

Cancer Association of South Africa (CANSA)



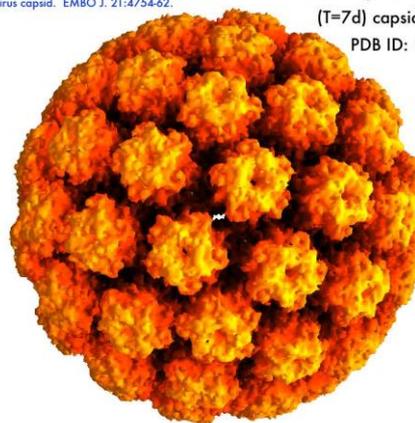
Fact Sheet on Human Papilloma Virus Infection and Cancer

Introduction

The human papillomavirus (HPV) is a DNA virus from the papillomavirus family that is capable of infecting humans. Like all papillomaviruses, HPVs establish productive infections only in keratinocytes of the skin or mucous membranes. While the majority of the known types of HPV cause no symptoms in most people, some types can cause warts (verrucae), while others can – in a minority of cases – lead to cancers of the cervix, vulva, vagina, penis, oro-pharynx and anus. Recently, HPV has also been linked to an increased risk of cardiovascular disease. In addition, HPV 16 and 18 infections, apart from being responsible for cervical cancer, are strongly associated with an increased risk of oropharyngeal (throat) cancer.

Modis Y, Trus BL, Harrison SC (2002). Atomic model of the papillomavirus capsid. EMBO J. 21:4754-62.

Human Papillomavirus 16 L1 (T=7d) capsid Model
PDB ID: 1LOT



QUAIR image by Juan Luis Soto ©2005
Images: www.docubio.wisc.edu

Coordinates from: PDB: www.rcsb.org/pdb/ VIPER: mmtsb.scripps.edu/viper/

[Picture Credit: HPV-16]

Kuo, H.K. & Fujise, K. 2011.

OBJECTIVES: The purpose of this study was to examine the association between human papillomavirus (HPV) and cardiovascular disease (CVD) among U.S. women.

BACKGROUND: Oncogenic proteins derived from tumor-associated HPV induce the degradation of tumor suppressor protein p53. Inactivation of p53 is associated with accelerated atherosclerotic process. However, the association between HPV infection with CVD remains unclear.

METHODS: Data were from 2,450 women (age 20 to 59 years) in the National Health and Nutrition Examination Survey, 2003 to 2006. Self-collected vaginal swab specimens were sent for HPV DNA analysis by L1 consensus polymerase chain reaction followed by type-specific hybridization. CVD was ascertained by self-reported diagnosis of myocardial infarction or stroke.

RESULTS: A total of 60 females (39 women were HPV DNA positive, whereas 21 were negative) had coronary artery disease. Presence of vaginal HPV DNA was associated with CVD. Odds ratio (OR) of CVD comparing women with presence of vaginal HPV DNA to those without was 2.30 (95% confidence interval [CI]: 1.27 to 4.16) after controlling for demographics, health/sex behaviors, medical comorbidities, cardiovascular risk factors, and management. At the same level of

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adjustment, OR of CVD comparing women with cancer-associated HPV types to those with negative HPV was 2.86 (95% CI: 1.43 to 5.70).

CONCLUSIONS: HPV infection, especially cancer-associated oncogenic types, is associated with CVD among women.

Joo, E-J., Chang, Y., Kwon, M-J., Cho, A., Cheong, H.S. & Ryu, S. 2019.

Rationale: Until now, no cohort studies have evaluated the relationship between high-risk human papillomavirus (HPV) infection and new-onset cardiovascular diseases (CVD).

Objective: We investigated an association between high-risk HPV infection and the development of CVD.

