



QUESTIONS AND ANSWERS ABOUT HUMAN PAPILLOMAVIRUS (HPV)



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QUESTIONS AND ANSWERS ABOUT HUMAN PAPILLOMAVIRUS (HPV)

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RESOURCES

ABOUT HUMAN PAPILLOMAVIRUS (HPV)

What is HPV?

HPV is a virus (human papillomavirus) that infects the skin or various mucous membranes (such as in the cervix or genital area). In some cases infection leads to the appearance of papillomas (wart-like growths).

There are over 200 types of HPV. Each type has a number (assigned in the order in which it was discovered).

Some HPV types, known as high risk types, are sexually transmitted and can cause cervical and other cancers. Low-risk HPV types can cause common warts, verrucae (warts on the sole of the foot), warts in the genital region, or in rare cases wart-like growths in the airway passages (causing a voice disorder called Recurrent Respiratory Papillomatosis or RRP).

What diseases can HPV cause?

The various HPV types infect different parts of the body, and can lead to different diseases, including cancer, genital warts or respiratory illness.

Most infections with any HPV type have no symptoms and clear naturally within 12-24 months.

However, at least 1 in 10 infections with high-risk, sexually transmitted HPV types may persist, becoming chronic infections. These can cause pre-cancerous growths called lesions. When these pre-cancerous lesions are located in the cervix they are also referred to as cervical intraepithelial neoplasia (CIN). If this cervical pre-cancer is not detected early and treated, it may progress to cancer. This usually takes 15-20 years.

Almost all cases of cervical cancer, most cases of vaginal, vulval and penile cancer and some cases of head and neck cancer are caused by HPV. 7 in 10 cases of cervical cancer are caused by HPV type 16 or 18.

Other HPV types cause genital warts, which are easily spread and can be difficult to treat. 9 in 10 cases of genital warts are caused by HPV types 6 or 11.

HPV can also cause a rare disease called Recurrent Respiratory Papillomatosis (RRP), which refers to growths in the larynx (windpipe) of newborns making it difficult for them to breath. RRP is caused by HPV types 6 and 11.

How is HPV spread?

HPV is spread from someone who has the virus through direct contact with infected skin, mucous membranes or bodily fluids. About 30 types of HPV are transmitted through sexual activity. This can be any intimate contact, such as during vaginal, oral or anal sexual intercourse or genital touching.

In rare cases, HPV can be spread from an infected mother to her newborn baby during childbirth.

How common is HPV infection?

HPV infection is the most common sexually transmitted infection worldwide.

About 8 in 10 men and women will be infected with one or more sexually transmitted HPV types at some time in their lives. The highest rates of HPV infection occur in sexually active men and women up to age 25.

What is cervical cancer?

Cervical cancer is cancer of the neck of the womb (or cervix). Almost all cases of cervical cancer are caused by HPV infection.

Infection with a high-risk type of HPV can lead to abnormal changes in the cells lining the cervix. These changes are called pre-cancerous growths (or lesions). If they do not heal or are not removed, they can develop into cancer. It takes years for these growths to develop into cervical cancer.

The most important risk factor is infection with a high-risk HPV type. Other risk factors include young age of first pregnancy, three or more full-term pregnancies, tobacco smoking, having a weakened immune system, HIV infection or the presence of other sexually transmitted infections.

The main treatments for cervical cancer are surgery, radiotherapy, and chemotherapy, which may lead to long-term health problems including infertility.

Every year, about 30 000 women die from cervical cancer in the WHO European Region (¹).

How common is cervical cancer?

Cervical cancer is one of the most common cancers affecting women, with about 69 000 cases and 30 000 deaths recorded per year in the WHO European Region (¹). In 2018, there were an estimated 570 000 cases of cervical cancer and 310 000 deaths due to cervical cancer worldwide (²).

Unlike most cancers, cervical cancer is more likely to develop among women aged 20–45 than among older women. Most cases occur in countries without effective cervical cancer screening programmes (which detect and treat pre-cancerous growths and early cancer before they progress).

Is it possible to get tested for HPV and cervical cancer?

