The Global Fund, Cervical Cancer, and HPV infections: what can low- and middle-income countries do to accelerate progress by 2030?



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Summary

The footprint of cervical cancer mirrors the impact of global inequity and inequality on the right to health for girls and women. While today, cervical cancer is a relatively rare cause of death in Europe, North America, and Australia, almost 94% of deaths in 2022 occurred in low- and middle-income countries (LMICs). Governments adopted the WHO global strategy to eliminate cervical cancer. Still, the stark reality is that many countries may not reach the 90:70:90 targets by 2030 without political commitment and a sense of urgency. We call for enhanced advocacy for the right to prevention services and political actions to mobilise global funding, local philanthropic support, and innovative financing. During the COVID-19 pandemic, an African coalition raised over \$20 million to mitigate the impact of the pandemic. Positive lessons from this response should be replicated to save millions of women and girls at risk of cervical cancer in LMICs. There is a need for a global fund for cancer; regional blocs like the African Union need to recognise the disproportionate burden and establish continental funding mechanisms to enable high-burden countries to make crucial upfront health systems investments that will put their countries on the pathway to cervical cancer elimination.

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Introduction

Cervical cancer disproportionately affects women and girls globally and is ranked the fourth most common cancer in both incidence (6.8%) and deaths (8.1%) in women worldwide in 2022.1 The World Health Organization's (WHO) director-general Tedros Adhanom Ghebreyesus said that "one woman dies of cervical every 2 min ... Each one is a tragedy, and we can prevent it."2 Cervical cancer is now labelled a disease of the poor,³ as most of the women who die from cervical cancer are poor, living in resource-constrained and marginalised communities. In 2022, Asia was ranked the continent with the highest cervical cancer incidence (60%) and mortality (57.3%), followed by Africa (19%, 23.1%) and Latin America and the Caribbean (9.5%, 9.6%); whereas Europe (8.8%; 7.7%), Northern America (2.4%; 1.9%) and Oceania (0.37%; 0.38%) have the

lowest incidence and mortality in 2022. Of all the 185 countries and territories included in the International Agency for Research on Cancer (IARC) estimates, cervical cancer is the leading cause of death in 37 countries, mostly low- and middle-income countries (LMICs) of sub-Saharan Africa, South America, and South-Eastern Asia. Clearly, where women live, their countries' income levels and human development index play a key role in whether they have the opportunity to prevent the disease or die of cervical cancer. While high-income countries (HICs) are approaching the elimination of cervical cancer through the prevention of human papillomavirus (HPV) infection, progress in LMICs is still emerging.

HPV is a sexually transmitted infection that causes virtually all cervical cancer.⁵ In 1991, the HPV vaccine was developed,⁶ and it became available to the public in 2006 after extensive clinical studies. The HPV vaccine is very safe and highly effective at preventing cervical cancer.^{7,8} The vaccine was added to the WHO list of childhood essential medicines in 2015⁹ and is

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recommended as part of routine immunisation in all the member countries.^{2,10} By March 2017, 71 countries had introduced HPV into their routine immunisation10; by the end of 2023, the number of countries has reached 14311; however, over 80% of these countries are HICs.12 See Fig. 1. As of 2022, the WHO regions of Europe and the Americas have achieved 40% and 77% first-dose HPV vaccination coverage for females aged 15; whereas the Eastern Mediterranean (0%), South-East Asia (3%), Western Pacific (11%), and the African region (22%) have been lagging behind.13 See Fig. 2. Women and girls' access to the life-saving HPV vaccine is clearly defined by the country's income levels and their geographical locations, and not necessarily by the burden of disease. LMICs like sub-Saharan Africa, where some of the highest burden of cervical cancer exists, still lack HPV vaccines, whereas most girls and even boys in HICs where the burden is lower have been vaccinated.12 For instance, using the UNICEF SD/Gavi HPV vaccine price of \$4.5 and operational cost \$11.07,14,15 Nigeria would need to invest USD 270 to \$664 million (i.e., over 50% of its 2024 total health

budget) to vaccinate over 60 million women and girls at risk of cervical cancer in this population. Due to the high cost of vaccines, global supply, inadequate global funding, and the COVID-19 pandemic, 16,17 securing investments and funding for the acceleration of the elimination of cervical cancer and meeting the 90/70/90 by 2030 has continued to be a herculean but possible task.

