

Questions and answers about human papillomavirus

Second Edition



European Region

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European Region

Abstract

This document provides evidence-based answers to frequently asked questions related to human papillomavirus (HPV), HPV vaccines, and prevention of cervical cancer and other HPV-related diseases. This second edition of the document includes updated information on the impact of HPV vaccination since its introduction in 2006 and on inclusion of the vaccine in national immunization programmes of the WHO European Region.

Keywords

HUMAN PAPILLOMAVIRUS CERVICAL CANCER HUMAN PAPILLOMAVIRUS VACCINE

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Corrigendum

Questions and answers about human papillomavirus, second edition

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1. Page 2

Paragraph rephrased:

However, about 5-10% of all infected women develop a chronic infection. The chronic infection with high-risk types can progress within months or years to

pre-cancerous growths called lesions. When located in the cervix they are also referred to as cervical intraepithelial neoplasia (CIN). If not detected and treated appropriately, these CINs may progress to cervical cancer.

This usually takes 15–20 years to develop.

High risk and low risk HPV types specified:

High-risk HPV types cause almost all cases of cervical cancer, most cases of vaginal, vulval and penile cancer and some cases of head and neck cancer. High-risk HPV types 16 and 18 are responsible for over seven in ten cervical cancer cases.

Low-risk HPV types cause genital warts, which are easily spread and need treatment. Nine in ten cases of genital warts are caused by HPV types 6 and 11.

Removed: Rarely, HPV may cause a rare disease called recurrent respiratory papillomatosis (RRP), which causes growths in the larynx (windpipe) of newborns leading to difficulty breathing. RRP is caused by HPV types 6 and 11.

2. Page 3

Removed: In rare cases, HPV can be spread from an infected mother to her newborn baby during childbirth. *Clarification added that HPV is most common before age 25 for women specifically:*

In women, the highest rates of HPV infection occur up to the age of 25 years.

Revised age:

Unlike most cancers, cervical cancer is more likely to develop among young women aged 35–45 than among older women.

Clarification of the role of screening (also on p. 15):

Yes, the widely used PAP or smear test is used to detect abnormal cell growth (pre-cancerous or cancerous lesions). Visual inspection of the cervix looks for precancer/cancer and the HPV test is used to detect high-risk types of HPV.

3. Page 4

Clarification of HPV types prevented by vaccination:

Vaccination before a person becomes sexually active significantly reduces the risk of infection because all vaccines protect against high-risk HPV types that cause up to nine in ten cervical cancer cases; and the quadrivalent and nonavalent HPV vaccines also protect against low-risk HPV types that cause nine in ten cases of genital warts.

These revisions were incorporated into the electronic file on 15 April 2024.

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Abbreviations

adverse events following immunization
cervical intraepithelial neoplasia
WHO Global Advisory Committee for Vaccine Safety
human papillomavirus
Recurrent Respiratory Papillomatosis

About human papillomavirus (HPV)

What is HPV?

HPV stands for human papillomavirus. There are over 200 types of HPV, which are referred to by number (assigned in the order in which they were discovered). All HPV types infect the skin or various mucous membranes (such as in the cervix or genital area).

Twelve HPV types known as high risk can cause cervical and other cancers. Low-risk HPV types can cause warts in the genital region, common warts and verrucae (warts on the sole of the foot).

What diseases can HPV cause?

HPV types infect different parts of the body and can lead to different diseases, including several types of cancer and genital warts.

Most HPV infections have no symptoms and clear or become undetectable within one to two years.

However, about 5–10% of all infected women develop a chronic infection. The chronic infection with high-risk types can progress within months or years to pre-cancerous growths called lesions. When located in the cervix they are also referred to as cervical intraepithelial neoplasia (CIN). If not detected and treated appropriately, these CINs may progress to cervical cancer. This usually takes 15–20 years to develop.

High-risk HPV types cause almost all cases of cervical cancer, most cases of vaginal, vulval and penile cancer and some cases of head and neck cancer. High-risk HPV types 16 and 18 are responsible for over seven in 10 cervical cancer cases.

Low-risk HPV types cause genital warts, which are easily spread and need treatment. Nine in 10 cases of genital warts are 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. Mucosal HPV types are transmitted through sexual activity. This can be any intimate contact with an infected area, such as during vaginal, oral or anal sexual intercourse or genital touching.

HPV is not inherited. There is no increased risk of being infected with the HPV virus in people with a family history of HPV-related disease.

How common is HPV infection?

HPV infection is the most common sexually transmitted infection worldwide.