Methods and Results: We conducted a cohort study of 63,411 women aged 30 or older without CVD at baseline who underwent a high-risk HPV test and were followed annually or biennially from 2011 to 2016. CVD was ascertained through the linkage to the Health Insurance and Review Agency database. A Cox proportional hazards regression model was used to estimate adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) of incident CVD. The prevalence of high-risk HPV infection was 7.6%. During 261,598.9 person-years of follow-up, 1,122 cases of new-onset CVD were identified (incidence rate of 4.3 per 103 person-years). High-risk HPV infection was significantly associated with incident CVD. After adjustment for possible confounders, and high sensitivity C-reactive protein, a significant association between high-risk HPV infection and incident CVD was still observed, with a corresponding HR (95% CI) of 1.25 (1.03-1.52). This association was stronger among individuals with obesity and those with metabolic syndrome (MetS). Multivariable-adjusted HR (95% CI) for incident CVD comparing high-risk HPV-positive- to high-risk HPV-negative participants was 1.10 (0.87-1.39) in the non-obese, whereas corresponding HR (95% CI) was 1.73 (1.19-2.51) in those with obesity (P for interaction by obesity=0.002). Similarly, multivariable-adjusted HR (95% CI) for incident CVD comparing high-risk HPV-positive- to high-risk HPV-negative participants was 1.09 (0.87-1.36) in those without MetS and 1.99 (1.28-3.08) in those with MetS (P for interaction=0.05).

Conclusions: In this large cohort, high-risk HPV infection was significantly associated with an increased risk of developing CVD, especially in obese individuals and those with MetS, indicating that high-risk HPV might affect CVD risk with possible effect modification by obesity and MetS.

High and Low Risk Human Papilloma Viruses

Most people infected with HPV never develop any symptoms, however, there are a number of conditions that can result from an HPV infection.

HPV Research Scientists have separated HPV types into those that are more likely to develop into cancer and those that are less likely. The so-called 'high-risk' types are more likely to lead to the development of cancer, while 'low-risk' viruses rarely develop into cancer.

The sexually transmitted varieties of 'high-risk' HPV types include:

HPV-16 HPV-18 HPV-31 HPV-33 HPV-35 HPV-39

HPV-45 HPV-51 HPV-52 HPV-56 HPV-58 HPV-59

HPV-68 HPV-69

A few other HPV types are also sometimes included on this list. These 'high-risk' HPV types cause growths that are usually flat and nearly invisible as compared to the warts caused by types HPV-6 and HPV-11.

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Up to 70% of cervical cancer cases are caused by HPV-16 and HPV-18.

'Low-risk' HPV types can cause no symptoms or may cause conditions such as genital warts, but do not cause cervical cancer. Warts can form weeks, months, or even years after sexual contact with a person who has genital HPV. It is also possible that warts may never appear. In fact, most people with 'low-risk' HPV types never know they are infected because they do not get warts or any other symptoms.

The following table lists various conditions along with their associated types of HPV:

Disease	HPV Type
Cervical cancer	16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58
Precancerous changes	16, 18, 34, 39, 42, 55
Laryngeal papillomas	6, 11, 30
Genital Warts	6, 11, 30, 40, 41, 42, 43, 44, 45, 51, 54
Common warts	1, 2, 4, 26, 27, 29, 41, 57
Flat warts	3, 10, 27, 28, 41, 49
Plantar warts	1, 2, 4
Other cutaneous lesions (e.g., epidermoid cysts, laryngeal carcinoma)	6, 11, 16, 30, 33, 36, 37, 38, 41, 48, 60, 72, 73
Epidermodysplasia verruciformis	2, 3, 10, 5, 8, 9, 12, 14, 15, 17, 19, 20, 21, 22, 23, 24, 25, 36, 37, 38, 47, 50
Recurrent respiratory papillomatosis	6, 11
Focal epithelial hyperplasia of Heck	13, 32
Conjunctival papillomas/carcinomas	6, 11, 16
Cervical intraepithelial neoplasia	
Unspecified	
Low risk	30, 34, 39, 40, 53, 57, 59, 61, 62, 64, 66, 67, 68, 69
High risk	6, 11, 16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 52, 74 16, 18, 6, 11, 31, 34, 33, 35, 39, 42, 44, 45, 51, 52, 56, 58, 66

Burd, E.M. 2003.

