

Investing in Global Cervical Cancer Prevention Resources for Low-Income and Lower Middle-Income Countries in 2021

- 2021 marked the first full year since Member States of the World Health Organization approved the launch
 of an ambitious strategy in November 2020 to accelerate the global elimination of cervical cancer through
 the scale-up of effective interventions.
- US\$ 94.7 million was invested in HPV vaccination programs and US\$ 66.6 million was invested in cervical cancer screen-and-treat programs in 2021, both representing large increases over 2020.
- Despite these increases, at the current pace only around \$1.6 billion (15%) of the \$10.5 billion necessary
 to achieve 2030 targets for cervical cancer elimination in low- and lower middle-income countries will
 be mobilized.

Cervical cancer's burden speaks directly to global inequities in health outcomes for women in low-resource settings. This preventable disease killed over 342,000 women worldwide in 2020 – 90% of whom resided in low resource settings.¹ Globally, cervical cancer is the leading cause of cancer death among women in 36 countries, with mortality rates in low-resource countries 18 times higher than in high-income countries.² The risk of developing cervical cancer for women living with HIV is six times higher than their HIV-negative peers.³ A recent analysis published in *The Lancet Global Health* estimates that only 8% of women in lower middle-income countries (LMICs) and 11% of women in low-income countries (LICs) have ever been screened for cervical cancer.⁴

To address the rising disease burden, the World Health Organization (WHO) launched its Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem in November 2020.⁵ The Strategy sets specific 10-year targets (e.g., "90-70-90 targets") for scaling up coverage of low-cost, effective cervical cancer interventions:

- Vaccinating 90% of girls against human papillomavirus (HPV) by age 15;
- Screening 70% of women at ages 35 and 45 for precancerous cervical lesions; and
- Ensuring that 90% of those women in need receive treatment for cervical disease.

This report, published annually by TogetHER for Health, provides a snapshot of global funding for implementation of cervical cancer prevention activities conducted in LICs and LMICs. Cervical cancer elimination is only possible with sufficient investment toward these evidence-based, effective interventions. Annual data on investments in cervical cancer prevention programs in LICs and LMICs can inform decision-makers and highlight areas of focus for advocates seeking to increase financial and political support for global elimination efforts. All reported figures are in US Dollars (\$).

Cervical Cancer Screening and Pre-Cancer Treatment

Early detection of cervical abnormalities through screening is a critical component of cervical cancer elimination. The WHO's Elimination Strategy stipulates that women be screened twice, ideally at ages 35 and 45 years, with a high-performance test. Although several screening methods exist, including cytology and visual inspection, the WHO's most recent guidelines recommend primary screening using HPV DNA testing. Notably, HPV DNA testing offers the potential to accurately screen women for high-risk HPV without requiring physical visits to clinics, provided women are given the opportunity to collect and submit vaginal samples (i.e., self-sampling). If women test positive for high-risk HPV and/or pre-cancerous lesions are detected on the cervix, these lesions can be treated using either cryotherapy or

NB: These data do not include research funding or funds allocated for the treatment of cervical cancer. It does include funds allocated for prevention: HPV vaccination, cervical screening, and treatment of pre-cancerous lesions.

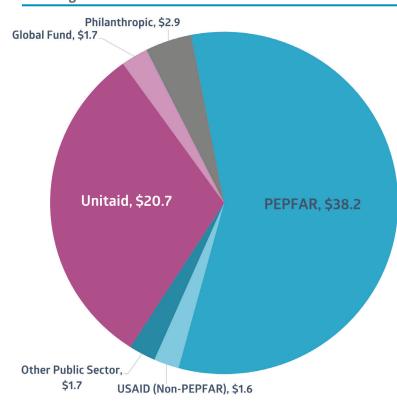


Figure 1. Support for Cervical Cancer Screen-and-Treat in LICs and LMICs totaled \$66.6 million in 2021.

thermal ablation. Women above the age of 50 and those with large lesions are generally referred for colposcopy and/or LEEP (Loop Electrosurgical Excision Procedure). Diagnosed invasive disease should be treated in medical facilities with appropriate cancer treatment capabilities.

