

Human papillomavirus (HPV) vaccine market shaping roadmap



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Read the article: <https://www.gavi.org/vaccineswork/bangladeshs-first-public-hpv-vaccine-roll-out-gathers-momentum>

Executive summary

Cervical cancer is the fourth most common cause of cancer and cancer death in women worldwide. [More than 348,000 women](#) die from this disease every year, and more than 90% of these deaths occur in low- and middle-income countries.

Yet cervical cancer is largely preventable. More than nine in ten cases are caused by human papillomavirus (HPV), for which we have a highly effective vaccine. The first HPV vaccine was granted regulatory approval in the United States of America in 2006, and it has been shown to be safe and effective in preventing cervical cancer.

For every 1,000 children immunised with the HPV vaccine, an estimated 17.4 deaths are averted, making it one of the most impactful vaccines supported by Gavi, the Vaccine Alliance. One modelling study found that 4.7 million deaths could be prevented in the 194 World Health Organization (WHO) member countries during 2021–2030, if Immunization Agenda 2030 (IA2030) coverage targets were reached.

In the decade or so after Gavi began funding HPV vaccine introductions and campaigns in 2012, significant supply-demand imbalances slowed progress. However, more recently, vaccine supply constraints have eased, thanks to the Alliance's market shaping activities and the efforts of manufacturers. Total supplies are expected to triple between 2022 and 2025. It is within this context that, in December 2022, Gavi revitalised its HPV vaccine programme, bringing its total investments to US\$ 600 million by the end of 2025, and set an ambitious goal to immunise 86 million adolescent girls by the same date.

While progress has been made in the creation of a healthy HPV vaccine market, there remains a range of challenges and uncertainties relating to supply, demand and the policy environment. Market shaping is a long-term undertaking, and further interventions are likely to be required to help establish a well-functioning, stable HPV vaccine market over the next decade.

Gavi currently provides eligible countries with support in funding three vaccines, two of which contain two types of HPV, while the other contains four types. They all protect against the main causes of cervical cancer. In 2022, WHO reported that all currently licensed vaccines, whether they protect against two, four or nine types of HPV, provide comparable efficacy in preventing cervical cancer. To help prevent cervical cancer cases and deaths, Gavi's priority is the launch of national HPV vaccination programmes, and for high vaccine coverage to be achieved and sustained using currently available products, regardless of how many types of HPV they contain.

The Vaccine Alliance's core market shaping partners – WHO, UNICEF, the Bill & Melinda Gates Foundation and the Gavi Secretariat – published an [updated Market Shaping Roadmap for HPV Vaccines](#) in December 2023. This insight paper provides a non-technical summary of that document. It highlights how working towards a series of key objectives and target outcomes can help achieve a healthy HPV vaccine market, and how doing so can play a major role in turning the ambitious vision of consigning cervical cancer to history into a worldwide reality.



Credit: Gavi/2023/Peter Caton

Read the article: <https://www.gavi.org/vaccineswork/zambia-launches-major-hpv-vaccine-campaign>

1 Introduction: Mapping out a path to cervical cancer elimination

Human papillomavirus (HPV) is a common, sexually transmitted virus that infects more than 80% of people by the age of 45. While HPV infection does not result in symptoms in most people, it can cause a number of different cancers, including [the vast majority](#) of cervical cancer cases. There were estimated to be [more than 661,000 cases of cervical cancer and more than 348,000 deaths from the disease](#) globally in 2022, making it the fourth most common cause of cancer and cancer death in women. More than 90% of deaths from cervical cancer occur in low- and middle-income countries.

The first HPV vaccine was licensed and approved for use in women and girls aged 9–26 years by the US Food and Drug Administration (FDA) in 2006. Since then, three additional HPV vaccines have been both approved by regulators and prequalified by WHO for procurement by UN agencies. All four have been shown to have good safety profiles and to be [highly effective in preventing HPV infection and HPV-related disease](#), including cervical cancer.

For every 1,000 children immunised with HPV vaccine, an estimated 17.4 deaths are averted, making it among the highest impact vaccines supported by Gavi. A modelling study published in 2023 by researchers at the University of Washington in Seattle, Imperial College London and WHO estimated [4.7 million deaths could be averted during 2021–2030](#) in the 194 WHO member countries if coverage targets set out in the Immunization Agenda 2030 (IA2030) were reached.

