

The human papillomavirus vaccine

The virus, the diseases and the HPV vaccine



Beating cervical cancer – the facts

Archived September 2017

This factsheet describes the human papillomavirus (HPV), the diseases that it causes and the vaccine that helps to protect against these diseases.

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What is HPV?

HPV is a virus that infects the deepest layer of the skin or genital surfaces (epithelium). There are approximately 100 types of HPV, of which about 40 infect the genital area (McCance, 2004). The majority of all HPV infections resolve on their own and cause no clinical problems. This factsheet focuses on those types of HPV that cause genital infections. Around 70% of new genital infections clear within one year and approximately 90% clear within two years (Ho *et al.*, 1998; Franco *et al.*, 1999).

What diseases can HPV cause?

Genital HPVs can cause cervical cancer, genital warts and other rarer anogenital cancers and some cancers of the head and neck (Parkin *et al.*, 2006; Stanley, 2007).

Genital HPVs are described as either:

‘high-risk’ types (also referred to as oncogenic) if they are associated with cervical cancer and the early changes in the cervix associated with cervical cancer, or

‘low-risk’ types, if rarely or never found in cervical cancer, although some lead to the development of genital warts and may be associated with some other cancers.

Cervical cancer

Infection with a high-risk type of HPV is detected in the vast majority of cervical cancers and is understood to be necessary for the development of cervical cancer (see table 1). Most high-risk HPV infections do not lead to cervical cancer. In some people, the infection can persist and can cause abnormalities of the cervix, which if left undetected and untreated, can lead to cervical cancer. The time span between being infected with a high-risk HPV and the development of cervical cancer is, in most cases many years (Moscicki *et al.*, 2006). While infection with genital HPV is most common among young adults (aged 18-28) (Koutsky *et al.*, 1997), cases of cervical cancer peak in women in their late 30s. Two high-risk types, HPV 16 and HPV 18, are responsible for over 70% of all cervical cancers in Europe (Smith *et al.*, 2007) and England (Howell-Jones, 2010). Other high-risk HPVs that can cause cervical cancer include HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 66 (WHO IARC, 2007), (see table 1).

Table 1. Prevalence of HPV types in cases of cervical cancer in a) Europe and in b) England.

HPV type	Europe		England	
	Percentage of cervical cancer cases by HPV type	Cumulative total (%)	Percentage of cervical cancer cases by HPV type	Cumulative total (%)
16	58.1	58.1	66	66
18	15.7	73.8	10.4	76.4
33	4.4	78.2	5.3	81.8
31	4	82.2	2.7	84.4
45	2.9	85.1	3.1	87.6
35	1.6	86.7	0.4	88
58	1.2	87.9	0.4	88.4
56	1	88.9	0.2	88.7
52	0.6	89.5	3.1	91.8
39	0.2	89.7	1.6	93.3
51	0.2	89.9	0.4	93.8
68	0.3	90.2	0.7	94.4
59	0.1	90.3	1.3	95.8
Other	1.4	91.7	0	95.8
No types identified	8.3	100	4.2	100

Adapted from Smith *et al.*, 2007 and Howell-Jones *et al.*, 2010

Other anogenital cancers

HPV can also cause some other anogenital cancers. These include cancer of the vagina, vulva, penis and anus. HPV is associated with 80–90% of anal cancers (Munoz *et al.*, 2006): HPV types 16 and 18 are found in most of these cancers (see table 2).

Table 2. Types of cancer associated with HPV and the percentages of cases that are caused by HPV infection.

Site	Percentage attributable to HPV infection	Percentage of which, HPV16 and/or 18	Reference
Cervix	>99	>75	Smith <i>et al.</i> , 2007, Howell-Jones <i>et al.</i> , 2010
Penis	47	74	Miralles-Guri <i>et al.</i> , 2009
Vulva,vagina	42	90	Vuyst <i>et al.</i> , 2003
Anus	84	93	Vuyst <i>et al.</i> , 2003
Mouth	16	95	Kreimer <i>et al.</i> , 2005 (European specific)
Oropharynx*	28	89	Kreimer <i>et al.</i> , 2005 (European specific)

Adapted and updated from Jit *et al.*, 2011

*for cancer of the oropharynx, notably different and higher percentages have been reported in other publications. This may partly reflect changes over time as well as variations between the populations studied and in the anatomical sites included in the definition of oropharynx. Variations in the prevalence of the other causes of oropharyngeal cancer such as smoking and alcohol, will also impact on the proportion of this cancer that is attributable to HPV in different parts of the world.

However, unlike cervical cancer, where HPV infection can be detected in almost all cases, only around 40% of vaginal and vulval cancers are associated with HPV. The development of vaginal and vulval cancers is not well understood. These cancers are usually preceded by abnormalities, known as vaginal intraepithelial neoplasias (VaIN) or vulval intraepithelial neoplasias (VIN).

