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## Fact sheet: HPV vaccine for protection against cervical cancer



Over the past few decades the number of women with cervical cancer has decreased drastically in many countries, including Germany. Yet this kind of cancer is still a life-threatening disease. Human papillomavirus (HPV) infections play a critical role in the development of cervical cancer. There is now a vaccine against some of these sexually transmitted viruses. It targets the most common of the carcinogenic (cancer-causing) viruses but does not provide complete protection against cancer.

## What is HPV?

HPV viruses only affect humans, attacking skin and mucous membranes. They can be spread through direct contact with infected skin or membranes. In most cases HPV infections go unnoticed, do not cause any symptoms, and clear up on their own.

So far, more than 100 different types (strains) of human papillomaviruses are known to exist. Some of these can lead to the development of warts (papillomas). About 40 HPV strains infect the skin or mucous membranes in the genital area and are transmitted through sexual contact. They are not spread through body fluids, but through contact with skin and membranes.

Because the viruses are very common, most people who are sexually active will become infected with HPV. It is thought that as many as 80-90% of all sexually active women will have an HPV infection at some point in their lives.

## What are the consequences of an HPV infection?

In most people, the body's immune system destroys the viruses relatively quickly on its own, without any consequences. An infection typically lasts about eight months. However, if the infection is not successfully fought off and the virus stays in the skin or membranes cells, the affected tissue may start to change over time. In women, this typically occurs in the region of the cervix, but it can also occur in the membranes lining the vagina, although this is extremely rare. The cervix is the lower end of the uterus (womb). The lower part of the cervix is referred to as the mouth of the womb, and opens into the vagina.

A number of risk factors other than HPV infections play a role in the development of cervical cancer, like a person's ethnic origin. The most decisive factor, however, is an HPV infection. Two strains of the virus, known as HPV 16 and 18, are considered to be particularly dangerous. It is

estimated that they are involved in the development of 70% of all cervical cancer cases. Infections with carcinogenic HPV viruses have been recognised as a cause of cervical cancer since the 1980s.

Infections with some other strains of HPV viruses can lead to irritating but harmless warts (condylomas) in the genital area. Many of these are not noticeable, others can be felt as small hard bumps with an uneven surface. 90% are caused by HPV strains 6 and 11. About 1% of the population has condylomas, but they are more common in sexually active young people. In 20-30% of all people who have them, the warts disappear on their own without treatment.

## How common is cervical cancer?

Cervical cancer affects about 6,200 women every year in Germany. This is about 12 to 14 out of every 100,000 women, and about 3% of all cases of cancer in women in Germany. Most of these women are diagnosed with cervical cancer when they are between the ages of 35 and 55.

In the early stages of the disease, cervical cancer does not cause any noticeable symptoms, so it can only be detected by means of a simple, specific medical examination. A cancerous tumour is considered to be in the early stages of development (an "in situ carcinoma") if the cancer cells have not invaded the surrounding tissue. About 30-40% of such pre-cancerous changes go away without treatment, but around 12-15% develop into cancer. Because cervical cancer tumours are usually discovered and treated early on, it is difficult to say how they would develop without treatment. The treatment possibilities are good in pre-cancerous and early stages.

## How can you protect yourself from HPV infections?

The careful use of condoms provides protection against many sexually transmitted diseases. Yet condom use alone is not enough to protect against HPV infections. Because these viruses are so common, it is very difficult to ensure 100% protection other than by avoiding sexual activity completely.

A vaccine against the HPV types 16 and 18, 6 and 11 became available in 2006. HPV 6 and 11 are not considered to be cancer-causing (carcinogenic) viruses, but they can cause genital warts. The vaccine which goes by the brand name "Gardasil" or "Silgard" provides

protection against these four types, but hardly protects against other types of HPV, and does not offer any protection at all against other sexually transmitted infections. This is also true for the other licensed vaccine, marketed under the name of “Cervarix”, which only targets HPV types 16 and 18. “Cervarix” does not protect against genital warts. No published scientific studies have directly compared the two vaccines to see how well they can protect women against pre-cancerous changes. The question of whether boys could or should be vaccinated too is still being discussed.