About eight in ten men and women will be infected with one or more HPV types at some time in their lives. In women, the highest rates of HPV infection occur up to the age of 25 years.

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 high-risk HPV types may lead to abnormal changes in the cells lining the cervix. These changes are called pre-cancerous growths (or lesions). If they do not heal spontaneously or are not removed, they can develop into cancer. It usually takes 15–20 years for these growths to develop into cervical cancer.

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

Every year, in the WHO European Region, more than 30 000 women die from cervical cancer.

How common is cervical cancer?

Cervical cancer is one of the most common cancers affecting women: in the WHO European Region, about 66 000 cases and 30 000 deaths are recorded per year. In 2020, there were an estimated 600 000 cases of cervical cancer with 341 000 deaths worldwide (1, 2).

Unlike most cancers, cervical cancer is more likely to develop among young women aged 35–45 than among older women. Most cases occur in countries without effective cervical cancer screening programmes (which aim to detect and treat pre-cancerous growths and early cancer before they progress).

What are the risk factors for developing 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.

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 of the cervix looks for precancer/cancer and the HPV test is used to detect high-risk types of HPV.

These tests are used in cervical cancer screening programmes to detect precancerous 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 protect themselves against cervical cancer.

Can HPV infection be prevented?

Without vaccination, eight 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.

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 significantly reduces the risk of infection because all vaccines protect against high-risk HPV types that cause up to nine in 10 cervical cancer cases; and the quadrivalent and nonavalent HPV vaccines also protect against low-risk HPV types that cause nine in 10 cases of genital warts. HPV vaccination will not protect against all HPV types so cervical cancer screening is still important even if a woman has been vaccinated.

Can cervical cancer be prevented?

The risk of cervical cancer can be reduced by timely HPV vaccination and cervical screening.

HPV vaccines protect against the HPV types that cause up to nine in 10 cervical cancer cases and nine 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. In countries where there is an organized cervical cancer screening programme, there has been a marked reduction in the incidence of invasive (advanced) cervical cancer. Unfortunately, screening programmes 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. About HPV Vaccines

Why get vaccinated against HPV?

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

About eight in 10 men and women will be infected by the virus at some time in their lives. In women, sexually transmitted HPV is most common up to the age of 25 years.

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 also cause cancers of the penis, anus, vulvar, vaginal, the head and neck, and genital warts.

If a person is vaccinated before becoming sexually active, he/she will be protected from most high-risk HPV types that cause cancer. Vaccination protects their sexual partners as well. However, vaccination cannot prevent all cases, so cervical cancer screening is still important for vaccinated and unvaccinated girls and women. HPV vaccination and cervical cancer screening programmes together provide the best protection against cervical cancer.

How does the HPV vaccine work?

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

HPV vaccines are 100% effective in preventing any future infections with the types of HPV virus it contains.

HPV vaccines currently in use contain virus-like particles 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: <u>How the HPV vaccine works</u> (3).

What HPV vaccines are available?

Various HPV vaccines are currently in use:

- Bivalent vaccines protect against two high-risk HPV types 16 and 18, and provide cross-protection against three additional HPV types: 31, 33 and 45. The first bivalent vaccine was licensed in 2007.
- Quadrivalent vaccines protect against four HPV types: 6, 11, 16 and 18. They also provide cross-protection against three additional HPV types: 31, 33 and 45. The first quadrivalent vaccine was licensed in 2006.
- Nonavalent vaccine protects against nine HPV types: 6, 11, 16, 18, 31, 33, 45, 52 and 58. It was first licensed in 2014.

All HPV vaccines are highly effective in preventing infection with the high-risk HPV types that cause the majority of cervical cancer and several other HPV-related cancers.

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

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

Number of types in the	HPV types in the	% of cases caused by these types	
vaccine (valents)	vaccine	Cervical cancer	Anogenital warts
2 (bivalent)	16, 18	71% (with proven cross- protection – up to 84%)	None
4 (quadrivalent)	6, 11, 16, 18	84%	90%
9 (nonavalent)	6, 11, 16, 18, 31, 33, 45, 52, 58	90%	90%

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

What is 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 hydroxide, a water-soluble aluminum salt) to help enhance the body's immune response, mineral salts (L-histidine, polysorbate 80 and sodium borate) and water.

How commonly are the constituents of HPV vaccines found in other products?

The constituents of HPV vaccines are commonly found in some other vaccines and in other medicines.