Mirghani, H., Sturgis, E.M., Aupérin, A., Monsonego, J. & Blanchard, P. 2017. Is there an increased risk of cancer among spouses of patients with an HPV-related cancer: a systematic review. *Oral Oncol.* 2017 Apr;67:138-145. doi: 10.1016/j.oraloncology.2017.02.024. Epub 2017 Feb 28.

BACKGROUND: High-risk human papillomaviruses (HR-HPV) are the cause of most ano-genital cancers and a fast growing subset of oropharyngeal cancer. As these malignancies occur as a result of an HPV- infection transmitted through intimate contact, many patients with HPV-induced cancer and their partners are concerned about HPV-transmission and the potential partners' cancer risk. Few studies have addressed this issue and whether the HPV-related cancer risk of partners of patients with HPV-related cancers is comparable to or greater than that of the general population.

METHODS: We performed a systematic review of the published literature addressing this issue. Out of 1055 references screened, 53 articles were found eligible for inclusion.

RESULTS: Regarding the issue of coincidence of HPV-induced oropharyngeal and/or anogenital cancers in couples, 13 case-reports or case-series were reported and 9 larger studies based on population-registries. Four of these registry studies showed an increased risk of cervical cancer in the partner while four did not. Among the four positive studies, odds ratios for the development of HPV-related cancer among spouses were between 2.6 and 6.7. One study showed an increased risk of tongue or tonsil cancer among husbands of women with cervical dysplasia or cancer. Overall the absolute risk increase in all these studies was small, on the order of 1-3%, although potentially

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underestimated. Indeed, all these studies have assessed partner's cancer risk at only one anatomical site whereas HPV-related malignancies can affect different locations.

CONCLUSION: This systematic review suggests a small trend of increase risk in HPV-associated cancers among spouses of patients with HPV-related cancer.

HPV Infection

Genital human papillomavirus (also called HPV) is the most common sexually transmitted infection (STI). There are more than 40 types of HPVs that can infect the anogenital areas of males and females. These HPV types can also infect the mouth and throat.

HPV can cause serious health problems, including genital warts and certain cancers. There is no certain way to tell who will develop health problems from HPV and who will not. In most cases HPV goes away by itself before it causes any health problems, and most people who become infected with HPV do not even know that they have it.

HPV is not the same as herpes or HIV (the virus that causes AIDS). Both viruses can be passed on during sexual contact but they have different symptoms and cause different health problems

Wang, M., Sharma, A., Osazuwa-Peters, N., Simpson, M.C., Schootman, M., Piccirillo, J.F., Huh, W.K. & Adjei Boakye, E. 2020.

BACKGROUND: Since the number of cancer survivors is increasing, it is imperative that we better understand the long-term consequences of these survivors. We assessed the risk of developing a second primary malignant neoplasm (SPMN) after an index potentially-HPV-associated cancers (P-HPV-AC).

METHODS: We constructed a population-based cohort of patients with P-HPV-AC using Surveillance, Epidemiology, and End Results registry data (2000-2015). We limited patients to those with invasive P-HPV-AC [cervical, vagina, vulva, penile, anal, and oropharynx] based on the International Classification of Diseases for Oncology, 3rd edition. Excess SPMN risks were calculated based on standardized incidence ratios (SIRs) and excess absolute risks (EARs) per 10,000 person-years at risk (PYR).

RESULTS: A total of 105,644 patients with an index P-HPV-AC were identified, and 7.8 % developed a SPMN. In all P-HPV-AC patients, the overall SIR was 1.73 (95 % CI: 1.69-1.77) and EAR of 70.72 per 10,000 PYR. All index P-HPV-AC sites showed statistically significant increases in the risk of SPMN, except for anal cancer among men, compared with the general population. The greatest increase in risk of SPMN was observed among patients diagnosed with an index P-HPV-oropharyngeal cancer (SIR = 1.83; 95 % CI, 1.70-1.82 and SIR = 2.29; 95 % CI, 2.12-2.47 for men and women, respectively). Men developed SPMN mostly in aero-digestive tract while women developed SPMN both in aero-digestive tract and other HPV-associated cancer sites.