Programs enabling access to these services have expanded in recent years, but only around one out of ten women in LICs/LMICs have ever been screened for cervical cancer. Total funding for cervical cancer screening and preventive treatment in LICs and LMICs totaled \$66.6 million in 2021, an increase of 49.2% from 2020. Funding in 2021 was 61.2% above the \$41.3 million three-year funding average for cervical cancer screening and treatment in LICs/LMICs from 2018 to 2020.

The United States government (USG) invests in cervical cancer screening and preventive treatment in LICs and LMICs, primarily through the U.S. Agency for International Development (USAID) and the Centers for Disease Control and Prevention (CDC) as implementing agencies of the U.S. President's Emergency Plan for AIDS Relief (PEPFAR). Starting in May of 2018, PEPFAR investments in cervical

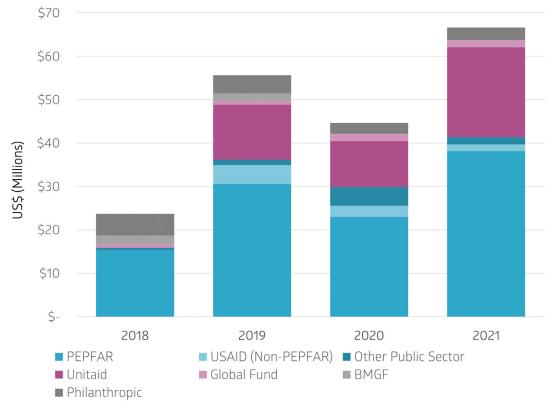


Figure 2. Support for Cervical Cancer Screen-and- Treat in LICs and LMICs increased by 49.2% in 2021.

cancer screening and treatment for women living with HIV were substantially increased under the Go Further program, a public-private partnership organized with the George W. Bush Institute, the Joint United Nations Programme on HIV/AIDS (UNAIDS), Merck, and Roche.⁷

The Go Further program was launched in eight African countries of high HIV burden (Botswana, Eswatini, Lesotho, Malawi, Mozambique, Namibia, Zambia, and Zimbabwe), aiming to screen all women ages 25-49 living with HIV and accessing antiretroviral drugs and, where necessary, treat all precancerous lesions found or refer suspected cancers for further management. In 2021, planned PEPFAR investments through the Go Further program totaled \$38.2 million, a year-to-year increase of 66.0% reflecting a major expansion into four additional countries (Ethiopia, Kenya, Tanzania, and Uganda).8

Other USG investments in cervical cancer screening and preventive treatment in 2021 included \$1.6 million spent in support from USAID and the National Academies of Sciences, Engineering & Medicine, toward the integration of innovative cervical cancer screen-and-treat services into voluntary family planning programs in Malawi and Mozambique under the Partnerships for Enhanced Engagement in Research (PEER) award.9

The multilateral partnership, Unitaid, provided \$20.7 million in 2021, a 95.3% increase of its support for introduction of innovative tools for screening and treatment of pre-cancerous lesions, including innovative service delivery models, HPV self-sampling, HPV testing, and expansion of portable thermal ablation devices, as well as developing an artificial intelligence-based screening tool. Unitaid's investments are implemented in collaboration with the Clinton Health Access Initiative (CHAI) in sub-Saharan Africa and India, and with Expertise France, the Union for International Cancer Control (UICC) and Jhpiego in Côte d'Ivoire, Burkina Faso, Guatemala, and the Philippines.¹⁰

The Global Fund to Fight AIDS, TB, and Malaria supports programs to integrate HIV treatment and cervical cancer services. 2021 represented the second year in the Global Fund's current three-year funding cycle, with a total allotted budget of \$8.1 million over those three years.

20 countries received Global Fund support for cervical cancer prevention services within their HIV prevention programs in 2021, totaling an estimated \$1.7 million for the year.¹¹ Public sector contributions to screen-and-treat programs from non-U.S. countries – the United Kingdom (including the Foreign, Commonwealth & Development Office and Scotland's International Development Fund), Canada, and Japan – fell to an estimated \$1.7 million in 2021. Philanthropic contributions to screen-and-treat programs totaled \$2.9 million in 2021.¹²