- Aluminium salts are found in the air, food, cosmetics such as deodorants, and toothpaste and is a component of several childhood vaccines. Aluminium salts have been used in many vaccines for over 50 years. The quantity of aluminium in the vaccine is very small. Most adults will get about 35 times more aluminium from the food they eat every day than is in the vaccine.
- L-histidine is an essential amino acid available in food. L-histidine is also a component of some hepatitis vaccines.
- Polysorbate 80 is used as an emulsifier in foods, such as ice cream. It is a component of several childhood vaccines and other medicines.
- Sodium borate is a component of some vaccines and medicinal compounds such as eye drops.

Sodium chloride in HPV vaccines is an ordinary salt that is necessary for the body's normal functioning, and can be harmful only if consumed in large quantities.

Sodium phosphate-based salts are widely used and harmless. They help maintain the acidity balance, and prevent sedimentation of the vaccine's active ingredients on the bottom of a vaccine vial.

The tiny amounts of the ingredients found in vaccines are not toxic regardless of how they enter your body (through ingestion, injections or eye drops).

Are aluminum-containing vaccines safe?

Yes. Based on a thorough review of all available evidence, the Global Advisory Committee on Vaccine Safety (GACVS) has stated that there is no evidence of a health risk from aluminium-containing vaccines (4).

The amount of aluminum contained in vaccines is very tiny. The majority of adults get approximately 35 times more aluminum through daily food intake than from a vaccine.

How long have HPV vaccines been in use?

HPV vaccines have been available since 2006.

The first quadrivalent HPV vaccine (against four HPV types) was licensed in 2006, the first bivalent (against two types) in 2007 and the nonavalent (against nine types) in 2014.

How many people have received HPV vaccines?

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 *(5)*.

How many countries have introduced HPV vaccines?

HPV vaccination is part of the routine immunization schedule for girls and in some cases also boys in 135 countries worldwide.

The majority of countries in the WHO European Region have introduced HPV vaccine, and the number of these countries is growing each year (6). As of 2023, 45 of 53 countries in the Region have introduced HPV vaccination.

Overall, high income or upper-middle-income countries are more likely to have introduced HPV vaccine compared to lower-middle-income countries, although more than 85% of all cervical cancer cases and deaths are in low or middle-income countries (7).

Who should get the HPV vaccine?

WHO recommends the vaccination of girls between the age of nine and 14 years as a priority.

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 more. Some countries also recommend the immunization of boys and young men (8).

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. Due to lack of evidence from well-controlled studies in pregnant women, as a precaution HPV vaccination is not recommended in pregnancy. No data indicate any negative impact of HPV vaccination when administered to pregnant women who had no knowledge of their pregnancy at the time of vaccination.

Why are girls the priority for HPV vaccination?

The main aim of HPV vaccination programmes is to protect women from cervical cancer, which is the most common disease caused by HPV.

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. This is why WHO and national authorities in most countries recommend HPV vaccination be offered to young girls aged 9–14 as the first priority.

Each country makes its own decision about who should be given the HPV vaccine, based on the national disease burden and available funding. If they have enough capacity and funding, a country may decide to expand coverage to girls older than 14 and to boys.

Should boys also be vaccinated?

Preventing cervical cancer is the priority objective for HPV vaccination programmes, but vaccinating boys where feasible offers additional benefits.

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, so boys can also benefit from receiving the vaccine.

Vaccinating boys protects them from genital warts and at least one HPV-related cancer affecting men, depending on the vaccine used. It also protects their sexual partners, thereby indirectly helping to prevent cervical cancer.

The highest rates of HPV infection are among men who have sex with men especially those who are also infected with HIV. Men who have sex with men do not benefit from the community protection or 'herd immunity' from vaccinating women.

When should a girl or boy be vaccinated?

The best time for a child to be vaccinated is from 9–14 years of age.

The vaccine gives the strongest immune response at that age, and it is most effective if given at an early age.

What is the HPV vaccine schedule?

WHO recommends one- and two-dose HPV vaccination schedules. Each country makes its own decision on the vaccine schedule for their immunization programme.

Persons with immunodeficiency conditions or persons who are on treatment that affects the immune system (immunocompromised) require at least two doses, and preferably three doses for a full vaccination course.

Immunization experts do not recommend getting more than one course of HPV vaccines. All licensed vaccines offer high protection against the cancer-causing high-risk HPV types.

Why is the vaccine not offered to children under nine?

The vaccine is not licensed for children under nine.

When the HPV vaccine was developed, the duration of protection was not known and the vaccine developers and health officials were concerned that if young children were immunized, the protection offered by the vaccine might not last long enough to protect them throughout the most at-risk period of getting the infection (up to age 25).

However, recent evidence shows that the duration of protection is at least 11 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.