CONCLUSIONS: P-HPV-AC survivors experienced excess risk of SPMN. These findings have the potential to affect future surveillance practices and improve preventive healthcare for survivors of P-HPV-ACs.

Key Statistics and Human Papilloma Virus Infection in South Africa

According to **Bruni, *et al.***, (2019), the following are key statistics for South Africa for 2018:

Population

Women at risk for cervical cancer (female population aged ≥ 15 Years) 20,2 million

Burden of cervical cancer and other HPV-related cancers

Annual number of cervical cancer cases 12 983

Annual number of cervical cancer deaths 5 595

Crude incidence rates per 100 000 and Year

	Male	Female
Cervical cancer	-	44.4
Anal cancer	0.2	0.0
Vulvar cancer	-	0.8
Vaginal cancer	-	0.2
Penile cancer	0.6	-
Oropharyngeal cancer	1.1	-.3

Burden of cervical HPV infection

Prevalence (%) of HPV 16 and/or HPV 18 among women with:

Normal cytology	3.2
Low-grade cervical lesions (LSIL/CIN-1)	21.1
High-grade cervical lesions (HSIL/CIN-2/CIN-3/CIS)	33.7
Cervical cancer	64.2

Other factors contributing to cervical cancer

Smoking prevalence (%), women	7.0 [5.5-9.1]
Total fertility rate (live births per woman)	2.5
Oral contraceptive use (%) among women	10.9
HIV prevalence (%), adults (15-49 years)	19.2 [18.4–20.0]

Sexual behaviour

Percentage of 15-year-old who have had sexual intercourse (men/women)	- / -
Range of median age at first sexual intercourse (men/women)	-/ 18.2-19.2

Cervical Cancer

The presence of 'high-risk' HPV types may lead to abnormal cell changes and can cause genital cancers: cervical cancer as well as cancer of the vulva, anus, and penis. In fact, researchers say that virtually all cervical cancers - more than 99% - are caused by these 'high-risk' HPV viruses. The most common of the high-risk strains of HPV are types 16 and 18, which cause about 70% of all cervical cancers.

Researched and Authored by Prof Michael C Herbst

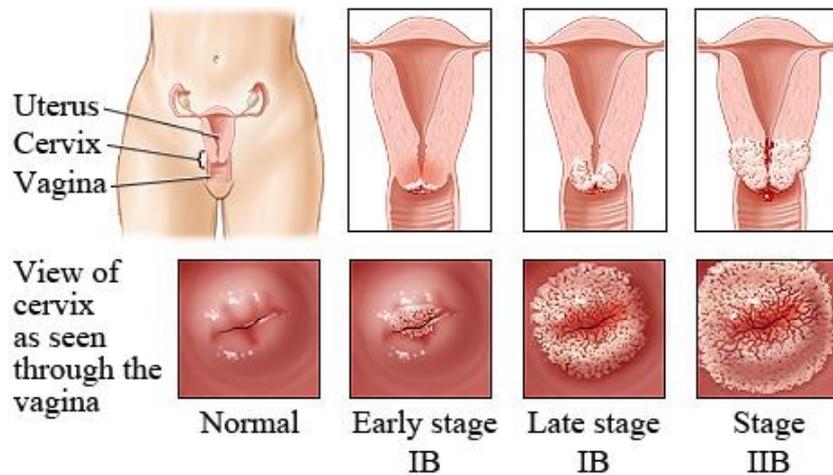
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[Picture Credit: Cervical Cancer]

If the body clears the infection, the cervical cells return to normal. But if the body does not clear the infection, the cells in the cervix can continue to change abnormally. This can lead to precancerous changes or cervical cancer (WebMD).



Please refer to CANSA's Fact Sheet on Cervical Cancer.

