

'Biggest killer' cancer thwarted by home tests, AI

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Adolescent girls ages 11 to 13 receive HPV Vaccination in Sao Paulo Brazil. This image has been cropped. Credit: HR@PAHO/WHO, CC BY-ND 2.0

Ugandan street vendor Saudah Namutebi found out about cervical cancer one day when she was listening to the radio.

"During a radio talk show a doctor was urging women to go and screen," says Namutebi. "I have never gone because I don't have time. And I don't

know where to go and get screened."

Fellow trader Madina Nakku, who sells fruit on the roadside in Entebbe, says she has no need to get checked for [cervical cancer](#). "I do not feel sick, no itching down there or anything. Why should I go for screening when I am feeling fine?"

Cervical cancer is preventable and curable. Yet it remains the leading cause of cancer death for women in many developing countries, and researchers say the burden of cervical cancer is an important indicator of global health inequality.

While some [wealthy countries](#) are making progress towards eliminating the disease, in line with global goals to significantly reduce rates by 2030, screening rates remain low in many [poorer countries](#), where access to services is limited and social taboos can deter women from seeking healthcare.

But, major breakthroughs in diagnostics and a newly approved [vaccine](#) could significantly reduce cervical cancer rates in the global South.

The cervical cancer challenge

Cervical cancer disproportionately affects women in low- and [middle-income countries](#). It is estimated that [85 percent](#) of the 570,000 new cases and 311,000 cervical cancer deaths in 2018 occurred in developing countries. Cervical cancer was the leading cause of cancer-related death for women in Sub-Saharan Africa, central America, south central Asia, and Melanesia.

Last year, the World Health Assembly endorsed the WHO's global [strategy for cervical cancer elimination](#). It calls for 70 percent of women globally to be screened regularly for cervical cancer with a high-

performance test—a rate that less than 20 percent of countries currently meet.

The WHO says that the global strategy, which recommends vaccinating 90 percent of girls under 15 against [human papillomavirus](#) (HPV), which causes nearly all cervical cancers—could prevent a staggering [62 million cervical cancer deaths](#) in the next 100 years.

While it is known that the cervical cancer burden is highest in the global South, the true numbers may be undercounted where women's health is overlooked by governments, or where data is poor.

Data coming from the 22 countries that make up the WHO's Eastern Mediterranean region—which includes the Middle East and North Africa, parts of central Asia, Djibouti and Somalia—suggests low rates of cervical cancer in those communities. But this could be due to poor diagnosis and reporting, with deaths attributed to secondary cancers that develop after cervical cancer.

Only one of the 22 countries in the region has implemented a HPV vaccine program, says Nasim Pourghazian, WHO Eastern Mediterranean technical officer for noncommunicable disease prevention, while only nine countries offer cervical cancer screening services, "of which most are opportunistic."

"One general problem with cancer registries in the region is the lack of communication between national cancer registries and death registration systems, which can also contribute to the low death rate attributed to cervical cancer," Pourghazian says.

"When you compare the number of deaths to the number of cases in the region—the mortality to incidence ratio—then our region has a significantly higher rate than the global average."

Culture and knowledge

A major challenge in Sub-Saharan Africa—which carries the world's [highest burden of cervical cancer](#)—is widespread lack of understanding about the disease.

Bernard Sawadogo, from the African Field Epidemiology Network, told SciDev.Net that most women were uninformed, with many believing that cervical cancer cannot be cured.

Christine Nakimuli, who works at a private clinic in Uganda's capital Kampala, said: "I ask women who come for any vaccine if they have had the HPV shot. Those who know about it say it is for young girls who are virgins. I encourage them to test anyway despite the age, and if they are negative to get vaccinated."

Social and cultural norms play a major role in the likelihood that a woman will go to be screened, particularly when health staff are male. Joyce Zalwango, a palliative care nurse in Uganda, said: "Most women are scared of who they will find when they go for screening—they do not want men to screen them."

Sawadogo says women who live in rural areas often need authorisation from their husbands in order to go for screening.

Emmanuel Bukalu, a reproductive health specialist and a consultant at the Uganda National Expanded Program on Immunization, says clinics always try to ensure a woman is present.

"If it gets to the stage of screening, then we maximize the use of females and even if it is a man we want a female counterpart to be present," says Bukalu. However, he says that most women are unaware of this rule.

Yet Zalwango says that, while female staff should perform smears, most health facilities are understaffed and a woman is often unavailable, particularly in remote areas.

Meanwhile, Ugandan hairdresser Aisha Nakitende said reports that the screening process was uncomfortable put her off from getting checked.

"I heard from a friend how she was screened and she said it was very painful," said Nakitende.

"Is there no other way they can screen for it?"

Do-it-yourself testing

At-home HPV tests are "poised to be a game-changer," according to Karen Canfell, director of cancer research at the Cancer Council NSW, Australia's leading cancer charity, and an adjunct professor at the University of Sydney's medical school.