Yes, the widely used PAP or smear test is used to detect abnormal cell growth (pre-cancerous or cancerous lesions). Visual inspection and the HPV test are used to detect high-risk types of HPV that may cause cancer.

These tests are used in cervical cancer screening programmes to detect pre-cancerous growths and early cancer, so they can be treated before they progress.

Unfortunately, screening programmes cannot detect or prevent all cases of cervical cancer. Even countries with an effective cervical cancer screening programme have significant numbers of cervical cancer deaths.

HPV vaccination in combination with regular screening offers the most effective way for women to be protected against cervical cancer.

Can HPV infection and cervical cancer be prevented?

Without vaccination, 8 in 10 men and women will be infected with the most common HPV types at some time in their lives, usually before the age of 25. The risk of cervical cancer can be greatly reduced through timely HPV vaccination and cervical screening.

Genital HPV infection can be prevented by abstinence from any sexual activity or lifelong monogamy. However, even if a person has only one sexual partner, that person could already be infected without knowing it because the HPV virus often has no symptoms. Reducing the number of sexual partners and the frequency of new partners can reduce the risk. Condom use and other barrier contraceptives reduce, but do not eliminate the risk of sexual transmission of HPV.

HPV vaccination before a person becomes sexually active greatly reduces the risk of infection because the vaccines protect against the most common HPV types, which cause up to 9 in 10 cervical cancer cases and 9 in 10 cases of genital warts. HPV vaccination will not protect against all types of HPV types, so cervical cancer screening is still important even if a woman has been vaccinated.

Cervical screening can detect pre-cancerous lesions and cervical cancer at an early stage, when treatment can be successful. Countries with national screening programmes have reduced the incidence of invasive (advanced) cervical cancer. Unfortunately, screening cannot prevent or detect all cases of cervical cancer. Even countries with an effective cervical cancer screening programme have significant numbers of cervical cancer deaths.

This is why vaccination in combination with regular screening offers the most effective way for women to protect themselves against cervical cancer.

ABOUT HPV VACCINES

Why get vaccinated against HPV?

HPV is the most common sexually transmitted infection. Vaccination protects against high-risk types of HPV that can lead to cancer.

About 8 in 10 men and women will be infected by sexually transmitted types of the virus at some time in their lives. Sexually transmitted HPV infection is most common in young people up to age 25.

HPV causes almost all cases of cervical cancer. Cervical cancer severely impacts the lives of women even if detected at an early stage. Cervical cancer is difficult to treat and can be fatal.

Sexually transmitted HPV can also cause cancer of the penis, anus, head and neck as well as genital warts.

A person who is vaccinated before becoming sexually active is protected from most high-risk HPV types that can cause cancer. But vaccination cannot prevent all cases, so cervical cancer screening is still important for vaccinated and unvaccinated girls. HPV vaccination and cervical cancer screening programmes together provide the best protection against cervical cancer.

Vaccination protects against most HPV-related cancers and, depending on the vaccine, also genital warts. It also indirectly protects a person's future sexual partners as well.

How do HPV vaccines work?

The body reacts to the vaccine by making antibodies that will help the immune system fight HPV infection.

HPV vaccines are up to 100% effective in preventing any future infections with the types of HPV virus they contain; all three licensed HPV vaccines protect against the most common cancer-causing types of HPV.

The three HPV vaccines currently in use contain virus-like particles (VLPs) produced from the protein shell of each HPV type in the vaccine, using recombinant DNA technology. These vaccines are not live vaccines and cannot cause HPV infection or cancer.

See also the video "How the HPV vaccine works":
<https://www.youtube.com/watch?v=qF7pBzU4D20&t=4s>

Are HPV vaccines safe?

Yes, all three HPV vaccines are among the safest and most tested vaccines ever licensed.

Each HPV vaccine was thoroughly tested for safety and effectiveness in clinical trials before being licensed and introduced to the general public. Monitoring of vaccine safety also continues in every country following introduction of the vaccine ⁽³⁾.