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Incidence of Cervical Cancer in South Africa (2019)

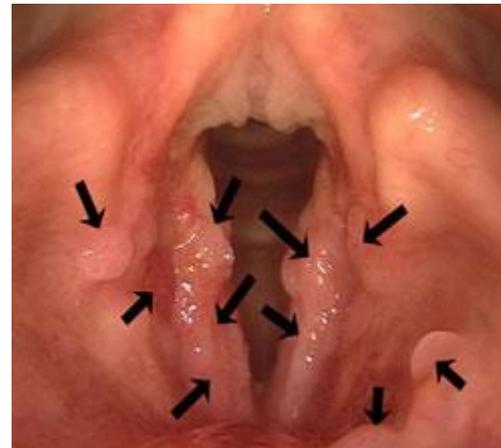
According to **Bruni, et al., 2019:**

- About 12 983 new Cervical Cancer cases are diagnosed annually in South Africa (estimates for 2018)
- Cervical Cancer ranks as the 2nd leading cause of female cancer in South Africa
- Cervical Cancer is the (1st) most common female cancer in women aged 15 to 44 years in South Africa.

Laryngeal Papillomas

Papillomas are benign epithelial tumours that are caused by infection with the human papilloma virus (HPV). They are the most common benign neoplasms affecting the larynx and upper respiratory tract. Malignant degeneration to squamous cell carcinoma can occur, but is very rare. Laryngeal papillomas are similar to verrucae on the skin (common wart) and *condyloma acuminatum*, or genital warts. Infection with the virus is ubiquitous (universal).

[Picture Credit: Laryngeal papilloma]



Why some infected people develop clinical expression of papilloma (respiratory, genital, or cutaneous) and some people never develop clinical disease remains uncertain. The reality is that some individuals appear to be susceptible to the virus and others do not. Although some individuals can acquire the virus through intimate contact, the virus can be transmitted from mother to foetus and laryngeal (respiratory) papillomatosis is not considered a sexually transmitted infection (Center for Voice and Swallowing).

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Genital warts

A genital wart is an infection of the skin, in genital or anal area, as well as the mucous membranes of the rectum, cervix and vagina. Genital warts are also known as venereal warts or *condylomata acuminata*. Genital warts are one of the most common kinds of sexually transmitted infections (Medical News Today).

[Picture Credit: Female Genital Warts]



HPV virus infection in men can also cause health problems. It is important for men to understand how to reduce the risks of HPV infection. HPV infection can increase a man's risk of getting genital cancers, although these cancers are not common. HPV can also cause genital warts in men, just as in women.

Warts are caused by viruses and can appear anywhere on the body. Those that show up in the genital area are caused by the human papillomavirus, commonly called HPV and are easily transmitted by sexual contact. HPV infection is one of the most common sexually transmitted infections. More than half of men who are sexually active will have HPV at some time in their life. Often, a man's body will clear the virus on its own with no health problems (WebMD).

Penile Cancer

Penile cancer is a disease in which malignant (cancer) cells form in the tissues of the penis.

[Picture Credit: Penile Cancer due to HPV Infection]

- Risk factors for developing penis cancer include human papillomavirus (HPV) infection, not being circumcised, being age 60 or older, phimosis (narrowing of the foreskin), poor personal hygiene, many sexual partners, and tobacco use
- Signs and symptoms of penile cancer include sores, redness, irritation, discharge, bleeding, or a lump on the penis
- A biopsy may be taken to determine if one has penile cancer
- Treatments for penile cancer include surgery, radiation therapy, and chemotherapy
- Prognosis and treatment options depend on the stage of the cancer, the location and size of the tumour, and whether the cancer has just been diagnosed or has recurred.



Common warts

Common warts are small, grainy skin growths that occur most often on the fingers or hands. Rough to the touch, common warts also often feature a pattern of tiny black dots - sometimes called seeds - which are small, clotted blood vessels.

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Common warts are caused by a virus and are transmitted by touch. Children and young adults are more likely to develop common warts, as are people who have weakened immune systems. Common warts usually disappear on their own, but many people choose to remove them because they find them bothersome or embarrassing.