Genital warts

Genital warts are the most common viral sexually transmitted infection in the UK (PHE, 2013). Over 90,000 new cases were reported throughout the UK in 2009 (HPA, 2011). HPV types 6 and 11 cause the majority of cases of genital warts (Lacey *et al.*, 2006). In a survey of the UK population, 4% of adults aged 18 to 44 years reported that they had genital warts at some time in their life (Fenton *et al.*, 2001).

Genital warts can be difficult to treat and patients may experience frequent recurrent episodes. Genital warts are not life threatening, but they can cause significant distress to the individual and substantial healthcare costs (Woodhall *et al.*, 2011; Desai *et al.*, 2011).

How is HPV infection spread?

Genital HPV infections are spread primarily by sexual contact, particularly through sexual intercourse but also by non-penetrative genital contact. Risk factors for acquiring HPV infection are related to sexual behaviour – risk increases with number of new sexual partners, the sexual history of partners and the number of previous sexual partners. Non-sexual routes of HPV transmission include transmission from mother to baby in the period immediately before and after birth, and hand to genital contact may explain some infections in childhood (Cubie *et al.*, 1998).

What are the main factors that cause HPV infection to lead to the development of cervical cancer?

Persistent infection with one or more high-risk HPV types is the most important known factor for the development of cervical intraepithelial neoplasias (CIN) and cervical cancer. Several co-factors are likely to be involved in the development of cervical cancer. The incidence of invasive cervical cancer is increased by cigarette smoking, increasing number of full-term pregnancies, and HIV infection (WHO IARC, 2007; Vaccarella *et al.*, 2008). Some other factors, such as the use of the contraceptive pill, have been suggested to increase the likelihood of developing cervical cancer. But, as it is difficult to separate this factor from other linked factors such as sexual behaviour, the findings are inconclusive (Munoz *et al.*, 2006).

How does HPV infection lead to cancer?

HPV can cause changes in infected epithelial cells. In some cases, HPV DNA integrates into host (human) DNA in the cervical epithelial cells at the site of infection. It is this process that is likely to be involved in changes to these cells that can progress to cancer (Woodman *et al.*, 2007). The exact nature of this process and the role of other factors are not fully understood. A description of how CINs can develop into cervical cancer is shown in figure 1 (see pages 10 and 11).

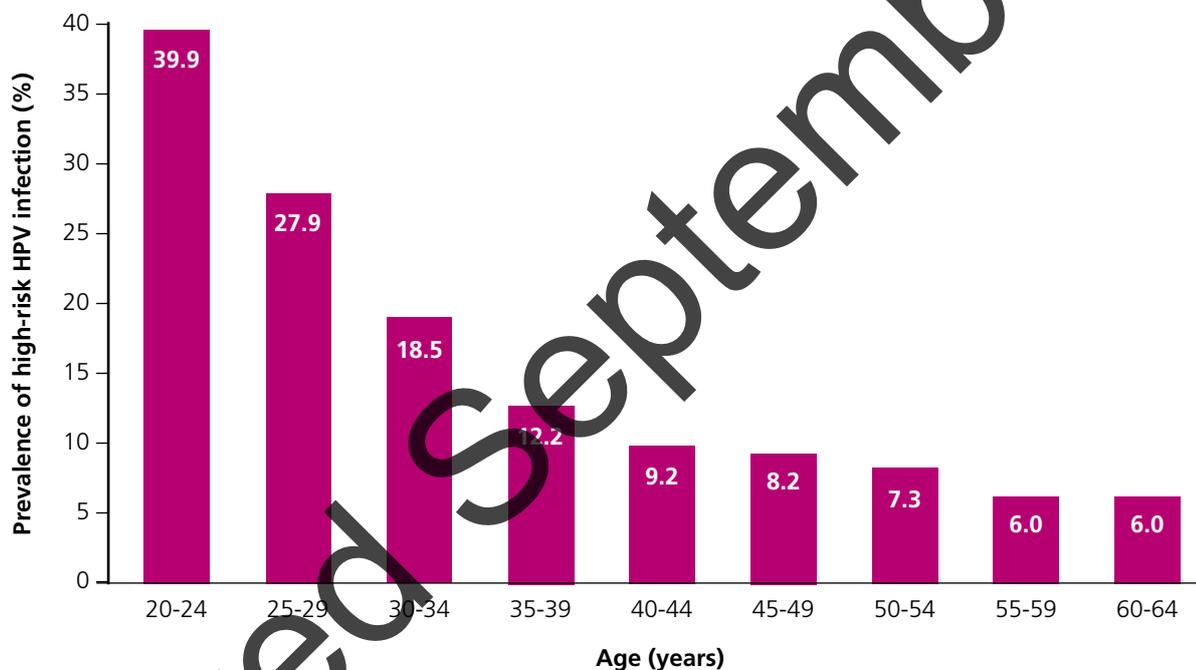


Figure 2. Prevalence of high-risk HPV infection amongst women attending for cervical screening. This shows that HPV infection is commonest in 20- to 29-year-olds and decreases rapidly after age 30. Data taken from Kitchener *et al.* 2006.