HPV Vaccination

Infection by high-risk types of human papillomavirus (HPV), the virus that causes over 99% of cervical cancers, can be prevented by safe and effective vaccines, first introduced in 2006. Most current country guidelines recommend that girls between 9-14 years of age receive two doses of HPV vaccine, although guidance from the WHO Strategic Advisory Group of Experts (SAGE) is being updated based on a review of evidence showing comparable preventive effects from just a single dose of HPV vaccine. (Notably, the same guidance continues to

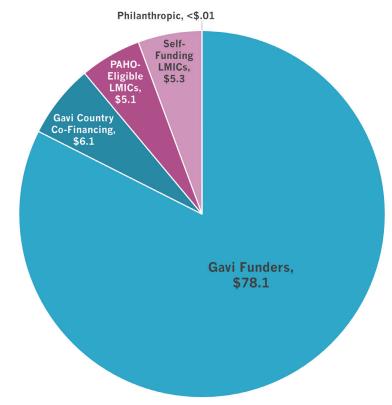


Figure 3. Support for HPV Vaccine Programs in LICs and LMICs Totaled \$94.7 Million in 2021.

recommend three doses for people living with HIV and other immunocompromised individuals.)¹³ Negotiated discounts have made HPV vaccines more affordable to programs in low- and lower middle-income countries, but the lowest available price of \$4.50 per dose is significantly higher than most other vaccines. Only 38% of low- and lower middle-income countries have introduced the HPV vaccine into national immunization programs, compared to more than 89% of high-income countries.¹⁴ 59% of cervical cancer cases occur in countries that have yet to introduce HPV vaccines.¹⁵ COVID-19 continued to disrupt HPV vaccination programs in many countries, with mean coverage of first (46%) and final dose (33%) declining further in 2021.¹⁶

Total funding for HPV vaccination programs in LICs and LMICs for 2021 – including both vaccine procurement and vaccine delivery – is estimated at \$94.7 million, a significant increase of 31.7% over 2020, driven by a \$22 million increase in support for HPV vaccination programs by Gavi, the Vaccine Alliance, alongside increased investment by Gavi-eligible countries co-financing their domestic programs as well as countries accessing vaccines through the Pan-American Health Organization's (PAHO) Revolving Fund. Funding for HPV vaccination in LICs/LMICs in 2021 was 60.4% above the \$59.0 million

three-year funding average from 2018 to 2020.

HPV vaccines for public program use in LICs and in some LMICs are funded by Gavi, the Vaccine Alliance, and procured through the services of UNICEF. 17,18 Gavi expenditures for HPV vaccination in 2021 - including country demonstration projects, national routine immunization programs, and operational costs for multiage cohorts – totaled 78.1 million, 19 with per-dose purchase prices (currently \$4.50 for Merck's Gardasil and \$4.60 for GlaxoSmithKline Biologicals' Cervarix) set through manufacturer offers during the most recent UNICEF tender exercise. HPV vaccine supply is expected to increase in the Gavi 5.0 program from both existing manufacturers and companies entering the market (Innovax, Serum Institute of India, and Walvax). Provided additional supplies are available and the impact of COVID-19 on demand and country uptake is minimized, Gavi aims to vaccinate as many as 84 million girls between 2021-2025.20

Gavi is funded from a diverse group of donors – including the United Kingdom, Norway, the United States, the Bill & Melinda Gates Foundation (BMGF) and the International Finance Facility for Immunisation (IFFIm). Gavi-eligible countries are also required to provide cofunding for routine HPV vaccination programs, with such



Figure 4. Support for HPV Vaccine Programs in LICs and LMICs Increased by 31.7% in 2021.

country contributions totaling \$6.1 million in 2021, an increase of \$1.8 million (41.5%) from 2020.²¹ Many LMICs are ineligible for Gavi support, and thus must procure HPV vaccines via other mechanisms. Middle-income countries (MICs) in the Americas that are Members of PAHO can purchase discounted HPV vaccines at a purchase price of \$9.98 per dose from suppliers through PAHO's Revolving Fund.^{22, 23} In 2021, lower middle-income PAHO Members supported their domestic HPV vaccination programs at an estimated \$5.1 million.²⁴

LMICs outside the Americas are eligible to purchase discounted vaccines for national use from UNICEF, and in some specific cases at the same price as Gavi-eligible countries. Estimated support by non-PAHO/non-Gavi LMICs funding their own HPV vaccination programs totaled \$5.4 million in 2021, a significant decrease (-\$2.1 million) primarily attributed to a large reduction in the number of HPV vaccinations reported in the Philippines between 2020 and 2021.²⁵

