

Reaching teenagers with three-times jab is a first for most countries

Now that the GAVI Alliance has agreed to subsidize the HPV vaccine, many low-income countries have the chance to roll out the HPV vaccine nationally – an opportunity for women's health. Patrick Adams reports.

In May 2010, the tiny mountain kingdom of Bhutan made very big news. By partnering with the pharmaceutical company Merck & Co. and the Australian Cervical Cancer Foundation, Bhutan became the first developing country to roll out a national vaccination programme against the human papillomavirus (HPV), the main cause of cervical cancer.

In the two and half years since then, others have followed suit. In 2011, Rwanda became the first country in sub-Saharan Africa to roll out HPV vaccination. A year later, Uganda launched the first phase of its national HPV vaccination introduction in September, aiming to reach girls in primary grade four – most between the ages of nine and 12 years – in 14 of the country's 112 districts in 2012, a further 40 districts in 2013 and full national rollout in 2014.

A 2008–2009 pilot points the way ahead, says Dr Emmanuel Mugisha, country manager for non-profit health organization PATH that is partnering with the Ugandan government in the pilot and, now, the national rollout in the east African country of 34.5 million.

"We found that we reached more girls by selecting them by grade rather than age, that it's feasible and cheaper to deliver the vaccine alongside other packages targeting schools," Mugisha says, referring to packages such as vitamin A and deworming medications distributed by health workers during the twice-yearly Child Days Plus programme. "Delivering it at the same time each year aids planning of health worker time and space in the cold chain while reducing disruption in schools."

Uganda has high school attendance rates, but some girls do not go to school and among those who do, there is a fair amount of absenteeism, so mop-up campaigns are also needed. "These girls may fall between the cracks or be lost to follow up, so we are developing a plan to urge them to go for HPV vaccination at the nearest health facility," Mugisha says.

Another worry for the Ugandans is that a full nationwide rollout beyond the initial 14 districts could be jeopardized by a lack of funds. "You need timely planning and implementation to ensure that vaccines are on hand when they are needed," Mugisha says. "But the Ministry

of Health and local government districts have in the past faced delays in funding which can, in turn, delay delivery of subsequent HPV vaccine doses."

Uganda and Bhutan are just two of some 40 countries that have included the HPV vaccine in their national vaccination schedules. Most are in the developed world, but with last year's announcement that the GAVI Alliance would subsidize the HPV vaccine, more low-income countries will be able to afford to immunize girls against HPV and join their ranks.

Dr Andreas Ullrich, cancer expert at the World Health Organization (WHO), calls GAVI's decision "a major step forward" for implementing WHO guidance. WHO recommends a comprehensive approach to cervical cancer prevention and control, of which vaccination is but one part. HPV vaccination should not divert resources from cervical cancer screening programmes.

The GAVI decision, Ullrich says, moves forward "the spirit of the United Nations (UN) High-level Meeting

on Non-Communicable Diseases" in September of last year, which aimed to generate greater awareness of the global burden of NCDs, shine a spotlight on new initiatives to combat them and shape the global health agenda for future generations.

The second most common cancer in women worldwide, cervical cancer affects close to half a million women ever year, killing an estimated 275 000 of them. About 77% of new cases and 85% of deaths occur in the developing world, where cancer screening and treatment services are scarce. The majority of cervical cancer cases are linked to infection with HPV and, while most sexually-active people become infected with HPV without realizing it and most such infections resolve without consequences, persistent infection of high-risk HPV types for more than a year increases the likelihood that a woman will develop cancerous lesions.

The two HPV vaccines currently available, GlaxoSmithKline's Cervarix and Merck's Gardasil, both target HPV



A girl, aged about 12 years, is being vaccinated in Ibanda district at a primary school

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types 16 and 18 and, thus, can avert an estimated 70% of cervical cancer cases. Whether they can accord any protection against the remaining 30% of cervical cancers caused by other HPV types is still being studied.

Since their approval over the last decade, more than 120 countries have licensed one or both vaccines for use and in 2009, WHO prequalified them under a system that guides the procurement decisions of UN agencies and others that buy in bulk to make quality priority products available to those in need.

In June of last year, Merck offered to sell Gardasil to the GAVI Alliance for US\$ 5 per dose and most of the 57 countries that are eligible for GAVI support would contribute only US\$ 0.20 a dose of the purchase price, according to Nina Schwalbe, Managing Director of Policy and Performance at GAVI. A tender is under way and GAVI has assurances from at least one manufacturer that an even lower price will be offered. GAVI would then start rolling out the vaccine to countries in 2013.