WHO has recommended the use of HPV vaccines in adolescent girls for the prevention of cervical cancer since 2009, initially on a three-dose schedule and then, from 2014, on a two-dose schedule for those aged under 15 at dose one. In April 2022, WHO issued a permissive recommendation for a one-dose HPV vaccine schedule after its Strategic Advisory Group of Experts on Immunization (SAGE) found that [a single dose provides comparable protection against HPV to two and three doses](#). Research has shown this equivalent level of protection [lasts for at least ten years](#).

Gavi began funding HPV vaccination programmes in 2012, although demand was lower than expected between then and 2016. Initially, Gavi encouraged

and worked with countries that lacked experience in delivering vaccines to young adolescents, to complete demonstration or pilot programmes in preparation for national introduction programmes.

This enabled countries and external partners to gain valuable experience in areas including planning, budgeting, defining delivery strategies and community consultation. However, it also led to lower demand than had previously been expected, which in turn led to reductions in supply and production capacity.

In October 2016, WHO recommended HPV vaccination of a multi-age cohort (MAC) of girls aged 9–14 years when countries first introduce HPV vaccine to achieve wider primary protection, quicker herd protection and economies of scale. In December 2016, Gavi redesigned its HPV vaccine programme to allow countries to apply for support for national introductions without the need for demonstration programmes and to enable MAC vaccination from the start. These developments, in combination with [WHO's call in 2018 for action towards the global elimination of cervical cancer](#) and the introduction of vaccination programmes for boys in higher-income countries, triggered a surge in global demand which could not immediately be met by available supply.

Gavi engaged in significant market shaping (see “What is market shaping?” box below) to help stimulate investments to increase production capacity and new product development. Improved vaccine supply and WHO's permissive recommendation of a single-dose HPV vaccine schedule led, in December 2022, to the Gavi Board approving a revitalisation of the Alliance's HPV vaccine programme. This provided an extra US\$ 142 million of funding to bring its total investment to US\$ 600 million by the end of 2025.

Gavi also set ambitious targets to reach 86 million adolescent girls by 2025 and avert more than 1.4 million future deaths from cervical cancer. By the end of 2022, Gavi had supported the vaccination of 16.3 million girls to protect them against cervical cancer; and by the end of 2023, it had supported the introduction of HPV vaccine into the national immunisation programmes of 38 countries.

In 2023, Gavi worked with populous countries such as Nigeria and Bangladesh to introduce the vaccine into their routine immunisation programmes. Through these efforts, more than 16 million girls in Nigeria and more than 10 million in Bangladesh could be reached by 2025. Careful planning is needed to ensure countries have the supplies they need in time to implement their programmes, however recent forecasts suggest the Alliance is on track to achieve its target of immunising 86 million girls with HPV vaccine by 2025.

New suppliers are expected to enter the market and overall supply is predicted to meet demand in 2025. At this point, there will be enough HPV vaccine doses not just for the 54 Gavi-eligible countries, but also the 46 countries eligible for support under [Gavi's Middle-Income Countries \(MICs\) Approach](#), which is designed to prevent backsliding in vaccine coverage in former Gavi-eligible countries and to drive the introduction of key vaccines that are not widely available in both former and never Gavi-eligible countries.

As of December 2023, there are three WHO-prequalified HPV vaccines in Gavi's vaccine portfolio: GSK's Cervarix and Inovax's Cecolin, both of which protect against two types of HPV (HPV2); and Merck's Gardasil, which contains four types of the virus (HPV4). Research has shown all currently licensed vaccines provide comparable efficacy in preventing cervical cancer, irrespective of whether they contain two, four or nine types of HPV. Demand is, however, currently skewed towards Gardasil, at least partly because of the protection it provides against genital warts that the HPV2 vaccines do not.

Two more HPV vaccines are expected to be prequalified by WHO during 2024 and 2025. This should enable improved balancing of demand with appropriate products and greater ability to supply products according to country preferences – both key attributes of healthy markets. Merck's Gardasil9, which protects against nine types of HPV (HPV9), is also prequalified by WHO but is not yet in Gavi's portfolio. Other HPV9 vaccines are in development.

What is market shaping?

When it comes to vaccination, market forces have often failed to serve the interests of people in lower-income countries. Uncertainties around costs and demand reduce incentives for manufacturers to invest in new vaccines at affordable prices for lower-income countries. As a result, vaccines have often only become available in low- and middle-income countries long after they have been introduced in wealthier countries.