In March 2007 the German authorities issued a recommendation that all girls between the ages of 12 and 17 be given an HPV vaccine. In response to this recommendation, the German statutory health insurance funds now cover the vaccine costs for all girls between 12 and 17. Girls and women who are younger or older than this can have the vaccine too, but the statutory health insurance funds do not generally pay for them to have it.

In order to prevent young women from becoming infected with HPV early on, it is recommended that they be vaccinated before they become sexually active, if possible. But it is not exactly clear at what age it is best to have the vaccine. Most of the research on how HPV vaccines influence the development of pre-cancerous changes was done in women who were 15 years old and above.

### **How well does the HPV vaccine work?**

In many women the vaccine successfully prevents pre-cancerous changes which may develop into cervical cancer. The scientific trials which looked at the vaccine that targets four HPV strains showed that the risk of pre-cancerous changes caused by HPV 16 and 18 is generally low. It was only 2-3% in women who had not been vaccinated, compared to 1-2% in those who had. In other words, the vaccine prevented the development of pre-cancerous changes in about 1 out of every 100 women during the trial. It is assumed that the vaccine works even better in girls and women who have not been infected with HPV – but researchers disagree about the estimates of possible benefit. The vaccine was also shown to reduce the frequency of genital warts from 4% in women who were not vaccinated to 1% in those who were (1 in every 100 women).

According to current knowledge, the protective effect of the vaccine lasts at least five years. It is not yet known whether a booster vaccination is needed after this. The vaccine

cannot be used to treat HPV infections or genital warts once women have them.

Because it is not yet known how well the vaccine works in the long term, and because cervical cancer usually develops very slowly, at the moment it is unclear whether the HPV vaccine really lowers the number of people who get cervical cancer. Being so new, there is also no evidence to show whether it reduces the number of women who die from this disease either.

One benefit of having the vaccine is that it can prevent pre-cancerous changes from developing. The diagnosis and treatment of these changes can be very stressful for women. Every year, thousands of women have surgery to remove pre-cancerous tissue – it is not known exactly how many women do though.

You can read more about clinical trials of the HPV vaccine [here](http://www.informedhealthonline.org/index.293.en.html) (URL: <http://www.informedhealthonline.org/index.293.en.html>).

### **How is the vaccine given?**

The vaccine is injected into the muscles of the upper arm. It does not contain any genetic material (DNA) of the viruses. Instead, genetically engineered virus-like particles are used. These have the same outer protein coat as the viruses do, but do not carry any genetic information. The particles activate the body's immune system and trigger the production of protective antibodies without causing an infection. Depending on the vaccine, the second dose is given one or two months after the first dose, and the third dose is given six months after the first dose.

### **What adverse effects does the HPV vaccine have?**

The adverse effects of the HPV vaccines have been studied in three ways:

- In small safety tests, including with young teenagers
- By information on adverse effects collected in the large trials
- Through monitoring reports of adverse effects from doctors and other health care workers, particularly in the USA

Based on the small, short-term safety tests, the authorities concluded that the vaccines are safe.

No serious adverse effects were reported in the large trials. According to the US authorities, HPV vaccines can cause local skin reactions at the site of injection, such as pain (in 8 out of 10 people), swelling (in 3 out of 10 people) and redness (in 3 out of 10 people). Fever is also among the more common adverse effects (just over 1 in 10 people). Problems such as indigestion, headaches, tiredness or muscle ache may occur but are less common.

The US authorities have set up a monitoring programme to collect data about adverse effects caused by the HPV vaccine. Early results are now available. The authorities say that the results are generally reassuring: given how many millions of girls have now been vaccinated, they believe that the vaccine is reasonably safe. But they do warn that, as with many vaccines in teenagers, there is a risk of fainting soon after having the vaccination. Doctors should therefore monitor girls who get the vaccine for at least 15 minutes afterwards, and the girls should not get up too quickly after having the shot.