Methods

We conducted a literature review on PubMed and Google Scholar using the following search words: "cervical cancer," "HPV infection," "HPV vaccine," "HPV interventions in LMICs," "innovative financing in Africa," "history of Global Fund," and "Global Fund interventions in AIDS, Tuberculosis, and Malaria." The review was conducted in September 2022 and December 2023. Data extraction and analysis were done using Microsoft Excel and the websites of the WHO (https://immunizationdata.who.int/) and Global Fund (https://data.theglobalfund.org/).





The boundaries and names shown and the designation used on the map do not imply the expression of any opinion whatsoever on the part of the Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the edimitation of its or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement. - Source: WHO Data portal - World Health Organization, WHO, 2024, All rights reserved.

Fig. 1: Introduction of Human Papillomavirus (HPV) vaccines across the world. Source: WHO Immunization Data Portal, generated 9th November 2024 via https://immunizationdata.who.int.



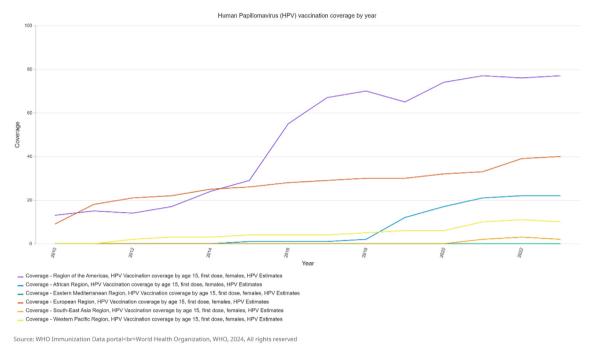


Fig. 2: Human Papillomavirus (HPV) vaccination coverage by year in six WHO regions. Source: WHO Immunization Data Portal, generated 9th November 2024 via https://immunizationdata.who.int.

Role of funding source

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Main

As we progress to 2030, challenges around the multiple cyclical replenishments of multilateral institutions tackling global causes are a concern. In a recent post, The Center for Global Development called this confluence the "2024-2025 Replenishment Traffic Jam." In the health domain alone, the Global Fund (GF), Gavi, the Pandemic Fund, the Global Polio Eradication Initiative, and the Global Financing Facility are preparing for crucial replenishments and funding rounds in this period. In addition, at the time of submission of this manuscript, the World Health Organization (WHO) had just instigated its inaugural investment round, responding to member states' call for increased sustainability and core funding.19 In this competition for health funder attention, how can the LMICs and African cancer community position for a small share of the global health funding pie but, more importantly, look to national funding mechanisms to support the implementation of national cancer control plans?

One question we ask national finance ministers is—are we taking maximum advantage of funds that are

already on offer? For example, in the last cycle, on September 19, 2022, global leaders, civil societies, and the private sector gathered in New York, USA, for the seventh GF Replenishment conference and raised over USD(\$)15.7 billion for the GF's fight against AIDS, Tuberculosis, and Malaria for the year 2023-2025.3,4 While most of the top pledges were from the governments of high-income countries (HICs), with the United States Government making the highest pledge (\$6 billion) followed by France and Germany pledging \$1.6 and \$1.3 billion, respectively, and low-and-middleincome countries (LMICs) also contributed (See Table 1 for the top ten pledges). In Africa, the Government of Nigeria made the highest pledge of \$13.2 million, followed by South Africa and Kenya pledging \$13 and \$10 million. See Table 2 for all the pledges by African Governments. The private sector and civil society organizations, including Bill & Melinda Gates Foundation, RED, Children's Investment Fund, AIDS Healthcare Foundation, Skoll Foundation, and other organizations cumulatively pledged over \$1.2 billion. In over 20 years of its existence, this is the second-largest amount ever pledged to the GF and possibly one of the largest fundraising efforts in global health.20,21 See Fig. 3.

