical

cancer. Now, there are several highly sensitive molecular tests for the detection of cervical HPV infection that could be used as first-line screening instead of cytology. Moreover, women could self-collect their own vaginal sample in the privacy of their home and submit it for testing. Because most HPV infections remit spontaneously and do not result in cancer, testing women starting at 30 years old would identify women with persistent HPV infection who are at a higher risk for cancer and who will require subsequent screening and treatment. This could result in savings and higher rates of screening. Some countries in LA have started with success in HPV testing with and without self-collection, involving community health agents.^{12-14,18} HPV self-collection could help achieve a high coverage for screening, which, together with other new technologies like thermocoagulation for treatment,^{19,20} could provide the opportunity to control and eliminate cervical cancer in LA.

However, important challenges remain. There is a need to promote political and economic support to establish stronger national test and treat plans. There is a need to ensure HPV tests are available and affordable for countries, promoting central procurement systems through cooperation agencies, similar to the PAHO revolving fund for vaccines, which allow economy of scale, lower costs, and quality assurance. And there is a need for national awareness campaigns about cervical cancer that break myths, stigma, and fears about the gynecologic examination and promote HPV self-collection. There is a lack in LA of enough trained human resources, especially in public health services and rural areas. It is critical to plan ahead how to effectively deploy health care and resources (human and technological) in poor or rural areas, assuring access to indigenous populations and migrants. Task shifting and task sharing are key. Professional midwives should be part of the see and treat system. However, there are conflicts between physicians, especially gynecologists who see their space as being invaded by midwives, as seen in Peru. Conservative groups could be also against HPV self-sampling, which is seen as too much empowerment for women. And from the physician's point of view, self-sampling could be seen as threat to their practice, because most of gynecologic practice is based on Papanicolaou smears. Discussion of the important opportunities for linking HPV-positive women to services should be made with physicians to ease these fears.

The opportunities to make the difference remain. Although most efforts for elimination of cervical cancer are focusing on African countries, a coalition of funding partners, academia, professional stakeholders, and cancer charities directed to LA could be the catalytic effort needed to change the history of and eradicate deaths from cervical cancer, fight inequities, and stop the suffering of so many women and families in LA.

SENEGAL'S SYSTEMATIC APPROACH TO IMPLEMENTING A NATIONAL CERVICAL CANCER PREVENTION AND CONTROL PROGRAM (BABACAR GUEYE AND J. ANDREW DYKENS)

Senegal is a French-speaking West African country with a population of 16.2 million people, of whom 45% live in urban areas and the remaining 8.9 million people are dispersed across rural areas.²¹ The Senegal Ministry of Health and Social Action (MSAS) oversees 77 health districts in 14 medical regions. Senegal has 13 referral hospitals and an additional 10 district hospitals that receive referrals from the 99 health centers in Senegal, which oversee a total of 1,456 community-level health posts and 708 health huts.²² Workforce coverage in the public sector in Senegal is one physician per 18,615 population, one nurse per 3,946, and one midwife per 4,183.²² Physicians direct the care at health centers whereas health posts are staffed by nurses and midwives. Health huts are staffed by community health workers and are the only immediate care available to those in many rural areas.

The MSAS oversees cancer prevention and control through the Direction of Noncommunicable Diseases, and the Direction of Vaccines launched a national HPV vaccination campaign in October 2018 alongside Gavi, the Vaccine Alliance, to combat HPV-related cancers.²³ The MSAS plans to launch the National Cervical and Breast Cancer Prevention and Control Program in 2019. Senegal has a decentralized health system²⁴ with dynamic leaders at national and regional levels dedicated to solving major challenges in low-resource settings. However, currently, there remains minimal access to cervical cancer screening throughout Senegal, especially in rural Senegal, leading to very low screening rates.²⁵ Senegal focuses on sensitization and early referral at the community level through health huts and is planning improved screening access with referral and case monitoring at the health-post and health-center levels. The plan also calls for the health-center level to have the ability to provide treatment of uncomplicated cases of identified dysplasia. Complicated cases will be referred for specialty care in the urban setting.

The actual prevalence of all cancers in Senegal is unknown,^{26,27} but national-level data from the main referral hospital indicate 379 confirmed cervical cancer cases nationwide in 2018. However, cervical cancer incidence is estimated at 37.8 per 100,000 (17th in the world).²⁶ Confirmed cases will likely increase with the implementation of the national cervical cancer screening program, given that current screening rates are very low at 10.9% nationwide.²⁸

Senegal is prioritizing its response to the mounting burden of cancer in the Senegal National Cervical Cancer Prevention and Control Plan (CCPCP) that will launch in late 2019, shaped alongside the National Health and Social Development Plan (2019 to 2028). These plans have been informed by Sustainable Development Goal 3, the Global