How common is HPV infection in the UK?

In a study conducted in the UK in 2001-2003, 40% of the cervical smears from 20- to 24-year-old women were positive for HPV DNA (indicating a current infection) (Kitchener *et al.*, 2006). Fifteen per cent of these women were infected with HPV types 16 or 18. In a study conducted in younger women undergoing chlamydia screening in England in 2008, prevalence peaked at 19 years of age (Howell-Jones *et al.*, 2012). As individuals get older the likelihood of infection with HPV decreases (see figure 2) (Kitchener *et al.*, 2006). The Centers for Disease Control and Prevention estimate that at least half of all sexually active women are infected by genital HPV in their lifetimes (CDC, 2004). Infection is likely to occur in their late teens and early twenties. A study of antibodies to four types of HPV infection (16, 18, 6 and 11) showed that the proportion of females who have been infected by HPV increases rapidly from 14 years of age to the early twenties (Jit *et al.*, 2007), (see figure 3).

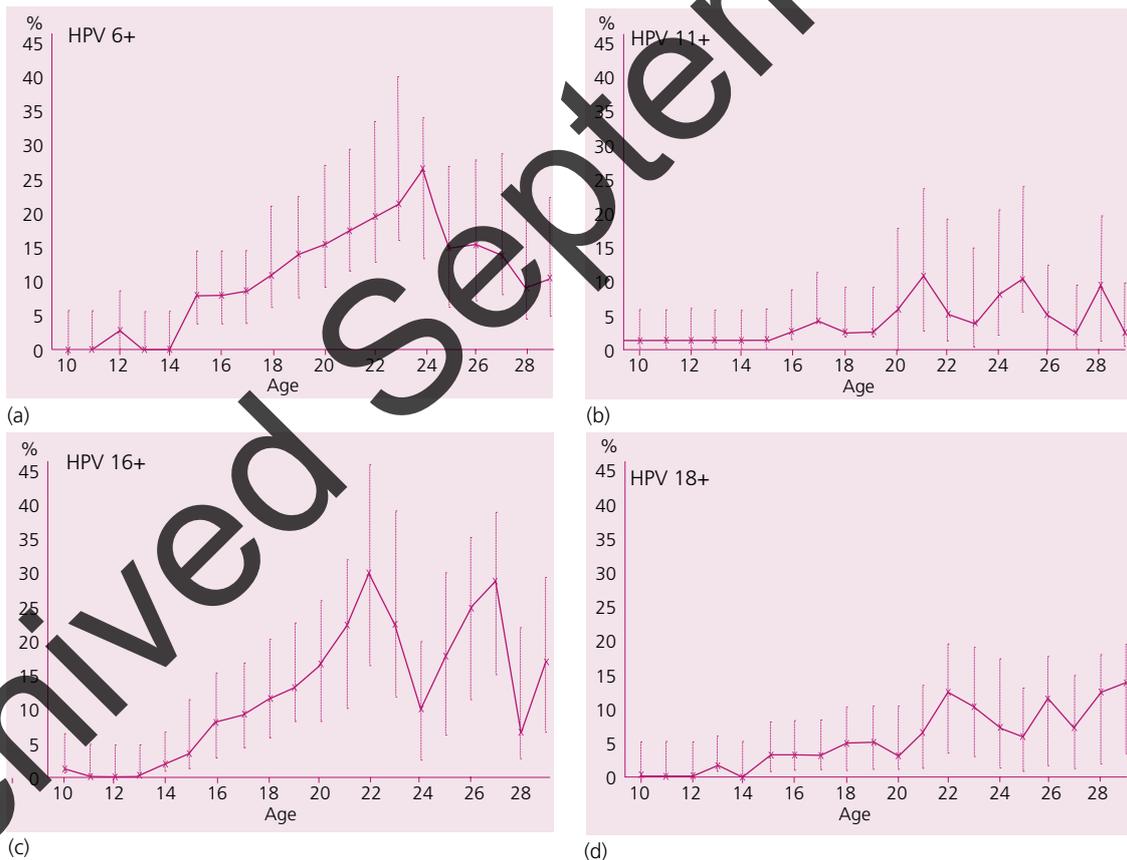


Figure 3. The percentage of females aged 10 to 29 years who have antibodies to (a) HPV 6, (b) HPV 11, (c) HPV 16 and (d) HPV 18. The error bars indicate the upper and lower confidence intervals. The presence of antibodies is evidence of past HPV infection. The graphs show that infection with HPV has already occurred in some girls shortly after age 14 years. Data taken from Jit *et al.*, 2007.