The WHO Global Advisory Committee for Vaccine Safety (GACVS) regularly reviews the scientific evidence on the safety of HPV vaccines provided by studies conducted around the world. Any serious event following immunization that could potentially be associated with the vaccine is investigated and the Committee looks at how often such events occurred before and after introduction of the vaccine.

GACVS first reviewed the safety data in 2007 and since then in 2008, 2009, 2013, 2014, 2015 and June 2017 ⁽⁴⁾. No severe or serious adverse reactions have been identified. Like all other vaccines, anaphylaxis (severe allergic reactions in 1.7 cases per million doses) and syncope (fainting) are possible but rare. GACVS considers HPV vaccines to be extremely safe.

The European Medicines Agency also conducted an independent assessment and concluded that HPV vaccines are safe and effective ⁽⁵⁾.

See also: Surveillance of side-effects of the HPV vaccine (video)
<https://youtu.be/z-B5jztdwog>

What HPV vaccines are available?

Three different HPV vaccines are currently in use:

- Gardasil® is a quadrivalent vaccine, meaning that it protects against four HPV types: 6, 11, 16 and 18. This is made by Merck Sharp & Dohme (sometimes called MSD or Merck) and was first licensed in 2006.
- Cervarix® is a bivalent vaccine (protects against two HPV types 16 and 18). This is made by GlaxoSmithKline (sometimes called GSK) and was first licensed in 2007.
- Gardasil 9®, is a nonavalent vaccine (protects against nine HPV types: 6, 11, 16, 18, 31, 33, 45, 52 and 58). This is made by MSD and was first licensed in 2014.

All three vaccines are very effective in preventing infection with the most common HPV types that cause cervical cancer and several other HPV-related cancers. The quadrivalent and nonavalent vaccines also prevent genital warts.

All three vaccines are WHO prequalified, which means that WHO has determined that they meet global standards of quality, safety and efficacy. Like other vaccines, HPV vaccine is given as an injection into the muscle of the upper arm.

Each country's national regulatory authority decides which vaccines will be available in that country and the technical advisory committee and the health authority decide which vaccine to include in the national routine immunization programme.

The following table shows which HPV types each of the vaccines protects against.

Name	HPV types		% of cases caused by these types	
	Number of types in the vaccine (valency)	HPV types in the vaccine	Cervical cancer	Anogenital warts
Cervarix®	2 (bivalent)	16,18	71% (with observed cross protection up to 84%)	None
Gardasil® (sometimes called Silgard)	4 (quadrivalent)	6, 11, 16,18	84%	90%
Gardasil 9®	9 (nonavalent)	6, 11, 16,18, 31, 33, 45, 52, 58	90%	90%

Who produces HPV vaccines and where are they manufactured?

The quadrivalent and nonavalent vaccines (Gardasil® and Gardasil 9®) are manufactured by Merck Sharp & Dohme (sometimes called MSD or Merck), whose corporate headquarters are in the United States. The bivalent vaccine (Cervarix®) is manufactured by GlaxoSmithKline (sometimes called GSK), whose headquarters are in the United Kingdom.

These companies have manufacturing facilities in many countries worldwide, where the vaccines are produced. All factories that produce HPV vaccines are regularly inspected by national and international authorities. An established procedure for prequalification is used by WHO to evaluate, and then regularly reassess, vaccines to ensure their continuing high quality and safety.

What are the ingredients in HPV vaccines?

HPV vaccines contain virus-like particles and other 'constituents' (ingredients) commonly found in vaccines and other medicines.

The virus-like particles contain the protein coat of the HPV virus, without any of the genetic materials from the virus itself. By resembling the virus, the vaccine stimulates the immune system to produce protective antibodies against HPV infection. To be as effective as possible, the vaccine also contains tiny amounts of an adjuvant (aluminium sulphate) to help enhance the body's immune response, mineral salts (L-histidine, polysorbate 80 and sodium borate) and water. The constituents of HPV vaccines are commonly found in some other vaccines and other medicines as well as food and cosmetics.

Aluminium salts have been used in many vaccines for over 50 years. The quantity of aluminium in the vaccine is very small and most adults will get about 35 times more aluminium from the food they eat every day than is in the vaccine.