The GF finances health investments via government agencies and local organizations. For instance, in

Countries	Amount
United States of America	\$6 billion
France	\$1.6 billion
Germany	\$1.3 billion
United Kingdom	\$1.2 billion
Japan	\$1.1 billion
Canada	\$ 905 million
European Commission	\$710 million
Sweden	\$274 million
Norway	\$193 million
Denmark	\$50 million

Source: The Global Fund, Pledges and Contributions, generated 15th July 2023 via https://data.theglobalfund.org/ Last updated on 11th May 2023.

Table 1: Top ten pledges to the global fund replenishment (2023–2025).

Countries	Amount (in U.S. \$million)
Nigeria	\$13.2
South Africa	\$13
Kenya	\$10
Congo (Democratic Republic)	\$6
Rwanda	\$3.3
Uganda	\$3
Ghana	\$2
Cote d'Ivoire	\$2
Togo	\$1.5
Morocco	\$1.3
Tanzania	\$1
Zimbabwe	\$1
Niger	\$1
Malawi	\$1
Eswatini	\$1
Burkina Faso	\$1
Central African Republic	\$1

Source: The Global Fund, Pledges and Contributions, generated 15th July 2023 via https://data.theglobalfund.org/ Last updated on 11th May 2023.

Table 2: African government pledges to the 7th global fund replenishment 2023–2025.

Nigeria, the GF has invested over \$3.4 billion since 2012, with the majority of funds directed toward strengthening the country's health system and supporting the delivery of malaria, HIV, and tuberculosis prevention and treatment services to local people who would never have been able to afford nor have access to those healthcare services. Today, HIV has been demystified and destigmatized, with 90% of people living with human immunodeficiency virus (HIV) knowing their status in Nigeria. HIV treatment is now available to about 98% of those who know their HIV status, 95% have suppressed viral loads, and 28% decrease in new HIV infections since 2012.

The impact of GF's health investment across the globe is commendable and needs to be sustained in all ramifications because health financing is a critical determinant of who lives or dies of curable, treatable, and preventable diseases in many poor and low-resource communities of LMICs. Founded in 2000, GF has interesting historical roots in Africa, where the United Nations Secretary-General Kofi Anan made the first explicit call to action for a new funding mechanism at the African Summit on HIV/AIDS, Tuberculosis and Other Infectious Diseases that took place in Abuja, Nigeria, on 24-27 April 2001.23 Secretary-General Anan proposed "the creation of a Global Fund, dedicated to the battle against HIV/AIDS and other infectious diseases." Anan underscored that "this Fund must be structured in such a way as to ensure that it responds to the needs of the affected countries and people, and it must be able to count on the advice of the best experts in the world."24 Secretary-General Anan later donated his \$100,000 Philadelphia Liberty Medal award to GF.²⁵ This donation in July 2001 was recorded as one of the first donations to the GF. As of July 2023, GF pledges and contributions amount to over \$88 billion²⁶ and over \$60 billion in disbursements to the fight against HIV/AIDS, Malaria, and Tuberculosis in more than 80 countries in Africa, the Americas, Asia, Europe, and Oceania.27

While the greater part of GF funding investment goes directly to HIV/AIDS, TB, and Malaria programmes, unknown to many, the GF invests and supports co-infections and co-morbidities associated with ageing, mental health, coronavirus, and other emerging pandemics.²⁸ Therefore, budget lines for cancer prevention and control are possible, such as via HPVrelated cervical cancer and hepatitis-driven liver cancer, as well as health systems strengthening for noncommunicable diseases (NCDs).28 Taking the GF as a marker for the current prioritisation of cervical cancer elimination services, it is commendable that 29 countries, including Ethiopia, Kenya, Nigeria, Togo, and Zambia,29 are starting to access financing support for human papillomavirus (HPV) and cervical cancerrelated interventions. However, these investments are far from a level for the national programming required to reach the 90:70:90 targets.2

What cause fits the description of SG Anan more than eliminating cervical cancer for the first time, a preventable and avoidable disease that is dominating the cancer statistics in Africa due to its causal links with HIV and weak health systems? First, girls and women living with HIV have a higher risk of getting HPV infection and lower chances of clearing the infection.³⁰ Second, this population tends to progress faster from HPV infection to precancer lesions and a higher recurrence following treatment.^{30–32} The consequences are that girls and women living with HIV present with cervical cancer at a younger age and are six times more