Still, for many developing countries, acquiring the vaccine is but one step towards the successful implementation of a national programme, a complex undertaking rife with logistical challenges.

“It is still early in the global HPV vaccine introduction process,” says Dr Susan Wang, a Medical Officer who works on immunization at WHO. “How to implement HPV vaccination successfully, affordably and sustainably in all countries is still being examined and we are still learning.”

HPV vaccine delivery, say experts, is unlike anything most immunization programmes have previously done before. But every challenge comes with new opportunities. “HPV vaccine offers countries the exciting opportunity to

galvanize new stakeholders and partners who are new to immunization and who are not the traditional child health partners of immunization programmes, but who bring experience from the fields of adolescent health, school health, women’s health, reproductive health, HIV prevention and treatment, cancer control, and NCDs,” says Wang.

With new partners, their ideas and their support, solving the challenges of sustainable HPV vaccine delivery in developing countries can be pivotal in making global progress in two major areas, she says: one, routinely delivering health services and health promotion messages to 9 to 13 year olds and two, preventing and controlling cervical cancer.

“Advances in those two areas are the phenomenal life-changing opportunities that HPV vaccine offers us, when we succeed,” says Wang.

But, while ultimate success may seem a long way off for some, there is “plenty of evidence to show that with good planning it is possible to deliver the HPV vaccine without severe logistical challenges,” says Dr Scott LaMontagne, country research manager for the PATH-supported HPV vaccination pilots.

One of the ways countries are deciding whether and how HPV vaccination should be introduced is by doing pilot studies of various delivery strategies, LaMontagne says, adding that already 26 countries had run such programmes and were building up a solid evidence base in the process for future decision-making.

Factors that proved critical to successful coverage include education and outreach in communities with little knowledge of the disease, establishing reliable cold chains, and targeting a new population that seldom accesses health services with a new service to be routinely delivered three times within a six-month time period, he says.

Rwanda, one of Uganda’s neighbours, introduced school-based HPV vaccination in 2011 in partnership with Merck, which donated two million doses of its vaccine Gardasil for a complete national rollout in the country of some 11 million people. It is part of Rwanda’s ambitious effort to eliminate cervical cancer by the year 2050.

So far, say health officials there, that effort has met with success. “This is a shining example of what is possible through a public-private partnership,” says Rwandan Minister of Health Dr Agnes Binagwaho.

Meanwhile, in the neighbouring United Republic of Tanzania, local physicians and researchers from the London School of Hygiene and Tropical Medicine and the Tanzanian National Institute of Medical Research evaluated school-based strategies for the delivery of HPV vaccination. Like the pilot in Uganda and the national programme in Rwanda, the Tanzanian study found that these were highly effective, so effective – the researchers point out – that they “achieved better coverage than programmes in countries such as Denmark, the Netherlands and the United States of America, which rely on health-centre visits, on-demand vaccination and private sector provision.”

The experience of the three low-income countries – Rwanda, Uganda and the United Republic of Tanzania – underscores the complex challenges posed by HPV vaccine introduction in poor countries and the rigorous pre-planning needed to ensure that scaling up is done in a sustainable way. That is why GAVI’s support is not limited to vaccine purchasing, says GAVI’s Schwalbe.

“We support health system strengthening, for example, training health workers or upgrading cold chains,” she says. “We are also focused on sustainability of programmes and our co-financing model (with countries) helps with this.”

However, aside from a one-time vaccine introduction grant from GAVI, countries must cover the cost of vaccine delivery themselves.

“There is no continuing support for vaccine delivery, even for eligible countries,” says Wang. “And this is an important cost that countries need to address.” For any programme, she says, “the proof of success will be in its duration”.

Although proof of concept on a small scale is encouraging, Wang adds, “that doesn’t mean it will be easy to do nationally or for a long time without adequate resources. And that’s the concern; people often ask ‘Why aren’t more countries introducing HPV vaccine nationally? And the reason is that HPV vaccine delivery requires creating new routine health service delivery to a new target population – in other words, delivering HPV vaccine requires health systems strengthening on a scale that is different from when a country introduces a new infant vaccine. And that is challenging, no question.” ■

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Health worker fetches the HPV vaccine from a fridge at a health centre in Ibanda district