Game-Changing Developments Fueling Optimism

Despite the negative impact of COVID-19 on HPV vaccination and cervical cancer screening and treatment programs, estimated overall investments in these programs rose to their highest point since the initiation of this funding analysis. Continued increases in funding for HPV vaccination from Gavi, pre-planned scale-up of the Go Further program, and a near doubling in Unitaid support all reflect the global values underpinning the WHO's elimination strategy and the understanding that each vaccinated adolescent and each woman screened represents one more step toward ending this preventable disease. The possibility that the United States Government will bolster investments in global cancer prevention through its revitalized Cancer Moonshot program may provide another political and financial boost to the elimination agenda.26

Evidence-based developments in the policy space hold the potential to accelerate the elimination agenda. In April of 2022, the WHO's Strategic Advisory Group of Experts on Immunization (SAGE) concluded that a single dose of HPV vaccine provides protection comparable to two- or three-dose regimens.²⁷ A transition to

single-dose HPV vaccination could greatly expand the number of adolescents that can be immunized without expanding vaccine supply, while also removing the significant logistical and financial cost of administering follow-up doses. Alongside the WHO's 2021 update of its global guidance for screening and treatment of cervical pre-cancer lesions listing HPV DNA testing as the preferred screening method,²⁸ the basic pillars of the WHO elimination strategy have begun a shift toward more efficient and effective strategies.

The global supply for HPV vaccines, once a major constraint in ensuring access in LICs and LMICs, is undergoing a rapid expansion thanks in large part to the entry of new suppliers in the market. UNICEF price lists for HPV vaccines have added the Chinese-manufactured Innovax HPV vaccine in 2022 at the per-dose price of \$2.90, 35% lower than Gavi prices for the Merck or GSK HPV vaccines.²⁹ Regulatory approval of the new Cervavac HPV vaccine produced by the Serum Institute of India could speed efforts to ramp up immunization in India, the country with the highest number of annual cervical cancer diagnoses and deaths, with another vaccine likely to be less expensive than current Gavi-negotiated prices.³⁰ The combination of expanded vaccine supply, the potential for continued price reductions due to competition, and a shift to single-dose regimens all portend an accelerated path toward achieving 90% coverage of HPV vaccines throughout the world.

Continued investments into new tools and strategies – which totaled US\$ 98 million in 2020 – are critical to improving and expanding efforts to prevent cervical cancer.³¹ The U.S. National Cancer Institute recently announced plans for new research funding through its HIV/Cervical Cancer Prevention 'CASCADE' Clinical Trials Network. CASCADE aims to conduct pragmatic clinical trials evaluating the effectiveness of proven interventions to optimize cervical cancer screening, management, and precancer treatment cascade for women living with HIV in low- and middle-income countries and in regions with health disparities in the United States.³²

Smaller, targeted support to determine the feasibility of innovative cervical cancer prevention strategies in low-resource settings has also been made available

through the Project to Eliminate Cervical Cancer from the International Federation of Gynecology and Obstetrics (FIGO) and TogetHER's Cervical Cancer Grants Program.^{33,34} Cutting-edge screening techniques using artificial intelligence to identify precancerous lesions are being tested in low-resource settings, as are lower-cost HPV DNA tests and less expensive, easier-to-use treatments.

An Uncertain Future

While optimism in the promise of cervical cancer elimination is warranted, challenges remain. As noted above, COVID-19 disrupted cervical cancer prevention programs in most countries – including high- and upper middle-income economies not represented in this analysis – and uneven progress is being made to catch up to women and girls lacking access to vaccination and screening. 35.36

Policy inaction can hinder progress toward cervical cancer elimination. Thus far only a handful of countries have begun incorporating HPV DNA testing as the primary form of cervical cancer screening. Major funders such as PEPFAR and Global Fund can play a critical role now by facilitating the transition to HPV DNA testing in the programs they support.³⁷

Ongoing financial uncertainty around the world threatens the long-term sustainability of cervical cancer prevention programming. While Gavi and the Global Fund both held successful replenishment campaigns in recent years, past shocks in the global economy have resulted in cuts to global development assistance.³⁸ Already, the United Kingdom has reduced funding for global health programs, including for cervical cancer prevention.³⁹