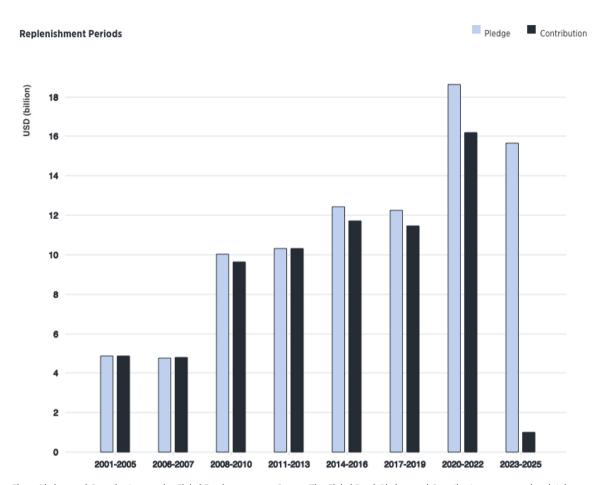


Fig. 3: Pledges and Contributions to the Global Fund 2001–2025. Source: The Global Fund, Pledges and Contributions, generated 15th July 2023 via https://data.theglobalfund.org/ Last updated on 11th May 2023.

likely to develop cervical cancer than women without HIV. On this premise, investing in HIV interventions with the integration of HPV and cervical cancer prevention and treatment yields a remarkable return on investment. WHO estimates that by investing to meet the 90-70-90 targets, an estimated 250,000 women would remain productive members of society, adding an estimated \$28 billion to the world's economy through 2050 (i.e., \$700 million directly through increased workforce participation and over \$27 billion through the indirect socioeconomic benefits of good health).33 We should add here that women and mothers have both crucial economic and social roles in families and communities; hence, their premature death from cervical cancer has intergenerational consequences.34

The sense of urgency expressed by the 2030 targets is responding to the fact that the burden of cervical cancer is increasing in many LMICs as women now survive and live well with HIV and other infectious diseases but die of cervical cancer.³⁵ In Europe, North America, and Australia today, cervical cancer is a rare cause of cancer

death, conversely, recent data from the International Agency on Cancer (2024) show that of 6,600,000 women who developed cervical cancer, 350,000 died from the disease in 2022 and 94% of these deaths occurred in LMICs. 36,37 Cervical cancer is clearly a sad marker of the inequity and inequality of the right to health for girls and women, exasperated by the fact that cervical cancer diagnostic and management services are relatively underfunded compared to infectious diseases in most LMICs. Most of the governments in LMICs are signatories to the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health problem via HPV vaccination of 90% of girls, screenings of 70% of women, and treatment for 90% of women diagnosed with cervical disease (pre-cancer and cancer).2 The reality is that most of the LMICs will likely not meet 50% of these targets without global funding and investment, political commitment, local philanthropic support, and other innovative funding strategies. The competing health needs are high and made worse by the COVID-19 pandemic that pushed many of these countries into or close to recession.

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The GF's 2023-2025 funding cycle and the publication of the 2023 guidance note places cervical cancer as priority three is promising.²⁸ The "2024–2025 Replenishment Traffic Jam" is a time for governments, private sectors, and partners in LMICs to collaboratively expand HPV vaccination, cervical cancer screening, and treatment. Many countries celebrate the November 17th anniversary of the launch of the WHO Global Strategy for the Elimination of Cervical Cancer with awareness activities. Now is the time to go beyond the celebration of anniversaries; high-level policy advocacy by all relevant partners is required to demonstrate demand for the right to cervical cancer prevention services and secure renewed national political will and action towards achieving the 90-70-90 targets. For instance, a few years ago, Rwanda had some of the highest cervical cancer rates in the world38; with government commitment, school-based delivery, and global support, it was reported that the country had reached over 98% HPV coverage and aspires to be the first country in Africa to achieve elimination of cervical cancer.38-40