How many countries vaccinate against HPV?

HPV vaccination is part of the routine immunization schedule for girls and in some cases also boys in over 96 countries worldwide.

Most countries in the WHO European Region have introduced the HPV vaccine and more countries join this list every year ⁽⁶⁾.

In general across the world, high-income or upper-middle-income countries are more likely to have introduced HPV vaccine than lower-income countries, even though 85% of all cervical cancer cases and deaths are in low-income or lower-middle-income countries ⁽⁷⁾.

Since 2006, when the first HPV vaccine was introduced, over 100 million people have been vaccinated with over 270 million doses of HPV vaccines around the world ⁽⁸⁾.

Who should get vaccinated against HPV?

WHO recommends vaccination of girls between the age of 9 to 14 years as a priority, as the main aim of HPV vaccination programmes is to protect women from cervical cancer.

Cervical cancer is the most common disease caused by HPV. Vaccinating girls also provides protection to their future partners, and this community protection or 'herd immunity' is very effective in stopping the spread of the virus.

When the vaccine is first introduced in a country, it is recommended that all girls aged 9–14 be offered the vaccine, and if feasible all girls and young women 9–18 years of age. Most countries share this recommendation, but some recommend vaccination of all girls and young women up to the age of 26 or even older.

Some countries also recommend the immunization of boys and young men. Although cervical cancer is the most common disease caused by HPV, HPV infection can also cause cancer of the penis, anus and head and neck and genital warts. Vaccinating boys protects them from genital warts and at least one of these HPV-related cancers affecting men (depending on which vaccine is used).

In the European Region, as of late 2019, Austria, Germany, Israel, Italy, Norway, Switzerland and the United Kingdom offer the vaccine to both boys and girls.

Who should not get the HPV vaccine?

HPV vaccine should not be given if a person has had a severe allergic reaction (anaphylaxis) to a previous HPV vaccine or to a constituent of the vaccine, such as yeast. As a precaution, HPV vaccination is not recommended in pregnancy due to a lack of evidence from well-controlled studies in pregnant women. There is no evidence that HPV vaccine caused any harm when administered to pregnant women who did not know about their pregnancy at the time of vaccination.

Is there a shortage of HPV vaccines on the global market?

Yes. There are currently three licensed vaccines, and the global supply of these vaccines is insufficient to meet demand. As a result, some countries have had to or will postpone introduction of the vaccine ⁽⁹⁾.

Supply shortages are expected until 2024. This expectation may change depending on HPV vaccination strategies in each country, planned capacity of the current manufacturers as well as the progress of three other HPV vaccines which are in their advanced stage of clinical development.

What is the vaccine schedule?

The best time for a child to be vaccinated is from 9 to 14 years of age with two doses of HPV vaccine.

The recommended age is based on when the vaccine will be most effective in building long-lasting immunity and give the strongest immune response. The vaccine is most effective if given before a person is exposed to HPV infection.

Those aged 15 and older require three doses for a full vaccine course. HPV is most common in those less than 25 years of age, so many become infected soon after starting sexual activity. This is true even for those who have only one sexual partner.

The vaccine is currently not licensed for children under 9. However, recent evidence shows that the duration of protection is at least 10 years and will most likely be much longer. Some scientists are therefore urging that research be done on the effectiveness of offering the vaccine to younger children.

Those who have an illness or are on treatment that affects the immune system (immunocompromised) require three doses for a full vaccine course.

Immunization experts do not recommend getting more than one course of HPV vaccines. All three licensed vaccines protect against the most common cancer-causing types of HPV.

HPV vaccines are not live vaccines and can be administered at the same time as or at any interval before or after other vaccines such as tetanus-containing or meningococcal vaccines.

Is the vaccine effective for someone who is already sexually active?

People who are already sexually active may still benefit from the vaccine.

This will protect them against HPV types in the vaccine that they have not been exposed to, but may not protect them if they are already infected with HPV.

To benefit fully from the vaccine, it is best to be vaccinated before starting sexual activity.

Do HPV vaccines work?

Yes. All three HPV vaccines are more than 99% protective against infection with cancer-causing HPV types.