Addressing vaccine market failures has been key to Gavi's success in expanding childhood immunisation since the Alliance was launched in the year 2000. Since then, Gavi has helped create healthy, sustainable vaccine markets through a deliberate market shaping approach which aims to foster: a sustainable and competitive supplier base; healthy demand driven by a supportive environment; and an environment that encourages transformational innovation.

Gavi has a successful track record of devising and implementing interventions to achieve these goals

in ways that improve the supply of vaccines for infectious diseases and other immunisation products at affordable, sustainable prices for both lower-income countries and vaccine manufacturers. These include:

- incentivising innovative product development;
- working with Gavi implementing countries to improve the accuracy of demand forecasting;
- designing innovative procurement mechanisms, including leveraging high demand to reduce prices to sustainable levels;
- bilateral and multi-party risk-sharing agreements;
- using discretion to accommodate multiple price points in different markets; and
- making the most of good working relationships with manufacturers.



Credit: Gavi/2024/Armend Nimani

Read the article: <https://www.gavi.org/vaccineswork/first-cohort-kosovan-kids-get-vaccinated-against-cancer-causing-hpv-part-routine>

2 HPV vaccine market shaping vision and strategic market objectives

Gavi published a summary of its [Market Shaping Roadmap for HPV Vaccines](#) in December 2023. This outlines the Alliance's vision of a healthy HPV vaccine market in which a competitive supplier base produces multiple products that meet varied and evolving country programme needs. Gavi envisages this can be achieved over a period of around ten years in three phases:

In the short term (2024–2025), additional HPV2 and HPV4 vaccines are expected to enter the market. However, countries that have adopted a one-dose schedule will be limited to existing products because the new vaccines are not expected to have sufficient evidence to support the use of a single-dose schedule during this period.

- This evidence is expected to be published **in the medium term (2025–2028)**, providing extra products and potentially lower-priced options to countries adopting a one-dose schedule.
- **In the long term (2028 and beyond)**, multiple HPV9 vaccines are expected to achieve WHO prequalification, creating a competitive market and further product options.

There is a range of ongoing and potential challenges and uncertainties relating to supply, demand and the policy environment. Deliberate interventions are therefore likely to be required to help a well-functioning, stable HPV vaccine market become established. To achieve its market shaping vision, Gavi has four key market objectives, each of which is underpinned by target outcomes.

- Objective 1 – Supply meets demand to support HPV vaccine programme implementation.
- Objective 2 – Predictability of medium- to long-term demand is enhanced to facilitate secure supply of affordable vaccines.
- Objective 3 – Diversity of products suitable for different country contexts is achieved, with healthy competition between suppliers.
- Objective 4 – Programmatically suitable future innovations are accommodated.

3 Enabling supply to meet demand

The increase in HPV vaccine supply since 2022 is a welcome development, however close monitoring is required to ensure that contracted volumes of vaccine doses are made available on time in the coming years. Unpredictable demand, largely due to uncertainties or changes in timing of MAC vaccination efforts, makes it difficult for manufacturers to plan their production.

Countries supported by Gavi are supplied with HPV vaccines through UNICEF Supply Division (UNICEF SD). In the short term, it is important that doses are made available in the contracted volumes, and that they are both delivered and used as planned in order to meet the target of vaccinating 86 million adolescent girls by 2025. In the medium to long term, countries

should have access to potentially lower-priced HPV2 and HPV4 vaccines that are supported by evidence showing the efficacy of one-dose schedules to ensure immunisation programme sustainability.

Gavi will seek to ensure supply meets demand by:

- monitoring country demand through regular meetings with agencies, non-governmental organisations and other partners, and providing countries with frequent updates on supply lead times to help facilitate vaccination programme launches.
- keeping vaccine suppliers informed of short- and medium-term changes in demand.



Credit: UNICEF/2023/Dwi Prasetya

Read the news release: <https://www.gavi.org/news/media-room/immunisation-partners-outline-ambitious-plan-protect-millions-girls-against-cervical-cancer>

4 Characterising longer-term demand to establish secure, affordable supply

The current UNICEF SD contracts with vaccine manufacturers run from 2021–2025, with the possibility of extensions of up to two years. Sufficient volumes of vaccines must be secured to cover projected demand for the next tender period, and greater supplier competition and product diversity is desired. To achieve this, greater clarity around outstanding policy uncertainties will be required to inform tendering and procurement strategies. These include the potential expansion of vaccination programmes to new target populations, additional Gavi support for HPV immunisation in middle-income countries and the potential availability of vaccines containing additional HPV types.