Access to cervical cancer prevention services in LMICs may once again be hindered by future changes in the composition of the U.S. government, whose outsized contribution to providing global access to these interventions is dependent on congressional appropriation. One area of potential concern is the future of the Go Further program beyond 2023, which hinges on appropriation from a United States Congress whose membership changes every two years. In one positive development, advocacy directed at the United

"Cervical cancer.—The Committee understands
OGAC and USAID are exploring partnerships to
prevent the spread of human papillomavirus and
cervical cancer through screening and treatment
programs in low-income countries with high
prevalence and directs OGAC and USAID to
consult with the Committees on Appropriations
on plans for and progress of such partnerships."
-U.S. State, Foreign Operations, and Related
Programs Appropriations Bill 2022⁴⁶

States Congress resulted in supportive language for global cervical cancer programs in the Department of State, Foreign Operations, and Related Programs Appropriations Act, 2022 (see text box above).

Beyond funding cuts specifically, U.S. policies will also have an outsized impact on access to cervical cancer prevention, which are often tied to the availability and scope of broader reproductive health services. A reduction in cervical screenings has been identified as an impact of the so-called Mexico City Policy or Global Gag Rule, a global policy denying funding for any U.S.-funded program providing abortion services that has been implemented by some recent U.S. administrations but is currently inactive under the Biden Administration.⁴⁰

This concentration of support for cervical cancer screening and treatment in LICs/LMICs from a small handful of funders bears significant risk that retrenchment from these donors will have an outsized impact on funding, and the importance of building a more diverse coalition of support for these lifesaving interventions.

The Case for Investing in Cervical Cancer Prevention

The upswing in financial support for cervical cancer prevention in LICs and LMICs over these past four years should be celebrated as a remarkable achievement, with total funding across vaccination and screening and treatment almost a full \$100 million more in 2021 than was reported for 2018. Yet, even at this unprecedented level, funding levels continue to fall short of estimates for the resources needed to fully fund the ambitious global elimination agenda.

Projections cited in WHO's global elimination strategy estimated that \$10.5 billion in total funding will be needed between 2019 and 2030 to fund HPV vaccination and screening and treatment programs in low- and lower middle-income countries.⁴¹ Estimates for actual funding between 2019 and 2021 – the first three years of the 12-year projections –total \$399.7 million, setting a funding pace of only \$1.6 billion for the 12-year period, approximately 15% of WHO's projected need. (Figure 5.)

Lauding the remarkable increase in funding over the past four years while highlighting a massive resource gap of almost 90% may seem dissonant. An updated analysis of resource needs for cervical cancer elimination may be warranted given the presumably lower projected cost of reaching 90% vaccination coverage of adolescents with single-dose regimens at lower per-dose prices – reducing the largest financial component of estimated need. Yet regardless of models and projections, the reality is this: failing to invest when the means to end a preventable killer of women are at hand puts lives, families, and communities at unnecessary risk.

At the current pace, cervical cancer will end the lives of 3.4 million women in the next decade – akin to wiping out the female population of Hyderabad, India. Almost 1.9 million children will lose a parent every decade to cervical cancer – comparable to the population of Lomé, capitol of Togo.⁴² The loss of mothers, colleagues, civic leaders, and entrepreneurs to a disease that is almost wholly preventable is a global health tragedy.

Beyond the humanitarian imperative, investing in cervical cancer elimination makes fiscal sense. Every dollar invested in cervical cancer prevention and treatment is projected to return at least \$3.20 to the global economy through 2050, making cervical cancer prevention a "Best Buy" for non-communicable diseases (NCDs).⁴³ Achieving WHO cervical cancer elimination goals by 2030 could add \$700 million to the global economy by keeping an estimated 250,000 women across the world participating in the workforce and add as a much as \$28 billion to the global economy through 2050.^{44, 45}

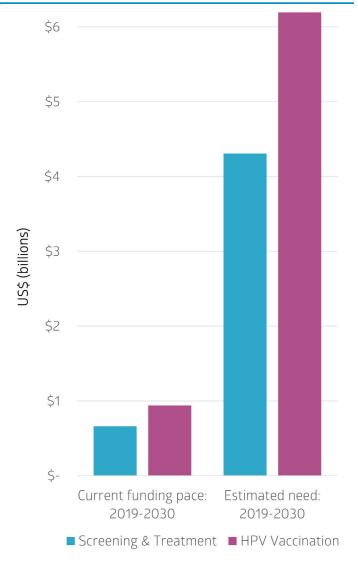


Figure 5. Pace of Funding for Cervical Cancer Prevention in LICs/LMICs (Based on 2019-2021 Data) Compared to Projected Resource Need for Cervical Cancer Elimination in LICs/LMICs 2019-2030.