Most infections with high-risk HPV types clear naturally, but some progress to pre-cancerous growths and some of these may over time progress to cancer. If HPV infection is prevented, pre-cancerous growths and cervical cancer cannot develop.

Rapid reductions of up to 90% in HPV infection and related disease in teenage girls and young women have been seen in many countries (¹⁰).

Countries with high vaccine uptake rates have seen the best impact. Research published from England, where 90% of girls have been vaccinated since 2008, shows that by 8 years after the introduction of HPV vaccine cancer-causing HPV infections had fallen 86% among women aged 16 to 21 who were eligible for the vaccine (¹⁰). In Australia, the HPV infection rate among women aged 18 to 24 dropped from 22.7% to 1.1% between 2005 and 2015 (¹¹). In Scotland, a study published in March 2019 reported that, compared with unvaccinated women born in 1988, vaccinated women born in 1995 and 1996 showed an 89% reduction in pre-cancerous growths (cervical intraepithelial neoplasia (CIN) grade 3) (¹²).

The rate of genital warts in vaccinated Australian girls aged under 21 has decreased dramatically, and the rate in unvaccinated heterosexual young men has also fallen, showing the impact of herd immunity – protection from vaccinated to unvaccinated persons (¹³).

How long does protection last?

Studies have shown that immunity lasts at least 10 years, but it may be as long as several decades.

There is no sign that this protection is decreasing in those who have been vaccinated, and many experts believe the vaccine will prove to be effective for several decades (^{14, 15}), affording potentially lifelong protection.

As protection does not appear to be waning among those who were vaccinated in 2006, there is no evidence as yet that a booster dose will be needed. Studies are ongoing to see if a booster vaccine may be needed in the future.

Is regular cervical cancer screening still needed for women who have been vaccinated?

Yes. Women who have been vaccinated should still be screened for cervical cancer as recommended in their country.

The vaccine protects against the HPV types that cause up to 9 in 10 cases of cervical cancer, but it cannot prevent all potential cases. Also, if a teenager or woman is vaccinated after she has become sexually active, the vaccine will not protect her against any types she had already been infected with before receiving the vaccine.

The widely used PAP or smear test is used to detect abnormal cell growth (pre-cancerous or cancerous lesions) and visual inspection and the HPV test are used to detect high-risk types of HPV that may cause cancer. These tests are used in cervical cancer screening programmes to detect and treat pre-cancerous growths and early cancer before they progress.

Do HPV vaccines have any side effects?

Like other vaccines and medicines, HPV vaccines often have mild side effects such as pain, redness and/or swelling at the injection site, headache or a mild fever. These usually last a few hours to one day.

Pain at the injection site is common (experienced by 8 people in 10). Fewer (3 in 10) will experience swelling or redness at the injection site and/or a headache following HPV vaccination. About 1 person in 10 will get a mild fever.

Sometimes people faint after any injection. This is more common in teenagers particularly when they are vaccinated in a group setting, such as in a school. This reaction is due to stress and anxiety, not to the vaccine itself.

Rarely a person will have a serious allergic reaction with difficulty breathing (known as anaphylactic shock) within minutes of a vaccination. Although severe allergic reactions to vaccines are very rare, patients and their caregivers should tell the healthcare provider about any known allergies before receiving any vaccine. The healthcare provider can then advise whether the allergy is relevant for the specific vaccine being given.

As a precaution, anyone receiving a vaccine of any kind should stay in the clinic for 15 minutes afterwards. If they feel light headed or have difficulty breathing, they should tell the healthcare provider, who is trained to treat faints and allergic reactions.

Can the risk of side effects be reduced?

It is very unlikely that a person will experience any serious side effects or anxiety-related reactions to HPV vaccination.

However, the following actions can help ensure that vaccination goes well.