WHO's permissive recommendation of a single-dose HPV vaccine schedule in 2022 meant that more girls could be reached with existing supply levels; and it stimulated interest in expanding vaccination programmes to include additional target populations. Gavi's current HPV vaccine programme eligibility covers girls aged 9–14 years (WHO's primary target population), as well as additional support for vaccines for girls aged up to 18, for countries with delayed MACs that adopt a single-dose schedule.

Countries that wish to reach other population groups, such as boys and other age ranges, must cover the full procurement costs. Over the medium term, the possibility of changes to target population groups as part of Gavi's HPV vaccine programme will affect vaccine demand and procurement planning.

In 2022, Gavi announced a package of support to help middle-income countries address gaps in vaccination programme capacities which can cause vaccine coverage backsliding and undermine vaccine equity. Funding was made available for HPV vaccine introductions in

former and never Gavi-eligible middle-income countries as part of Gavi's MICs Approach.

This support is currently available until 2025, however there are ongoing discussions about its potential continuation and design beyond that date as part of Gavi's next five-year strategic period, 2026–2030 (known as Gavi 6.0). This could also affect demand and procurement planning.

Gavi's current co-financing policy requires low-income, initial self-financing countries (defined under [Gavi eligibility criteria](#)) to contribute a set payment per dose regardless of product chosen. This means product choice is not subject to appropriate customer price sensitivity. Changes may be considered to introduce price sensitivity into these product choices, especially if vaccines that contain greater numbers of HPV types become available.

Gavi will help clarify medium- and long-term demand to facilitate secure supply by:

- defining any changes to target population groups as part of its HPV vaccine programme;
- generating more detailed middle-income country HPV vaccine demand forecasts, and defining the scope and extent of Gavi support to middle-income countries during 2026–2030;
- UNICEF SD optimising tendering processes to secure future supply, with close monitoring of potential changes to the scope of Gavi support; and
- considering changes to the HPV vaccine co-financing formula to support meaningful price sensitivity and encourage supplier competition.

5 Enabling healthy supplier competition and product diversity

In April 2022, WHO issued a permissive recommendation for the use of one-dose schedules for Cervarix, Gardasil and Gardasil9 based on a review which found that a single dose of these vaccines provides comparable protection against HPV to two and three doses.

The use of a single dose of these HPV vaccines is considered to be ‘off-label’ until vaccine manufacturers file evidence with regulators in support of this change to the approved indications for their products. It is therefore for countries to decide whether to implement a one-dose or a two-dose schedule. It will take some time for sufficient clinical evidence to be generated to support WHO recommendations permitting a one-dose schedule for newer vaccines. This may make newer vaccine products unattractive to some countries that have adopted a single-dose schedule.

HPV9 vaccines are not currently available as part of Gavi’s vaccine product menu. This will remain the case in the short term, but might change once a competitive, sustainable supplier base and market develops. The Alliance will need to monitor ongoing development of vaccines that protect against greater numbers of HPV types than those in its current portfolio, and re-evaluate its policies as market dynamics change.

As more HPV vaccines become available, country product choices will become more complex. These are affected by Gavi’s product menu, Gavi’s co-financing policy, WHO guidelines on single-dose schedules, as well as individual country contexts such as financial and epidemiological factors. New suppliers and products will make HPV vaccine markets more competitive. In the medium term (2025–2027), Gavi will seek to facilitate the additional availability of at least two competitively priced HPV2/HPV4 vaccines supported by one-dose data; and

in the longer term (2028–2030), multiple HPV9 vaccines supported by one-dose data and that meet Gavi product menu inclusion criteria.

For increased product diversity and supplier competition to enable healthy markets and sustainable vaccination programmes, Gavi-supported countries must have access to the information they need to inform their vaccine choices in this more complex environment. These decisions should be evidence-based.