How common are cervical cancer and other anogenital cancers?

Cervical cancer

Cervical cancer is the second most common cancer of women worldwide with approximately 500,000 new cases and 270,000 deaths annually (Parkin *et al.*, 2006; Munoz *et al.*, 2006). In some countries, routine cervical screening programmes and subsequent treatment have prevented many invasive cancers and deaths by detecting and preventing cervical changes at an early stage (Peto *et al.*, 2004).

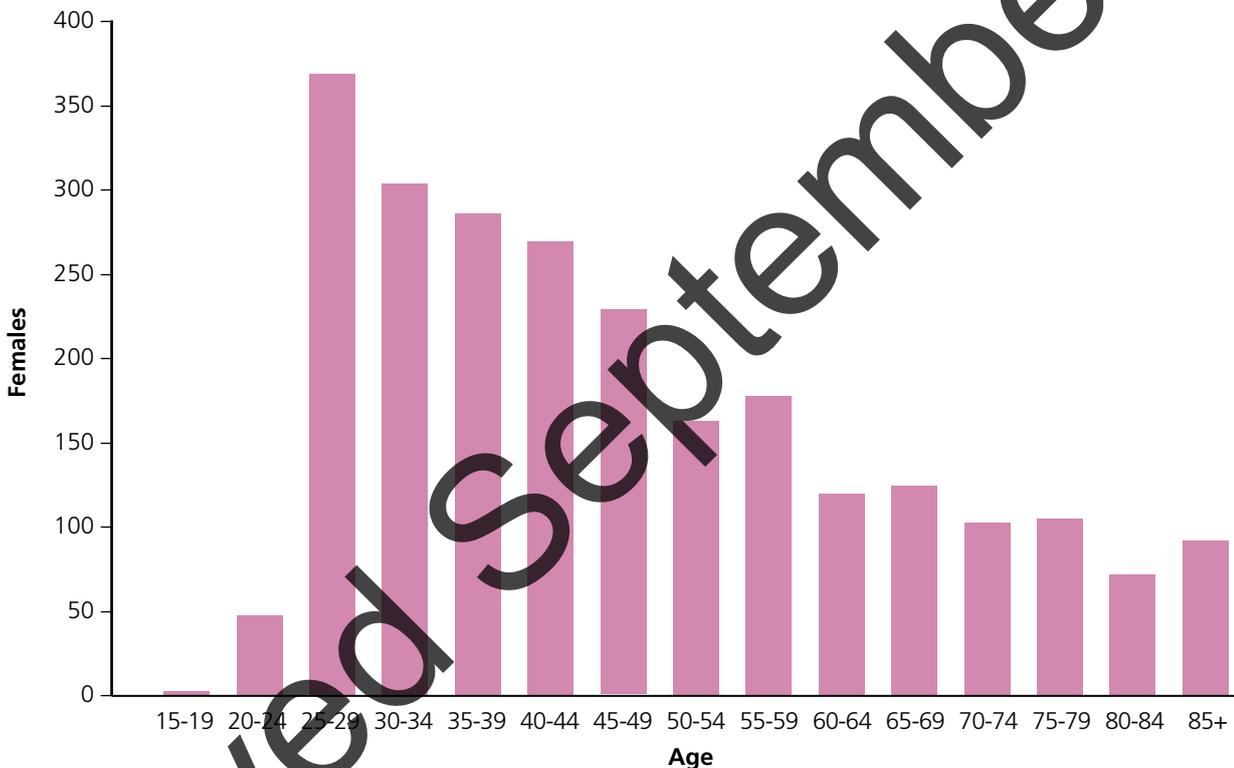


Figure 4. Number of cases of newly diagnosed cervical cancer in England, 2012 (source: Office for National Statistics, 2013)

In England, around 2500 new cases of invasive cervical cancer were diagnosed in 2012. Cervical cancer is the most common cancer among women who are 15 to 34 years old and unlike the majority of cancers, is primarily a disease of the young with 62% of cases occurring in women who are less than 50 years old (National Statistics, 2013).

Vaginal and vulval cancer

In England, there were around 210 cases of cancer of the vagina and 1050 cases of cancer of the vulva in 2012. (National Statistics, 2013) Around 70% of both types occur in women over the age of 60 years.

Anal cancer

In England, there were around 1043 cases of anal cancer diagnosed in 2012 (National Statistics, 2013). Nearly two-thirds of anal cancers occur in women.

How common are genital warts?

Genital warts are the most common viral sexually transmitted infection in the UK, with over 90,000 cases of new infection reported from GUM clinics in 2009 (HPA, 2011).

Can HPV infection be treated?