[Picture Credit: Common Warts]

Plantar warts



Plantar warts are noncancerous skin growths on the soles of the feet caused by the human papillomavirus (HPV), which enters the body through tiny cuts, breaks or other vulnerable sites on the skin of the feet. Plantar warts often develop beneath pressure points in the feet, such as the heels or balls of the feet. This pressure also may cause a plantar wart to grow inward beneath a hard, thick layer of skin (callus).

[Picture Credit: Plantar Warts]

Most plantar warts are not a serious health concern and may not require treatment. However, plantar warts can be bothersome or painful. If self-care treatments for plantar warts do not work, one may need to see one's doctor to have them removed (WebMD).

Round warts

In most cases, the body's immune system defeats an HPV infection before it has a chance to create any warts. When warts do appear, they may vary in appearance depending on which variety of HPV is involved. Flat warts are flat-topped, slightly raised lesions darker than one's regular skin colour. They usually appear on the face, neck, hands, wrists, elbows or knees. HPV infections that cause flat warts usually affect children, adolescents and young adults (Mayo Clinic).



[Picture Credit: Round Warts]

Anal Cancer

95% of anal cancers are caused by the human papillomavirus (HPV). There are many types of HPV. Some HPV types cause benign warts, but some cause lesions (also called dysplasia) that can progress to invasive cancer. HPV-16 and HPV-18 are the high-risk strains responsible for the majority of HPV-associated cancers. Nearly 80% of sexually active people will have a genital HPV infection at some point in their lives.

Men who have sex with men (MSM) are especially at risk of anal cancer due to HPV infection.

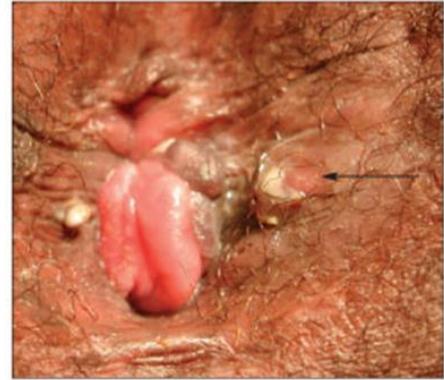
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[Picture Credit: Anal Cancer due to HPV Infection]



Risk Factors for HPV Infection

HPV infections are common. Risk factors for HPV infection include:

- Number of sexual partners - the greater your number of sexual partners, the more likely you are to contract a genital HPV infection. Having sex with a partner who has had multiple sex partners also increases your risk
- Age - common warts occur most often in children and adolescents. While plantar warts may occur in adults, they're more likely to initially surface during childhood. Genital warts occur most often in adolescents and young adults
- Weakened immune systems - people who have weakened immune systems are at greater risk of HPV infections. Immune systems can be weakened by HIV/AIDS or by immune system-suppressing drugs used after organ transplants
- Damaged skin - areas of skin that have been punctured or opened are more prone to develop common warts. For example, people who bite their fingernails are more likely to develop warts around their fingernails
- Personal contact - touching someone's warts or not wearing protection before contacting surfaces that have been exposed to HPV - such as public showers or swimming pools - may increase one's risk of HPV infection

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CONCLUSIONS: P-HPV-AC survivors experienced excess risk of SPMN. These findings have the potential to affect future surveillance practices and improve preventive healthcare for survivors of P-HPV-ACs.

Reducing the Risk for HPV Infection

Consider Abstinence - the only 100 percent effective way to prevent HPV transmission is abstinence from any sexual contact, including oral, anal, and vaginal sex. However, for most adults, complete abstinence is not a realistic option. There are other effective ways to prevent HPV from spreading and infecting one and one's sexual partners.

Get Vaccinated for HPV Prevention – two vaccines have been approved to protect women against the types of HPV that causes most cervical cancers (Cervarix and Gardasil). Gardasil also protects against most genital warts. It is best to be vaccinated before becoming sexually active. The vaccine is recommended for girls and women ages 9 to 26, but it can be given to older women as well. Gardasil also protects males against genital warts and is approved for boys and males ages 9 to 26. The FDA recently approved Gardasil for the prevention of anal cancer in both males and females ages 9 to 26. But the HPV vaccine does not protect against all types of HPV.