It would be inadvisable to inject the second vaccine dose if, for example, the person is ill with a fever at the time when it is due. If the first dose causes an allergic reaction, a second dose may not be given. The possible adverse effects of the vaccine in the long term are not yet known.

### **What can you do to prevent cervical cancer?**

Although the HPV vaccine provides protection against certain types of HPV that can cause cancer, it is not clear to what extent it can prevent cervical cancer. So at this stage it cannot be called a “cancer vaccination” as such, even if an HPV infection sometimes leads to cervical cancer. Both vaccines provide protection against the two most common cancer-causing (carcinogenic) HPV viruses, and they appear to halve the risk of pre-cancerous changes in the short term.

Researchers still do not agree about how much young women can benefit from the HPV vaccine. Some say there is a great benefit, some say there is a small benefit, and others question the vaccine in general. Further research has to be done to be more certain about all these issues.

The vaccine does not replace regular smear tests for the early detection of cervical cancer. These make it possible to discover and treat pre-cancerous cell changes at an early stage.

As part of a cancer screening programme organised by the

statutory health insurance funds, every woman above the age of 20 in Germany is entitled to a smear test or so-called “Pap test” (named after the Greek doctor George Papanicolaou, who developed it) once a year. During this screening test, a doctor removes some cells by gently scraping the membranes lining the mouth and neck of the womb (cervix) using a special spatula and brush. The cells are then “smeared” onto a glass slide and examined under a microscope. If any abnormal cells are found, further tests are needed.

### **What should be considered when vaccinating girls and young women?**

As already mentioned, the vaccine should not be seen as an alternative to regular smear tests for the early detection of cervical cancer and does not provide protection against other sexually transmitted diseases. One of the potential dangers of the vaccine is that it might make young women feel so safe that they do not feel the need to take precautions, such as using condoms, during sexual activity.

Girls and young women should avoid getting up too quickly or doing things like riding a bike immediately after having the vaccine, as there is a risk of fainting.

Because there are still a number of unanswered questions about the HPV vaccine, it is not easy to weigh up the pros and cons. As well as being well informed about the HPV vaccine, it is particularly important for young women to know how they can protect themselves against sexually transmitted diseases and cervical cancer. In our article (URL:

<http://www.informedhealthonline.org/index.568.en.html>) and <http://www.informedhealthonline.org/index.567.en.html>) leaflet (URL: <http://www.informedhealthonline.org/index.567.en.html>) – written especially for girls – we have put together information for girls who are still deciding whether or not to have the vaccine.

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## Glossary

### screening

Screening is a systematic approach to trying to find illnesses among people who do not have symptoms or other obvious signs of disease. An example is screening for breast cancer with mammography.

### evidence

Evidence is what we call scientific proof from well-conducted, good-quality scientific trials that have been carefully designed to answer specific questions. Depending on the types of questions, different scientific research methods (types of study) are most appropriate to find reliable answers to these questions. Randomized controlled trials (RCTs), for example, are the best way to get reliable evidence on the effectiveness of medical treatments (interventions). This type of study, however, is not the best form of evidence for all possible questions, and does not provide the best answers to all kinds of questions, either. Epidemiological studies, for example, are very suitable for establishing well-founded proof for the spreading of a disease in the population.

### infection

In medicine, we speak of an infection when a person has caught a germ (an infectious agent). This germ can be a bacterium, a virus, a fungus or a worm. The germ multiplies and then either spreads throughout the body or only attacks one particular organ. As long as there are no signs of a disease, this is called an asymptomatic infection. When the body shows a reaction to the germ in the form of symptoms, this is called a symptomatic infection (an infectious disease). The period between the moment the germs enter the body and the moment the first symptoms of the disease appear, is called the incubation period. It may last a few hours or days, or even many years. An infection does not necessarily have to lead to the onset of a disease.