Although HPV infection itself cannot be treated, the diseases it causes can often be treated quite successfully.

Cervical, anal, vaginal and vulval abnormalities may be treated by removal, or by using cryotherapy, electrocautery and laser therapy.

The main type of treatment for cervical cancer (when the cancer is restricted to the cervix) is surgery. Surgery may also be used to treat anal, vaginal and vulval cancers, either alone or in combination with radiotherapy and chemotherapy.

In the UK, approximately two-thirds of women diagnosed with cervical cancer are alive five years after diagnosis (National Statistics, 2004).

There is a variety of treatments for genital warts. They can be treated using topical agents, cryotherapy and electrocautery, all of which may require repeated applications. None of these approaches treats the infection and treated individuals may continue to be a source of infection to other people, and may suffer recurrence of genital warts.

Can HPV infection be prevented?

Abstinence from any sexual activity greatly reduces the risk of genital HPV infection. For sexually active people, condoms reduce the risk of HPV infection, but they are not 100% effective (Koutsky, 1997). This is because HPV can be transmitted by skin-to-skin contact of genital areas not covered by condoms.

Can the development of cervical cancer be prevented?

The NHS National Cervical Screening Programme has led to a significant fall in the incidence and death rate from cervical cancer. Death rates in 2004 were approximately 60% lower than 30 years before, mainly due to the introduction of systematic screening (Peto *et al.*, 2004). Cervical screening does not prevent HPV infection nor does it prevent the early changes that may indicate the later development of cervical cancer.

The HPV vaccine

Vaccines are available to protect against the two high-risk HPV types (16 and 18) that cause most cervical cancer and the two HPV types that cause the majority of genital warts (6 and 11). The national immunisation programme began in 2008 using a vaccine (Cervarix) against HPV 16 and 18. In 2012, the programme changed to use a vaccine (Gardasil) against HPV 6, 11, 16, and 18. In September 2014 the programme changed, from a three-dose to a two-dose schedule.

“to protect against the two high-risk HPV types (16 and 18) that cause most cervical cancer”

Why has the vaccine changed?

Cervarix was chosen for the initial vaccine supply. When this was reviewed in 2011, Gardasil offered the best value and so was chosen for the next contract.

Why has the schedule changed from three to two doses?

Since the HPV vaccination programme started in the UK in 2008, the vaccine has proved to be very effective. Studies conducted since then suggest that two doses of the HPV vaccine will provide excellent, long-lasting protection for young girls and so countries, such as Switzerland, have moved to this new schedule. From September 2014, the HPV vaccination programme in the UK will consist of two doses of HPV vaccine.

How effective is the HPV vaccine in preventing cervical cancer?

Both HPV vaccines are over 99% effective in preventing cervical abnormalities associated with HPV types 16 and 18 in women who have not already been infected by these types (Lu *et al.*, 2011).

The vaccines have not been shown to protect against disease if a woman has an active HPV infection. However, they may protect a woman who has already been exposed to HPV infections and is no longer infected. The vaccines will protect individuals against infection with the HPV vaccine types they have not already contracted.

These vaccines do not protect against all HPV types that cause cervical cancer. However, there is evidence of some protection against some of these types that are not in the vaccines (cross protection).