Non-Communicable Disease Action Plan 2013-2020, to reduce premature mortality from NCDs by 25%, and the global strategy to eliminate cervical cancer.^{29,30}

The Senegal CCPCP responded to the Investing in Cervical Cancer Prevention (2015–2020) London Meeting³¹ and advances Senegal's National Strategic Plan for Cancer Control³² by including a vaccination and information and education communications plan; human resources development; efforts for early detection, and diagnostic and therapeutic management; epidemiologic surveillance, research, and monitoring; and evaluation of the strategic plan. In 2018, Senegal underwent an exercise to document standards and protocols for early detection of precancerous cervical lesions and early detection of breast cancer. Participants included health officials, clinicians, non-governmental organizations, and academic partners. The Senegal CCPCP will also build on a history of significant achievements including the Tobacco Control Law of 2014^{31,33} and the more recent introduction of HPV vaccination nationally. To ensure access to cancer treatment, Senegal has acquired three linear accelerators and has secured a subsidy to aid dispensing of chemotherapy. Senegal has also secured equipment for health districts to support the screening and treatment of precancerous lesions in eight rural regions.

Senegal continues to strengthen decentralized primary health care services with a robust community-level component as its central strategy for a high-quality CCPCP that covers primary, secondary, and tertiary care, as well as the intersection of these health care levels with health promotion and primary (ie, vaccination) and secondary (ie, screening) prevention. The implementation of cervical cancer screening programs in rural areas, for example, will not be isolated in focus. Senegal is planning concurrent attention to demand-side determinants such as client knowledge, cost of access, and social support, while ensuring focus on supply-side access determinants such as well-trained personnel, equipment maintenance, supply chain, and quality control at the health-service level. Reliable referral systems will need to ensure follow-up at the primary care level to manage uncomplicated cervical dysplasia (through treatment with cryotherapy) as well as referrals to tertiary care for advanced cervical cancers.

Senegal's developing comprehensive response to the challenge of cervical cancer aligns individual components with the strengthening of primary health care services in general. Senegal is taking great strides, as well, to advance research and routine monitoring and evaluation across multiple settings. This fosters the advancement of critical evidence-informed policy. Senegal has implemented the infrastructure to support a national cancer registry and a District Health Information System, which is a widely used platform for the reporting, analysis, and dissemination of data for all of Senegal's health programs.³² To further develop tertiary-level cancer care, Senegal is developing

a national oncology center, including building workforce capacity by training oncology specialists. Senegal now boasts 12 gynecologists trained in colposcopy and one public health doctor trained in the management tools for strategic planning, monitoring, and evaluation of cervical cancer programs. However, there remain shortages of human resources, especially in rural zones. The MSAS is continuing to train gynecologic oncologists and medical oncologists to support referral services and public health doctors and communication specialists for prevention strategies of gynecologic cancers. There is a focus on task sharing in rural areas by training nurses and midwives in visual inspection of the cervix with acetic acid and treatment methodologies such as cryotherapy for precancerous lesions. Senegal is developing a plan for universal health coverage that will comprehensively cover cervical cancer prevention as well as care for advanced cervical cancer cases.

Senegal currently finds itself confronting the challenge of complexity, because cervical cancer is an issue that requires an approach at multiple levels of the health system but is reflective, as well, of equity and gender disparities. To achieve our collective goals, a resilient system is not optional nor can it be an afterthought. Our hope is that the global community can learn from our thoughtful, measured approach to this challenge, including Senegal's focus on responding across contexts and engagement with the international community to advance this cause collectively.³⁴

CONCLUDING REMARKS (GELILA GOBA)

The WHO's 2030 cervical cancer control targets provide an excellent platform for the global health community to work

together to eliminate death from preventable cervical cancer. As all panelists writing in the previous sections highlighted, we have proven tools for prevention and care, as well as implementation strategies that have worked in resource-limited settings, and successful examples of collaboration between academia and public health systems. We also want to highlight opportunities and challenges for all stakeholders. Strengthening advocacy and information to prevent misconceptions about vaccines and increasing the availability of vaccines in low- and middle-income countries are essential when implementing national HPV vaccination programs. Exploring service delivery options, including a single-dose vaccine and spacing the current two-dose regimen by 36 months, are also worth considering.

Strategies to reduce global and local disparities in survival by improving early detection and introducing new technologies to diagnose and treat HPV-related cancers, enhancing preservice and in-service education in cancer treatment and care, as well as providing corresponding infrastructure support for surgery and radiotherapy will be crucial to meeting targets. Strategies to reach vulnerable populations, including underserved, displaced, and migrant populations, in cancer prevention and care should be strengthened. Last, but not least, research targeting high-risk HPV subtypes and environmental and endogenous factors that contribute to the irreversibility of precancerous lesions and/or their rapid progression to cancer are crucial as we put all efforts together to curtail cervical cancer.

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