### vaccination

Vaccination involves stimulating the body's production of antibodies to a particular virus or bacteria, so that the person has increased resistance if they are exposed to the real infection. A vaccine aims to launch the body's defence system, without actually causing the disease. Depending on the vaccine, it could take some time after vaccination to develop immunity. With most vaccines, more than one

vaccination is needed. Sometimes the immunity from a vaccine lessens over time. That means there are some types of vaccination that need be repeated after a few years to stay active. There are several types of vaccines. Some vaccines are "inactivated" or "killed", which means that even though they are made from a virus, for example, no "live" part of the virus remains. That means the vaccine itself cannot cause infection. Other vaccines are "live attenuated vaccines". This means that the virus has been made so much less infective than the real virus, that it should not be able to cause symptoms.

### immune system

The immune system is the body's defense system and its task is to protect the body against germs or degenerated cells (like cancer cells). The immune system is very complex and has not been understood in every detail yet. There are two components: the cellular immune defense (for example "scavenger cells" and "killer cells") and the complement system ("antibodies", for example).

### virus

Viruses are germs that enter living cells (plant, animal or human cells) to multiply. Viruses cause illnesses and diseases such as smallpox, influenza, colds, hepatitis, herpes and AIDS.

### diagnosis

The term diagnosis (from the Greek word *diagnosi*: "distinguishing") is used to mean the identification and naming of an illness or a disease. A diagnosis is usually made by evaluating the medical history, symptoms and test results. The tests include both comprehensive physical examination and blood tests or examinations using medical instruments such as ultrasound or x-ray.

**Sources**

IQWiG health information is based on research in the international literature. We identify the most scientifically reliable knowledge currently available, particularly so-called “systematic reviews”. These summarise and analyse the results of scientific research on the benefits and harms of treatments and other health care interventions. This helps medical professionals and people who are affected by the medical condition to weigh up the pros and cons. You can read more about systematic reviews and why these can provide the most trustworthy evidence about the state of knowledge here (URL: <http://www.gesundheitsinformation.de/evidence-based-medicine.61.en.html>) . The authors of the major systematic reviews on which our information is based are always approached to help us ensure the medical and scientific accuracy of our products.

Agency for Healthcare Research and Quality. *Screening for cervical cancer. Systematic evidence review Number 25.* Rockville: Agency for Healthcare Research and Quality. 2002. [Full text (URL: <http://www.ahrq.gov/clinic/uspstf/uspstfscerv.htm>) ]

Brown DR, Kjaer SK, Sigurdsson K, Iversen O-E, Hernandez-Avila M et al. The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in generally HPV-naïve women aged 16-26 years. *J Infect Dis* 2009; 199: 926-935. [Full text (URL: <http://www.journals.uchicago.edu/doi/pdf/10.1086/597307>) ]

FDA (US Food and Drug Administration). *Information pertaining to labeling revision for Gardasil - Reminder to healthcare providers: 15-minute observation period needed after vaccination.* Rockville: FDA. June 2009. [Full text (URL: <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm165145.htm>) ]

Gesellschaft der epidemiologischen Krebsregister in Deutschland e.V. (GEKID – Association of Population-Based Cancer Registries in Germany). *Cancer in Germany: Incidence and Trends.* Saarbrücken: GEKID and Robert Koch Institute. 2006. [Full text (URL: [http://www.rki.de/clin\\_169/nn\\_205770/DE/Content/GBE/Gesundheitsberichterstattung/GBEDownloadsB/KID2008,templateId=raw,pr... - in German](http://www.rki.de/clin_169/nn_205770/DE/Content/GBE/Gesundheitsberichterstattung/GBEDownloadsB/KID2008,templateId=raw,pr...))]