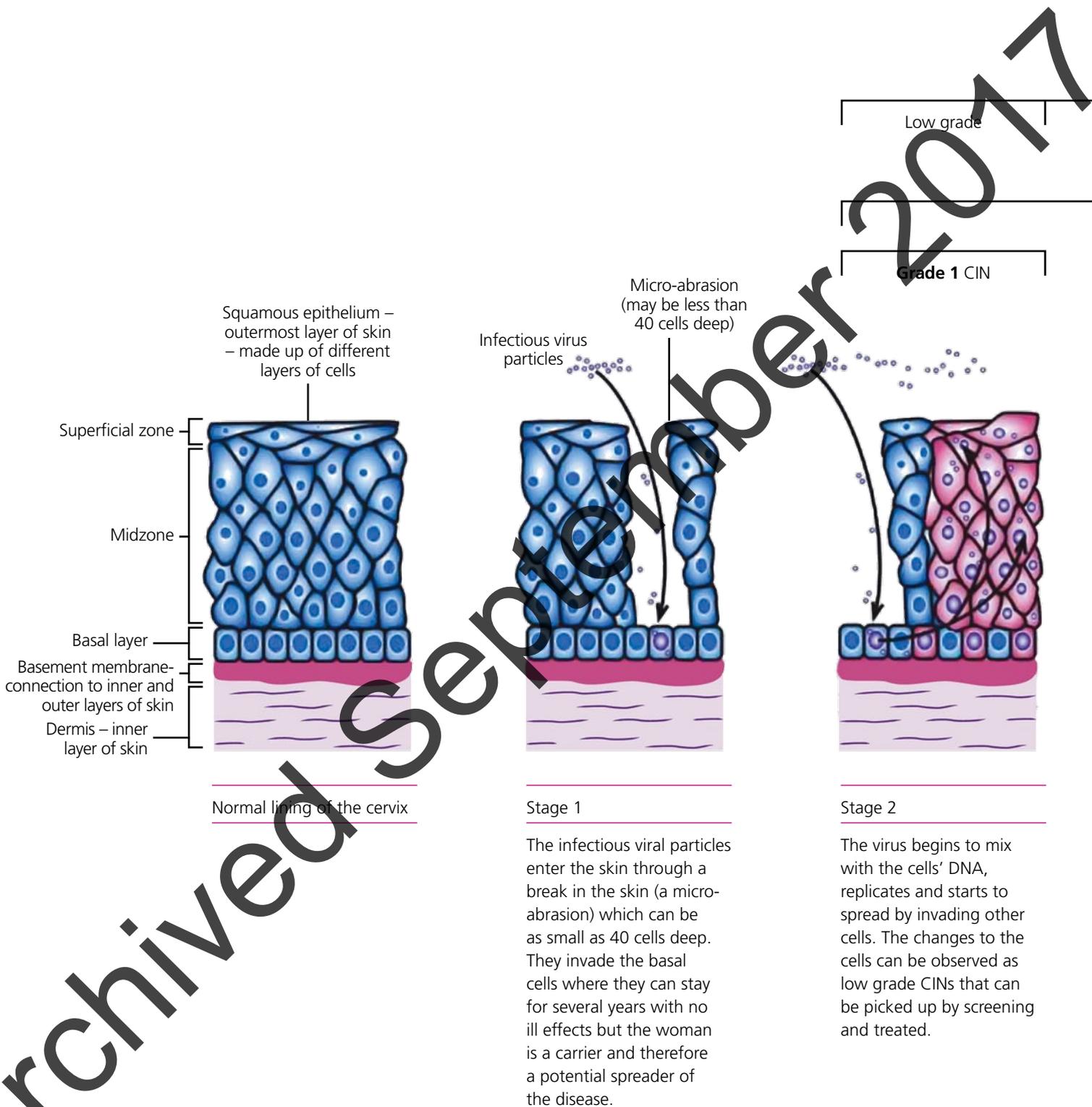


Figure 1. How the human papillomavirus affects the surface of the cervix and produces a cancerous growth. (from Woodman *et al.*, 2007)

Squamous intraepithelial lesion

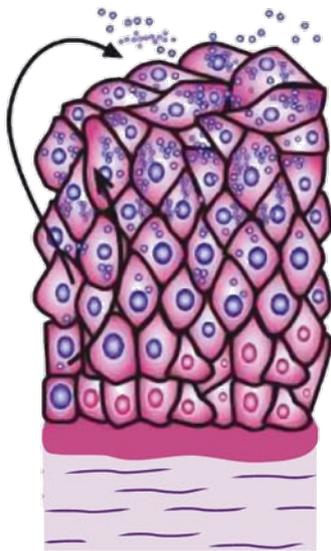
High grade

Cervical intraepithelial neoplasia (CIN)

Grade 2 CIN

Grade 3 CIN

Invasive cancer



Stage 3

The cells become more damaged and disorganised – resulting in a high grade lesion.



Stage 4

The high-grade CIN grows and occupies almost the entire thickness of the skin.



Stage 5

All the cells have been infected and are completely disorganised producing an invasive cancerous growth or tumour that can break through the basement membrane into the inner layer of the skin and spread to other parts of the body.

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How does the vaccine work?

The vaccine is made from the proteins that make up the outer coat of the virus types. These proteins assemble into small spheres that are called virus-like particles (VLPs). The VLPs are not infectious and cannot cause cervical cancer or genital warts.

When a person is vaccinated, their immune system mounts a response against these VLPs. If the person is exposed to the real virus infections, the body's immune system reacts quickly to stop the infection.

Who will receive this vaccine?

The vaccine is offered routinely to girls aged 12 to 13 years (school year 8). Older girls under the age of 18 were offered the vaccine through a catch-up programme that began in September 2008. This programme has finished, but girls aged under 18 years who have not received the vaccine can still receive it free of charge if they ask their doctor.

How will the vaccine be given?

The vaccine will usually be given in the upper arm by intramuscular injection. Two doses of HPV vaccine are given. The second injection should be given anytime between six and 12 months after the first but it can be given up to 24 months after. Your school or GP will inform you when your daughter will actually have the second dose. Both doses are needed for full protection.

What if my daughter has not had her first HPV vaccine by the age of 15?

Girls who have not received any HPV vaccine by the age of 15 will need three doses of the vaccine to have full protection. This is because the response to two doses in older girls is not quite as good, so to be on the safe side they should receive three doses, with the second dose given around a month after the first dose, and a final dose given around six months after the first dose.