In the long term, eliminating cervical cancer as a global health problem would not only represent an inspiring, unprecedented global accomplishment. Investments to forever remove this threat to women's health would increase in effectiveness with each successive generation free of cervical cancer. Thus, the financial value of eliminating cervical cancer for the remainder of human history is potentially infinite.

Recommendations

2021 data outlined in this report supports recommendations to critical stakeholders that can better enable the global response against cervical cancer:

 Funders – including government agencies and private foundations – must sustain commitments in cervical cancer prevention programs to preserve momentum toward cervical cancer elimination, prioritize investments that keep programs in lowresource settings apace with global standards of care (including HPV DNA testing), and continue to support development of innovative cervical cancer prevention strategies appropriate for low-resource settings.

Funders can also strengthen uptake of cervical cancer prevention interventions by providing sufficient support for community-led research and implementation efforts, including those combating misinformation and stigma associated with both HPV vaccines and screening and treatment.

Diversifying the donor base through new commitments from high-income countries not yet funding cervical cancer prevention in LICs/LMICs can not only play a role in closing the massive funding gap to fund the elimination agenda. It also can help shield funding levels from catastrophic reductions if major funders reprioritize their support.

Governments in low- and middle-income countries
 should continue to expand HPV vaccine and screen and-treat programs and develop budgeted national
 cancer control plans – following the examples of
 Zambia, Tanzania, Mongolia, and others – that
 incorporate cervical cancer prevention programs
 and enhance disease surveillance through national
 cancer registries. These plans should incorporate
 WHO guidelines emphasizing HPV DNA testing as the
 primary method of screening.

Where prevention programs have experienced delays in vaccine implementation or reductions in screenings, catch-up programs will be critical to get back on track to meeting elimination goals. As vaccine supplies expand, governments should also consider expanding HPV vaccine programs to target boys.

- Vaccine suppliers should increase manufacturing capacity to ensure sufficient supply, and work with procurers to support fair pricing for procurement and distribution of HPV vaccines in LICs and LMICs. As new suppliers continue to enter the field, donors and partners should leverage their purchasing power and competition between manufacturers to advocate for lower vaccine prices while increasing vaccine supply.
- Multisectoral partnerships between donors, countries, and the commercial sector should prepare to invest in the rapid deployment of new approaches to preventing, screening and treating cervical cancer as their effectiveness is demonstrated in low-resource settings.
- Implementers including nongovernmental organizations and private sector partners – should continue to seek synergies in women's health by integrating cervical cancer screening and treatment into existing HIV, family planning, and reproductive health programs.
- Civil society must continue to inspire policymakers, funders, and implementers to make cervical cancer elimination a signature generational effort, arguing for evidence-based strategies to ensure access to cervical cancer prevention regardless of geography.

Methodology and Request for Data

Data included in this brief have been compiled from multiple sources, including documented budgets, data on HPV vaccine administration, program disbursements, and funding information obtained directly from donors and implementers. This brief provides a high-level aggregate of global funding data; the authors acknowledge that such aggregation can reduce the visibility of specific country and regional contexts for cervical cancer prevention programs. TogetHER seeks feedback and contributions from donors, experts and advocates to expand our sources and to improve future iterations of this analysis. Please contact us at info@togetherforhealth.org.

This brief was written by Tom Harmon with Heather White of TogetHER. TogetHER would like to acknowledge the efforts of individuals who contributed data and review assistance to this project. This analysis would be impossible without their support.

TogetHER for Health is a global partnership igniting the movement to end cervical cancer everywhere around the world by driving awareness, supporting catalytic programs, and fighting for the political and financial resources needed to end this preventable disease.

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