Herrero R. Human papillomavirus (HPV) vaccines: limited cross-protection against additional HPV types. *J Infect Dis* 2009; 199: 919-922. [Full text (URL: <http://www.journals.uchicago.edu/doi/pdf/10.1086/597308>) ]

Hildesheim A, Herrero R, Wacholder S, Rodriguez AC, Solomon D et al. Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: a randomized trial. *JAMA* 2007; 298: 743-753. [Full text (URL: <http://jama.ama-assn.org/cgi/reprint/298/7/743>) ]

Markowitz LE, Dunne EF, Saraiya M, Lawson HW et al. Quadrivalent human papillomavirus vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *CDC MMWR Recommendations and Reports* 2007; 56 (RR02); 1-24. [Full text (URL: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5602a1.htm>) ]

Munoz N, Manalastas R, Pitisuttithum P, Tresukosol D, Monsonog J et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24-45 years: a randomised, double-blind trial. *Lancet* 2009; 373: 1949-1957. [Full text (URL: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)60691-7/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60691-7/fulltext)) ]

Paavonen J, Naud P, Salmeron J, Wheeler CM, Chow S-N et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvant vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young woman. *Lancet* 2009; 374: 302-314. [Full text (URL: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(09\)61248-4/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)61248-4/fulltext)) ]

Raffle AE, Alden B, Quinn M, Babb PJ, Brett MT. Outcomes of screening to prevent cancer: analysis of cumulative incidence of cervical abnormality and modelling of cases and deaths prevented. *BMJ* 2003; 326: 901-. [Full text (URL: <http://www.bmj.com/cgi/content/full/326/7395/901>) ]

Rambout L, Hopkins L, Hutton B, Fergusson D. Prophylactic vaccination against human papillomavirus infection and disease in women: a systematic review of randomized controlled trials. *CMAJ* 2007; 177: Online 1-11. [Informed Health Online summary (URL: <http://www.informedhealthonline.org/index.293.en.html>) ] [Full text (URL: <http://www.cmaj.ca/cgi/content/full/177/5/469>) ]

Robert Koch-Institut. Impfung gegen HPV – Aktuelle Bewertung der STIKO. *Epidemiologisches Bulletin* 2009; 32: 319-328. [ Full text (URL: [http://www.rki.de/nn\\_199596/DE/Content/Infekt/EpidBull/Archiv/2009/32\\_\\_09,templateId=raw,property=publicationFile.html](http://www.rki.de/nn_199596/DE/Content/Infekt/EpidBull/Archiv/2009/32__09,templateId=raw,property=publicationFile.html)) - in German]

Robert Koch-Institut. *Dachdokumentation Krebs*. RKI, 2009. Accessed 22.09.2009: [http://www.rki.de/DE/Content/GBE/DachdokKrebs/krebs\\_\\_inhalt.html](http://www.rki.de/DE/Content/GBE/DachdokKrebs/krebs__inhalt.html) (URL: [http://www.rki.de/DE/Content/GBE/DachdokKrebs/krebs\\_\\_inhalt.html](http://www.rki.de/DE/Content/GBE/DachdokKrebs/krebs__inhalt.html))

Slade BA, Leidel L, Vellozzi C, Woo EJ, Hua W et al. Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. *JAMA* 2009; 302: 750-757. [Full text (URL: <http://jama.ama-assn.org/cgi/reprint/302/7/750>) ]

Wheeler CM, Kjaer SK, Sigurdsson K, Iversen O-E, Hernandez-Avila M et al. The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in sexually active women aged 16-26 years. *J Infect Dis* 2009; 199: 936-944. [Full text (URL: <http://www.journals.uchicago.edu/doi/pdf/10.1086/597309>) ]

## **The German Institute for Quality and Efficiency in Health Care (IQWiG)**

The German Institute for Quality and Efficiency in Health Care (IQWiG) was established by legislation to provide evaluations of the effectiveness, quality and efficiency of healthcare services. This includes the assessment of medicines as well as the publication of health information for consumers and patients.

## **Evidence basis of our health information**

Our information is based primarily on systematic reviews of the effects of health care. Systematic reviews are necessary to gain an objective picture of health care. In order to do this, a clear question is formulated. Researchers then find all the relevant studies that could answer this question. They then evaluate those studies.

You can find a list of the evidence and other scientific literature on which this information is based at [\*\*www.informedhealthonline.org\*\*](http://www.informedhealthonline.org)

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