- Tell the healthcare provider if the child or adult to be vaccinated has an allergy before the vaccine is given. The healthcare provider can then advise whether the allergy is relevant for the specific vaccine being given.
- Make sure to stay for 15 minutes in the clinic after the vaccine is administered, so the clinic staff can observe the person and respond to any faint or serious allergic reaction.
- After vaccination, be aware of the usual side effects (redness or soreness at the injection site) as well as possible fever or body aches. Reassure a child or adolescent that these side effects are common, not serious and will only last for a day.
- Report anything unexpected to the healthcare provider. These reports are taken seriously and investigated to see if they are related to the vaccination or may have other causes.

Do HPV vaccines have long-term side effects?

All three HPV vaccines are among the safest and most tested vaccines ever licensed. There is no credible evidence pointing to any long-term side effects.

There have been case reports hypothesising that a range of rare and poorly understood conditions, such as premature ovarian failure (POF), postural orthostatic tachycardia syndrome (POTS) and complex regional pain syndrome (CRPS), could be induced by HPV vaccines. These reports lack scientific and epidemiological credibility and do not provide sufficient evidence to suggest a causal link between the vaccine and these illnesses. One country, Japan, has suspended promotion of the use of HPV vaccine, despite an expert Japanese committee and all respected scientific groups worldwide finding no evidence that the vaccine is responsible for causing these conditions.

How can I be sure HPV vaccines are high quality?

WHO, the European Medicines Agency, national regulatory authorities and many others take the safety of vaccines very seriously. Rigorous systems have been put in place to ensure the quality and safety of vaccines during all steps of testing, production, transportation and administration. These systems also ensure that any potential safety issue is reported and properly investigated.

Before any HPV vaccine is licensed, it is tested in clinical trials that carefully look for side effects. In clinical trials the vaccine is given to thousands of volunteers, and the outcomes for this group are compared to the outcomes for a group of people who did not receive the vaccine.

After a vaccine is shown to be safe and effective, national regulatory authorities in each country then still need to examine the evidence to decide if the vaccine should be made available (licensed) in each country. Once a vaccine is licensed and used for routine immunization, national and global systems monitor and investigate any adverse effects following immunization. Post-licensing vaccine safety studies are also carried out by countries and manufactures to detect any rare AEFIs that cannot be found during clinical trials.

The WHO Global Advisory Committee for Vaccine Safety (GACVS) regularly reviews the scientific evidence on the safety of HPV vaccines provided by studies conducted around the world. Any serious event following immunization that could potentially be associated with the vaccine is investigated and the Committee looks at how often such events occurred before and after introduction of the vaccine.

The high manufacturing and quality standards are the same in every country where HPV vaccines are produced.

Do HPV vaccines affect fertility?

No. HPV vaccines do not affect fertility. They do help protect a woman's health and fertility.

Clinical trials before the first HPV vaccine was licensed in 2006 and safety monitoring and studies since its introduction have confirmed that the vaccine does not cause any reproductive problems in women ⁽¹⁶⁾.

In fact, the HPV vaccine helps to protect fertility by preventing pre-cancerous cervical growths ('lesions') and cervical cancer caused by HPV. Surgical treatment of pre-cancerous cervical lesions can make it more difficult for a woman to become pregnant, and surgery during pregnancy can lead to premature labour and loss of a foetus. Treatment for cervical cancer (removal of the cervix and uterus, chemotherapy and/or radiation) leaves a woman unable to bear children.

Do HPV vaccines cause early menopause (primary ovarian failure/ premature ovarian insufficiency)?

No. There is no evidence of a link between early menopause (primary ovarian failure/ premature ovarian insufficiency) and HPV vaccination.

Primary ovarian failure, also known as premature ovarian insufficiency, occurs when the ovaries stop working, leading to early menopause. The cause of premature ovarian failure is often unknown but in some cases it may be due to cancer treatment or an autoimmune disease.

The WHO Global Advisory Committee on Vaccine Safety (GACVS) reported in 2017 after reviewing large population level data from several countries including Denmark and the United States that it saw no evidence for a causal association between HPV vaccine and primary ovarian failure/ premature ovarian insufficiency.

About 90 million doses of HPV vaccine were administered in the United States in the period from 2009 through 2017. The United States Centers for Disease Control and Prevention (US CDC) monitoring in this period through the Vaccine Adverse Event Reporting System (VAERS) did not detect any increase in incidence of primary ovarian failure/ premature ovarian insufficiency following HPV vaccination ⁽¹⁶⁾.