Would it be better to vaccinate children when they are older than the recommended age?

No. The recommended age is based on when the vaccine will be most effective in building long-lasting immunity.

The HPV vaccine produces the strongest immune response at the recommended age.

In addition, the vaccine is most effective if given before a person is exposed to HPV infection. HPV is most common in those less than 25 years of age.

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

People who are already sexually active can still benefit from vaccination. This will protect them against HPV types in the vaccine that they have not been exposed to, but may not protect them if they have already been infected with HPV.

To benefit fully from the vaccine, it is best to be vaccinated at 9–14 years of age.

How is HPV vaccine given?

Like many other vaccines, HPV vaccine is given as an injection into the muscle of the upper arm.

Can other vaccines be given at or around the same time?

Yes, 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.

Do HPV vaccines work?

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

A recent systematic literature review and meta-analysis highlighted the substantial impact of routine vaccination in countries that adopted HPV vaccines early (9). The average impacts of HPV vaccination include:

- up to 90% reduction in infections caused by high-risk HPV types (16 and 18) among age groups targeted by national immunization programmes;
- up to 88% reduction in genital warts incidence; and
- up to 70% reduction in pre-cancer risk (CIN grade 2 and 3) in young women compared to the pre-vaccine era.

Moreover, compelling evidence from the United Kingdom (England), Finland and Sweden demonstrates significant declines in the incidence of invasive cervical cancer in young women (10-12).

How long does protection last?

For more than 12 years researchers have been monitoring persons who had received a bivalent or quadrivalent vaccine, and there is no sign that the protection is decreasing with time. Many experts believe the vaccine will prove to be effective for several decades (13), providing potentially lifelong protection.

Will a booster vaccine be needed?

So far there is no evidence that protection is waning among those who have been vaccinated since the first HPV vaccine was introduced in 2006.

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?

The vaccine protects against the HPV types that cause up to nine in 10 cervical cancers but it cannot prevent all potential cases. If women are vaccinated after they became sexually active, the vaccine does not protect them against HPV types with which they were already infected.

The widely used PAP or smear test is used to detect abnormal cell growth (pre-cancerous or cancerous lesions); visual inspection of the cervix looks for precancer/cancer; and the HPV test is 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 lesions 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 swelling at the injection site, headache and a mild fever. These usually last a few hours to one day.

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.

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

How many people experience side effects?

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

Sometimes people faint after any injection (14). 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.

About one person in a million people vaccinated (with any vaccine) will have a serious allergic reaction.

Can HPV vaccination cause an allergic reaction?

Yes, but only for people with very specific allergies to the constituents in the HPV vaccine. All medicines and vaccines (and some foods and insect bites) can cause allergic reactions. The most serious allergic reaction, called anaphylactic shock, occurs in about one in a million people who receive a vaccine of any kind.

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 an extra precaution, every person receiving a vaccine should stay in the clinic for 15 minutes afterwards for observation by the healthcare provider, who is trained to recognize and treat allergic reactions.

Can the risk of side-effects be reduced?

It is very unlikely that a person will experience any serious side effects or anxietyrelated 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 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 hypothesizing 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.

Are HPV vaccines safe?

Yes, all 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 (4).

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. No severe or serious adverse reactions have been identified. As with all other vaccines, there is a very rare chance of anaphylaxis (severe allergic reactions in 1.7 cases per million doses) and syncope (fainting). 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 (15).

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. After conducting a thorough investigation, in November 2021, the Ministry of Health, Labour and Welfare of Japan concluded that HPV vaccines a safe and officially resumed active recommendations of the human papillomavirus (HPV) vaccine for girls aged 12–16 years (*16*).

See also the video: Surveillance of side-effects of the HPV vaccine (17).

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. After a vaccine is licensed and introduced for routine immunization, national and global systems continue monitoring and investigating any adverse events following immunization (AEFIs). Countries and manufacturers also conduct post-licensure vaccine safety studies to identify any rare AEFIs that cannot be detected 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 AEFI that could potentially be associated with the vaccine is thoroughly 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 (18-21).

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 both non-surgical and surgical treatment 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 (22).

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 monitoring in this period through the Vaccine Adverse Event Reporting System did not detect any increase in incidence of primary ovarian failure/premature ovarian insufficiency following HPV vaccination (23).

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World Health Organization Regional Office for Europe UN City, Marmorvej 51, DK-2100 Copenhagen Ø, Denmark

 TEL
 +45 45 33 70 00

 FAX
 +45 45 33 70 01

 EMAIL
 eurocontact@who.int

 WEB
 www.who.int/europe