Girls who started the three-dose course of the HPV vaccine before September 2014 should complete it as originally planned.

How long does protection from HPV vaccination last?

Studies suggest that vaccinated people maintain high levels of protection for at least seven years, and it is expected to last many years. The long-term effectiveness of the vaccine will continue to be monitored carefully.

Is the HPV vaccine safe?

Both vaccines are very safe. Safety has been established through rigorous testing in clinical trials (e.g. Paavonen et al, 2007; Reisinger et al, 2007), followed by use of many millions of doses across the world over the past few years. As with any vaccine, some people may experience a side effect, but these are generally of short duration and are far outweighed by the expected benefits of the vaccine.

What side effects does the vaccine cause?

The most common side effect is mild to moderate swelling, redness and pain at the site of injection. Other mild side effects such as raised temperature, sickness, dizziness, diarrhoea and muscle aches were reported in more than one in 100 people.

Very rarely, some people have an allergic reaction soon after immunisation. This reaction may be a rash or itching affecting part or all of the body. Even more rarely, some people can have a severe reaction soon after the immunisation which causes breathing difficulties and may cause the person to collapse. This type of reaction (anaphylaxis) is extremely rare and health professionals administering vaccinations are trained to deal with it. Fainting, sometimes accompanied by shaking or stiffening, has also been reported associated with the vaccination procedure.

A full list of potential adverse reactions is provided in the patient information leaflet that comes with each vaccine and can also be accessed [here](#). Suspected side effects should be reported to the Yellow Card Scheme www.mhra.gov.uk.

Are there any reasons why individuals should not have this vaccine?

There are very few individuals who cannot receive HPV vaccine.

Immunisation is contraindicated only in persons who have had:

- a confirmed anaphylactic reaction to a previous dose
- a confirmed anaphylactic reaction to any part of the vaccine.

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If a person is acutely unwell with a very high temperature, immunisation may be postponed until they have fully recovered. This is to avoid wrongly associating any cause of fever, or its progression, or other symptoms to adverse effects of the vaccine. Allergy to yeast is not a contraindication to immunisation.

Is HPV vaccine safe if it is given to a pregnant woman?

There is no known risk associated with giving HPV vaccine during pregnancy. HPV vaccine is an inactivated vaccine, which means that it does not contain any live organisms, and so cannot cause infection in either the mother or her baby. However, as a matter of precaution, HPV vaccine is not recommended in pregnancy. This is not because of any specific safety concerns with giving HPV vaccine during pregnancy but due to limited information on using the vaccine in pregnant women.

Although pregnant women were specifically excluded from the HPV vaccine trials and safeguards were in place during the trials to prevent pregnant women from receiving the vaccine some women were unknowingly pregnant when they were immunised, or were immunised just before becoming pregnant. The women who received HPV vaccine were no more likely to have problems with their pregnancies than women in the trials who did not receive HPV vaccine. There were no increased risks found for the babies born to women who had received the vaccine.

What should happen if HPV vaccine is given to a pregnant woman?

If a woman finds out she is pregnant after she has started a course of HPV vaccine, she should discuss this with her GP who can then report this to the Public Health England (PHE, formerly Health Protection Agency) register directly by visiting this website: www.hpa.org.uk or by telephone: 01788 540298 or 0208 327 7471.

There is no evidence that having the vaccination during pregnancy will harm her or her baby and there is no reason to believe that the pregnancy cannot continue safely. Once the woman has completed her pregnancy, she can finish the full course of HPV vaccine.

Due to the relatively limited experience of using HPV vaccine in pregnant women to date, it is important to follow up women who have been given the vaccine during pregnancy. This is to provide further information on the safety of the vaccine when it is given in pregnancy. This follow-up is being conducted by the National Immunisation Team of Public Health England.

Can the vaccine be given to people who are immunocompromised?

Women and girls whose immune systems are compromised, due to either disease or medication, can still receive HPV vaccine. However, the immune response to this vaccination and its effectiveness may be less than that observed among those who are immunocompetent. The two-dose schedule has not been used in girls who have conditions that reduce the effectiveness of their immune system. For this reason these girls should receive three doses of the HPV vaccine within a six month period.

Is HPV vaccination recommended in other countries?

HPV vaccination is in use (as a three-dose or two-dose schedule) in many European countries, as well as many other countries worldwide, including the US, Australia, Canada and New Zealand. Numerous other countries are considering implementation of HPV vaccine.

What about older girls – are they at risk and will they get the vaccine?

All women who are sexually active are at risk of HPV infection. Risk of a new HPV infection decreases quite markedly for most women over the age of 25 years – by this time many women will already have become infected and/or change sexual partners less frequently. For sexually active older women who are already likely to have been infected by HPV, participation in the NHS Cervical Screening Programme (to detect disease caused by existing infection) remains the best way to protect themselves against cervical cancer.