Does HPV vaccination lead to promiscuity?

No. There is no evidence that HPV vaccination has any impact on sexual activity.

Like every vaccine, it is best to be vaccinated before exposure to the infection.

HPV infection is the most common sexually transmitted infection worldwide. The highest rates of HPV infection occur in sexually active men and women up to age 25. HPV vaccination before a person becomes sexually active reduces the risk of infection because the vaccines protect against HPV types that cause up to 90% of cervical cancer cases and 90% of genital warts.

Several studies have found no evidence that HPV vaccination leads to increased sexual activity ^(17, 18, 19, 20).

Has an HPV vaccine been withdrawn in any country?

No. The HPV vaccine has not been withdrawn in any country.

Misinformation suggesting that HPV vaccines cause long-term adverse effects have long circulated in the media and on the internet. This misinformation has led at different times to a reduction in the numbers of girls getting the vaccine in some countries, including Denmark, Ireland and Japan. No country has withdrawn access to a HPV vaccine.

Denmark

The Danish Health Authority has recommended HPV vaccination for girls as part of the national childhood immunization programme since 2009. Initially vaccine uptake was 80-90% and studies soon showed clear benefits of the vaccine ⁽²¹⁾. But from 2014, the uptake dropped to below 40% because of adverse publicity about chronic conditions thought to be associated with the vaccine, though no evidence of such a link has been found.

After extensive public consultation, a new campaign was launched, “Stop HPV, Stop Cervical Cancer,” to help build confidence in the vaccine and remind people that the risk of getting cervical cancer far outweigh the risk of adverse vaccine events. Information from health authorities in Denmark shows uptake of the first dose of HPV vaccine in girls born in 2003 has increased from 27% in April 2016 to 76% in September 2018 ⁽²²⁾.

Ireland

The HPV vaccination school-based programme for girls aged 12–13 years began in Ireland in 2010. Initially, the uptake was greater than 80% but from 2015-2016 the uptake dropped to an estimated 50% in 2016-2017 due to parental concerns and misinformation about vaccine safety that were spread by lobby groups.

The Irish health authority formed powerful cross-sectoral alliances, implemented a comprehensive training programme for a wide range of health professionals and revised information for parents following focus group discussions and social media analysis of parents’ concerns. This led to a rapid improvement in vaccine uptake to 65% for 2017-2018 and 70% for the first dose in 2018-2019 ^(22, 23, 24).

Japan

In Japan, local municipalities introduced HPV vaccination for girls in 2010 and the vaccine was included in the national immunization programme in April 2013. Initially uptake was around 70%. However, in June 2013, the Japanese government suspended proactive recommendations for the HPV vaccine after unconfirmed media reports of adverse events (such as Chronic Regional Pain Syndrome (CRPS) and other symptoms) following vaccination. Uptake plummeted to 1%.

These adverse events were investigated by the WHO Global Advisory Committee on Vaccine Safety (GACVS) in 2013, 2014, 2015 and June 2017, which stated there was no evidence for a causal association between HPV vaccine and CRPS. GACVS considers HPV vaccines to be extremely safe. In February 2018, a Japanese study reported no difference in the rates of a wide range of symptoms in vaccinated and unvaccinated girls ^(25, 26).

The Japanese Expert Council on Promotion of Vaccination and other expert groups continue to actively campaign for the resumption of recommendations for HPV vaccination given the high rates of cervical cancer deaths in Japan. In July 2017, WHO reported the mortality rate from cervical cancer in Japan increased by 3.4% from 1995 to 2005 and is expected to increase by 5.9% from 2005 to 2015 (²⁷).

HPV vaccines are available in Japan but to date the government's proactive recommendations are still suspended.

GACVS has stated that young women in Japan are being left vulnerable to HPV-related cancers that otherwise could be prevented; and policy decisions based on weak evidence, leading to lack of use of safe and effective vaccines, can result in significant harm (^{28, 29}).

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The WHO Regional Office for Europe

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