Recent evidence has shown that self-collected vaginal swabs to check for the presence of HPV can be similarly accurate to clinician-collected swabs, when a polymerase chain reaction (PCR) test was used, she said.

"The potential of self-collection is immense," Canfell tells SciDev.Net. "Women worldwide are embracing the self-determination that it enables."

Self-sampling could be used to reach women in low- and middle-income countries who have never been screened for HPV or cervical cancer.

The WHO's cervical cancer screening and treatment guidelines, released in July, suggest samples can be self-collected or taken by a healthcare provider, as both methods "may have similar effects."

A [study published in June](#) in the *Medical Journal of Australia* found that some participants in Australia's initial self-collection program said they would not have been screened had the option to self-screen not been available.

A [systematic review](#) of the literature, primarily in high-income countries, found that HPV testing by self-sampling was likely to improve screening uptake, although the WHO says that some healthcare providers perceived that self-sampling could reduce their opportunities to provide additional care.

"Self-collection underpins several major initiatives to eliminate cervical cancer in low- and middle-income countries, such as the Western Pacific, where there has been a lack of any cervical screening or HPV vaccination programs and limited access to cancer treatment services," Canfell says.

Australia will expand the option of self-collection to all women from July 2022. "Australia is already on track to be the first country in the world to eliminate cervical cancer, but with self-collection as a universal option, we should get there sooner and in a more equitable way," says Canfell.

"We know there are significant barriers to cervical screening for many women and people with a cervix, particularly Aboriginal and Torres Strait Islander peoples, culturally and linguistically diverse people, and gender and sexually diverse people.

"Self-collection gives women more choice and control in the screening process, and should help to overcome some of these barriers."

Vaccine success

Successful HPV vaccine programs can lead to remarkable drops in cervical cancer rates, studies are now finding.

[Analysis published in *The Lancet*](#) in October found that cervical cancer rates were 87 percent lower for women in England who were offered an HPV vaccine between the ages of 12 and 13 than in previous generations.

Study co-author Peter Sasieni, from King's College London, said the observed impact of England's HPV vaccine program was "even greater than the models predicted."

Gavi, a global vaccine alliance, says the high cost of vaccines and the challenges of reaching adolescent girls worldwide have been barriers in low-income countries.

Gavi is a public–private partnership that aims to increase immunization access in poor countries. It says that 27 countries have been approved for HPV vaccine support, with 18 beginning programs—including countries with the highest cervical cancer rates such as Malawi, Uganda, Tanzania and Zambia.

The Gavi HPV vaccine program aimed to reach 40 million girls by 2020, however "surging global demand and vaccine supply shortages" mean the alliance has reduced this goal to about 14 million girls.

Fourth HPV vaccine

But now, it is hoped that a fourth HPV vaccine prequalified by the World Health Organization in October will increase supply worldwide.

A WHO prequalification is a 'seal' that attests that a vaccine meets safety and efficacy standards. Countries that do not have regulatory agencies

use this prequalification to ensure that vaccines are safe.

"With a WHO prequalification, a vaccine can enter the market more easily. It can be included in funds that buy vaccines in larger quantities to distribute them among countries," says Renato Kfourri, president of the Brazilian Pediatric Society's Scientific Department of Immunisations. "Foundations that distribute vaccines around the world use vaccines that were prequalified, which favors its use in countries even if they don't have full approval."

The new vaccine is Cecolin, manufactured by China's Xiamen Innovax, a subsidiary of Beijing Wantai Biological Pharmacy. Cecolin was licensed in China in 2019. It is a bivalent vaccine, which means it is active against two types of the human papillomavirus—HPV types 16 and 18, which are the cause of more than 70 percent of cervical cancers.

The three previously approved HPV vaccines are the bivalent Cervarix, the quadrivalent Gardasil—which is active against four HPV types—and the nine-valent Gardasil 9, which also prevents genital warts.

All of the vaccines protect against HPV types 16 and 18.

"Rich countries have abandoned [the bivalent vaccine], because they can buy the quadrivalent and are migrating to the nine-valent," says Kfourri. "But the bivalent vaccine is still being widely used around the world, in South-East Asian and African countries, for instance.

"It is nice to have this bonus [protection] in the quadrivalent vaccine, but the main goal is to prevent cancer, and the protection against 16 and 18 HPV types is the same in both vaccines."

A key difference for developing countries is expected to be cost-related.

Researchers from South-East Asia [reported in *The Lancet*](#) that Cecolin was priced at around US\$50 per dose in China, while Cervarix could cost around \$260 for three doses, Gardasil cost about \$360 for three doses and Gardasil 9 was \$586 for three doses.

Cost of care

News of the fourth WHO-approved HPV vaccine has delighted health advocates in Burkina Faso, where the government had promised the introduction of the Gardasil vaccine for girls aged nine to 14.