What about boys – are they at risk and do they need the vaccine?

As boys do not suffer from cervical cancer, the benefits of HPV vaccination are different and less clear for boys than for girls, and vaccination of boys has not been found to be cost-effective in the UK. The protection against genital warts offered by Gardasil has been clearly shown for both boys and girls. There is emerging evidence of benefit against other non-cervical cancers, including some in men.

The vaccination of girls will reduce the transmission of infections to boys. This should lead to a reduction in HPV-related diseases in unvaccinated boys as well as girls.

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Glossary

Abstinence

To refrain, to stop doing something

Allergic reaction

A reaction by your immune system to a substance that does not usually affect most people

Anal

Of the anus which is the opening at the end of the digestive system where solid waste leaves the body

Anaphylaxis

An immediate and severe allergic reaction which needs urgent medical attention

Anogenital

Of the genital area including the anus

Antibodies

Proteins produced by the body to neutralise or destroy toxins and disease-carrying organisms

Cancer

A group of diseases in which cells grow unrestrained in an organ or tissue in the body; can spread to tissues around it and destroy them or be transported through blood or lymph pathways to other parts of the body

Cervical cancer

Cancer of the cervix (neck of the womb)

Cervical intraepithelial neoplasias (CIN)

A cervical abnormality that can progress to cancer. CINs are classified as CIN 1, 2 or 3 depending on how much of the epithelium is affected

Cervical screening

Cervical screening is a method of preventing cancer by detecting and treating early abnormalities which, if left untreated, could lead to cancer in a woman's cervix. The first stage in cervical screening is either a smear test or liquid based cytology

Cervical screening programme

The NHS Cervical Screening Programme was set up in 1988 when the Department of Health instructed all health authorities to introduce computerised call-recall systems and to meet certain quality standards

Cervix

The lower part of the uterus (womb) separating it from the vagina

Chemotherapy The treatment of infections or cancer using drugs that act on disease-producing organisms or cancerous tissue

Co-factors

Other factors that may influence an outcome

Contraindicated

Contraindications are reasons not to use a particular treatment or medication. An aspect of a patient's condition that makes the use of a certain drug or therapy an unwise or even a dangerous decision

Cross-protection

The ability of a vaccine that protects against one strain of a virus to provide protection against other, similar strains

Cryotherapy

A treatment that uses extreme cold to freeze and destroy diseased tissue

DNA Deoxyribonucleic acid

The molecules inside cells that carry genetic information and pass it from one generation to the next

Electrocautery

The cauterisation of tissue using electric current to generate heat

Epithelium

The layer of cells that covers the body and lines many organs

Fetal/fetus

The unborn baby, from the eighth week of pregnancy until birth

Genital tract

The organs that make up the reproductive system

Genital wart

A growth on the skin in or around the vagina, penis, or anus, transmitted by sexual contact.

Genito-Urinary Medicine (GUM) clinic

Specialist clinics for the diagnosis and treatment of sexually transmitted diseases

Immune response

The body's response to an immunisation or infection

Immune system

The immune system is one of the body's defence systems, which helps protect it from disease

Immunocompetent

With a well- functioning immune system

Immunocompromised

When the body's immune system does not work properly
Intramuscular Into the muscle

Laser therapy

The use of a laser (a concentrated beam of light) to perform medical procedures, such as the destruction of tumours

Lesions

A lesion is an abnormal change in an organ or body tissue because of injury or disease.

Oncogenic genes

that, when altered by environmental factors or viruses, can cause abnormal cell growth

Pre-cancerous

Describes a condition from which cancer may develop

Proteins

One of the essential constituents of living organisms

Radiotherapy

Treatment of a disease, such as cancer, using forms of radioactivity that damage or destroy abnormal cells

Thiomersal

A mercury-based preservative used in some vaccines to prevent microbial contamination, or in the process of producing inactivated vaccines.

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Treatment

Medical care for an illness or injury

Tumour

An abnormal growth of tissue

Vagina

The muscular passage connecting the uterus to the outside genitals; a component of the female reproductive system

Vaginal intraepithelial neoplasias (VaIN)

A vaginal abnormality that can progress into vaginal cancer. Like cervical intraepithelial neoplasia (CIN) it is classified as VaIN 1,2 or 3 depending on how much of the epithelium is affected

Vulva

The female external genitalia

Vulval

Of the vulva

Vulval intraepithelial neoplasias (VIN)

A vulval abnormality that can progress into vulval cancer. Like cervical intraepithelial neoplasia (CIN) it is classified as VIN 1,2 or 3 depending on how much of the epithelium is affected

Warts

Small growths on the skin caused by the human papillomavirus

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Beating cervical cancer



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