In parallel, there is an urgent need for country-level accountability in global health financing. Corruption in the health sector is simply stealing from the sick, the weak, and the vulnerable. It places a huge barrier to any progress in achieving any of the Sustainable Development Goals (SDGs).41 Recent reports estimate that of the \$7.35 trillion spent on health care globally, \$455 billion is lost to corruption and fraud. 42-44 The public and civil society organisations in LMICs need to lead advocacy for open governance; government agencies in many LMICs need to be more transparent and put accountability at the fore of their work, including HPV and cervical cancer interventions. Today, the healthcare sectors of some LMICs are in the hands of donor agencies and not the hands of the people or their governments. While most LMICs have competing priorities, it is also important to note that health is the bedrock of other sectors; hence, an investment in health may directly or indirectly translate into investment in different sectors. Innovative financing, such as indigenous private sector and philanthropic investment for health is more urgently needed now than ever, especially in vaccine manufacturing in LMICs. Continuous importation of vaccines may not be sustainable in many LMICs, considering the volume of vaccines needed to serve the population.

The positive lessons of GF, COVID-19 in Africa, and local initiatives should be replicated in HPV and cervical cancer control. The rapid and innovative fundraising initiatives of the Coalition Against COVID-19 (CACOVID) in Nigeria are important examples. CACOVID is a private sector initiative that raised over N30 billion (\$20 million) in 4 months to support Nigeria's Federal Government efforts in combating the coronavirus pandemic. Founded in March 2020, CACOVID was led by chief executives of industries and companies in

Nigeria. Pulling resources from 181 companies and individuals, they built intensive care units (ICUs), distributed thousands of hospital beds, treatment and testing equipment, constructed isolation centres, research and response centres, and provided palliative support to states across the entire country. The coalition had three committees, namely funding, technical, and operational committees. The members of the committees are residents of Nigeria and business leaders, including the richest African man-Aliko Dangote and the richest African woman—Folorunso Alakija.46 CACOVID played a crucial role in Nigeria's effort to control the COVID-19 pandemic and mitigate the effects of the pandemic on Nigerians. Other local initiatives such as Project PINK BLUE's patient engagement and evidence generation from women living with cervical cancer are important ways to show the faces behind the cervical cancer statistics and how the HPV vaccine would have prevented the incursion of cervical cancer in these women.⁴⁷ Similarly, the Aspire Coronation Trust Foundation has invested over \$245,484 in grants for cancer interventions across nine African countries.48 Many other initiatives abound in many LMICs. With the commendable strides and successes of GF, we argue that there is an urgent need for a global fund for cancer control, and LMICs regional blocs like the African Union need to consider the establishment of continental funding mechanisms for cancers, women's cancers, and non-communicable diseases (NCDs).

The impact of CACOVID is evidence that private sectors of a particular community or country can come together to become catalysts and take action to address pressing issues. COVID-19 lessons and infrastructures should be employed in HPV and cervical cancer interventions. Evidence generation and patient engagement should be at the forefront of the interventions for sustainability. Women and girls are surviving HIV and dying from cervical cancer caused by HPV infection35 due to the service gap in the intersection between infectious and non-communicable diseases (NCDs). Health investment in both infectious diseases and NCDs will accelerate the LMICs' capacities to achieve SDGs by 2030. We call for enhanced advocacy to demonstrate demand for the right to prevention and drive national political action to secure global funding, local philanthropic support, and other innovative financing strategies. LMICs regional blocs like the African Union need to recognise the disproportionate impact of cervical cancer within their borders and consider continental funding mechanisms to enable highburden countries to make crucial health systems investments that provide girls and women with the highest risk equal access to prevention and treatment services.

Outstanding questions

More research is needed on innovative funding and financing in LMICs. Many emerging private sector-led initiatives and philanthropists in LMICs are providing funding to non-profits and governments to bridge community health challenges; however, these funding models and approaches are largely underreported. More data and evidence are needed to show how the integration of cervical cancer and HPV into HIV/AIDs interventions is reducing the burden of cervical cancer in LMICs. Understanding the view of government leaders and philanthropists on innovative funding will be crucial in developing the most useful model and approach for sustainability.

Contributors

RCWC conceived the subject of this viewpoint and outlined its contents. RCWC wrote the original draft of this paper. JST and OA provided editorial changes and edited the manuscript. RCWC extracted and analysed the data in this manuscript. JST supervised the writing. All the authors have accessed, verified, and approved the final draft of this manuscript.

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Declaration of interests

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