The Gardasil vaccine is available at pharmacies "at an exorbitant price," says Djeneba Ouédraogo, president of Yerelon, a research and support organization. "The dose[s] cost US\$200. However, two doses were needed. The population could not afford this vaccine.

"We had made a plea and the government and its partners had agreed to finance the vaccine," says Ouédraogo. But, she said they were still waiting for the government to launch the vaccination campaign.

While screening has been made available at no cost in Burkina Faso, uptake remains low according to Issoufou Bélem, from the country's cancer sufferers' group l'Association des Femmes Atteintes et Affectées par le Cancer (AFAAC).

Ouédraogo attributes this to a range of issues, including a shortage of trained staff and equipment, while women report avoiding screening because of the fear that cancer will be discovered.

Prohibitive treatment costs are a major concern in Burkina Faso. Madjara Cissé was diagnosed with cervical cancer last year, but she is unable to pay her medical bills.

"The doctor asked me to start chemotherapy, but I have no money. Before discovering my illness, I was able to save US\$1000. I had a first chemotherapy session, but for lack of funds, I stopped," she tells SciDev.Net.

Bélem, whose wife had cervical cancer, said: "Just for the exams I spent more than US\$200 per month, without taking medication into account."

Artificial intelligence

Machine learning could revolutionize the process and cost of cervical cancer screening in low-income communities.

Last month the WHO released a first-of-its-kind [framework for research into artificial intelligence](#). Special adviser to the director-general, Princess Nothemba Simelela, said that AI-driven tools will be the "game-changer" for low- and middle-income countries battling cervical cancer.

The global strategy to accelerate the elimination of cervical cancer says that initiatives to secure affordable, high-quality diagnostics and related supplies should be prioritized. As AI improves, it could allow medical providers to make faster, more accurate diagnoses, and the WHO suggests that AI could be harnessed to quickly detect both cervical and breast cancers.

Unitaid, a United Nations agency for improving diagnosis and treatment of infectious diseases in developing countries, launched a partnership with the Clinton Health Access Initiative in 2018 to test AI-based screening tools in India, Kenya, Malawi, Rwanda, South Africa and Zambia.

Unitaid executive director Philippe Duneton said: "We believe that by the end of 2022 we could be on track to treat over 1 million women."

He said despite COVID-19 interruptions the project was still aiming to produce a test-and-treat tool for US\$1 per woman. The \$33 million Unitaid project is deploying improved screening tools and introducing new portable devices for treatment, along with a phone application that uses artificial intelligence to detect signs of cancer.

Johan Lundin is a research director at the Institute for Molecular Medicine Finland and a professor at the medical research Karolinska Institute in Stockholm, Sweden. He told SciDev.Net that artificial intelligence could save pathologists hours of time currently spent analyzing cell samples.

Lundin and research partners in Kenya reported success with a proof-of-concept digital microscopy with artificial intelligence–based study. Cervical smear results from 740 women were collected and digitized, then analyzed with a deep learning algorithm. The [peer-reviewed results](#) showed the AI was 96 percent accurate.

"The AI seems to be more efficient since it can run through the entire sample at high magnification," Lundin says. "Human experts typically view only a part of the sample, because it would otherwise take too long. The AI can look at each and every corner."

When combined with human oversight, Lundin's cloud-based tool was powerful and fast, he said. "Analyzing a sample, a human expert typically spends about ten minutes or more. AI analysis takes a few seconds—less than a minute—once it's scanned with a digital microscope scanner, which takes a few minutes," he said.

Scans are viewable from anywhere in the world, but Lundin said the plan was to make the digital diagnostic tool locally sustainable, using Kenyan pathologists.

The team has received two grants to continue research, which will include determining cost effectiveness, and Lundin hopes that the service could become more widely available in the not-too-distant future—perhaps within five years.

Sweden has an average of around 30 pathologists per one million people, Lundin said, where many countries in Africa had less than one pathologist per million. He said he expected that the implementation of AI diagnosis would be fastest in resource-limited settings.

"Once the AI has matured and there is consensus that this reaches a high enough accuracy, then that is for sure a revolution in how you can provide services in settings where you don't have experts," Lundin said.

Strategies and campaigns

Health authorities will need to develop multi-pronged strategies to eliminate cervical cancer as a public health burden, say medical staff as well as patients. Gavi says that immunization against HPV infection, coupled with screening and treatment, is the best strategy to rapidly reduce the burden of cervical cancer.

Bélem in Burkina Faso says that if the WHO can help poor states like his to increase uptake of the newly approved HPV vaccine, countless lives will be saved. Fellow Burkinabe Hamidou Compaoré, from Doctors of the World, believes that artificial intelligence and the additional approved vaccine will drive down cervical [cancer](#) rates. But he says that communication will be critical to success.

"Populations are wary of anything that is free, especially for vaccination," Compaoré says. "They think that it's because it's not good that it's free."

For Yerelon's Ouédraogo, success will come through strengthened health systems and human resources: "Today, in Burkina Faso, we need more health workers and state support."

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