To facilitate greater supplier competition and product diversity, Gavi will:

- continue to advocate for the conduct of studies of single-dose use of new HPV vaccine products to inform country decision-making;
- encourage manufacturers to file evidence on one-dose schedules with regulators in support of changes to product labelling;
- define and communicate the conditions under which it would, in the longer term, finance HPV9 vaccines alongside HPV2 and HPV4, including co-financing criteria;
- update its product menu as new vaccines become available;
- provide timely WHO guidance on single-dose schedules for new HPV vaccines when supporting evidence becomes available; and
- continue to monitor demand for HPV vaccines with different characteristics and the ways countries choose between them.

6 Facilitating HPV vaccine innovation

Vaccine microarray patches (MAPs) are clusters of microscopic projections that are applied to the skin to painlessly deliver a vaccine. The technology [has the potential to significantly simplify vaccination administration and logistics](#), especially for vaccines like HPV that are delivered outside of traditional routine immunisation settings. Vaccine-containing MAPs currently in development include [those to protect against HPV, influenza, measles, rubella and rabies](#). Further research is required to better understand their precise benefits and value proposition.

A number of manufacturers are developing HPV vaccines that protect against more types of HPV than HPV9 vaccines. These are currently being investigated in preclinical and clinical trials. The public health benefit of

these higher valency HPV vaccines is not yet understood and may be marginal. The potential uses and benefits of both HPV vaccine MAPs and vaccines that protect against more than nine types of HPV require further investigation.

Gavi will:

- assess the potential of HPV vaccine MAPs and communicate its findings to industry and Alliance stakeholders;
- continue monitoring the development of vaccine MAPs including for HPV; and
- monitor the progress of development of vaccines that protect against more types of HPV than HPV9.



Credit: Gavi/2023/Latitude Space Africa

7 Conclusion: Shaping the market to consign cervical cancer to history

Cervical cancer is one of the most treatable and preventable forms of cancer, yet every two minutes a woman dies from the disease. In May 2018, WHO issued a global call to action to eliminate it. The Cervical Cancer Elimination Initiative (CCEI) was launched by WHO in November 2020, aiming to reduce incidence of the disease to fewer than 4 women per 100,000.

While 194 countries pledged to meet the CCEI targets, there remain major disparities between countries in cervical cancer burden, access to HPV vaccines and screening capabilities. The COVID-19 pandemic exacerbated existing problems by [undermining cervical cancer prevention services, including HPV vaccination programmes](#). As well as being critical to cervical cancer elimination, HPV vaccination is also a bridge to women and girls' health and therefore provides an opportunity to positively impact gender equality.

The complexities of vaccine manufacturing mean that market shaping is a long-term endeavour. To overcome supply challenges during 2017–2021, the Vaccine Alliance worked with manufacturers to support the development of a healthy HPV vaccine market. This provided a more promising environment for the revitalisation of Gavi's HPV vaccine programme in 2022. Supply is expected to triple from that date to 2025.

WHO's permissive recommendation of a one-dose HPV vaccine schedule has opened up opportunities to accelerate introductions and increase coverage. Single-dose HPV vaccine use is expected to remain

off-label in the short term, and it is up to countries whether to take this approach. Updated [Gavi Vaccine Funding Guidelines](#) nonetheless encourage the use of a single-dose schedule, and estimates suggest its widespread adoption could enable an additional 11 million girls to be reached per year.¹

Country introductions and high HPV vaccine coverage are key to achieving Gavi's goal of reaching 86 million girls by 2025 and making progress towards cervical cancer elimination. The 2022 update to the WHO position paper on HPV vaccines highlighted that all currently licensed vaccines (HPV2, HPV4 and HPV9) provide comparable efficacy in preventing cervical cancer. The priority in the short and medium term (up to 2028) is for HPV vaccines to become part of national immunisation programmes, and for high coverage to be achieved and sustained using currently available products, as guided by the WHO [Global strategy to accelerate the elimination of cervical cancer as a public health problem](#). New products should be assessed as they become available.

Many lower-income countries are a decade or more behind high-income nations in realising the life- and health-saving benefits of HPV vaccines, in part due to vaccine market failures. While supply-demand imbalances have slowed progress since Gavi first began supporting HPV immunisation programmes in 2012, market shaping and manufacturers' efforts are paying off. Many challenges remain, yet stakeholders now have a major opportunity to turn the vision of consigning cervical cancer to history into a worldwide reality.

References

1. Presentation to Gavi Board, December 2022 (Annex B: HPV volume forecast scenarios): <https://www.gavi.org/news/document-library/07-annex-b-hpv-volume-forecast-scenarios-pdf>