Staples, J.N. & Duska, L.R. 2019.

“The Pap smear is the only proven screening intervention in the field of gynecologic oncology. Women should receive treatment for precancerous conditions of the cervix, vulva, vagina, and endometrial lining. Women with inherited conditions should consider having a risk-reducing surgery once they have finished childbearing. The human papilloma virus vaccination should be offered to all girls and boys aged 11 to 12 years, and can also be given as early as age 9 and through 26 years of age.”

Joura, E.A., Kyrgiou, M., Bosch, F.X., Kesic, V., Niemenen, P., Redman, C.W. & Gulteken, M. 2019.

“Vaccines against human papillomavirus (HPV) are available in Europe since 2006. They have been highly effective in preventing infection and disease caused by the vaccine types. Clinical efficacy data are available for cervical, vulvovaginal and anal precancer and invasive cervical cancer. Disease reduction is best with early vaccination and a coverage of more than 70%. Gender-neutral vaccination provides direct protection for all men and improves the coverage. A good coverage is followed by herd protection of the unvaccinated men and women. School-based programs appear to be most effective; under the age of 15 years, two doses with an interval of 6-12 months are sufficient. From the age of 15 years, the standard regimen with three doses is recommended. A broad catch-up program for young adult women and men improves the effectiveness. The vaccines are also effective in sexually active women and men with previous but cleared infections. Vaccination in addition to local treatment of HPV-related disease appears to reduce recurrent or subsequent HPV-related disease. Combination of HPV vaccination and screening with HPV testing is the most effective approach to prevention of cervical cancer. The screening intervals may increase in the vaccinated cohorts. The upper age limit for vaccination remains to be evaluated, is country specific and depends on cost-effectiveness. The European Society of Gynaecologic Oncology and the European Federation for Colposcopy strongly support gender-neutral vaccination programs for children and young adolescents, with a catch-up program for young adults.”

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Limit the Number of Sexual Partners - another HPV prevention strategy is to limit the number of sexual partners one has and to be monogamous while one is in a sexual relationship. The more sexual partners one has, the more possible exposure one has to HPV. Some studies also suggest that knowing a new partner for eight months or longer before having sex can reduce one's risk of HPV transmission. The risk is lowered because that time period allows any HPV infection that is present in the potential partner to clear.

Use a Condom – if one is sexually active, using a condom can help lower the risk of HPV transmission. It is important to use a condom from start to finish of every sex act, including oral and anal sex. HPV is transmitted by skin-to-skin contact. Because HPV can infect areas that are not covered by the condom, condoms will not fully protect one against contracting HPV, but condoms do help in HPV prevention. Also, never reuse a condom.

Male Circumcision - research shows that the risk of HPV in men is lowered when they are circumcised. The risk for infecting their female sexual partners is also lower. There are more than 50 subtypes of HPV that are associated with cervical, penile, and other cancers, such as head and neck cancers, so by protecting oneself and one's partner from the spread of HPV, one could also be protecting oneself and one's partner from some forms of cancer.

Get the Pap Test – it is important for women to have regular check-ups, which include Pap smears to look for cervical cancer in its earliest stages - when it is most treatable. The Pap smear is a test that checks for abnormalities in the cells that line the cervix and is one of the best ways to detect cervical cancer. Every woman over age 21 should be getting routine Pap testing. The Pap test is now emerging as an important screening test for men at risk for anal lesions. Men at risk include gay, bisexual men, and HIV+ people. If one has health concerns or thinks one might have HPV, talk to a doctor.

Staples, J.N. & Duska, L.R. 2019.

“The Pap smear is the only proven screening intervention in the field of gynecologic oncology. Women should receive treatment for precancerous conditions of the cervix, vulva, vagina, and endometrial lining. Women with inherited conditions should consider having a risk-reducing surgery once they have finished childbearing. The human papilloma virus vaccination should be offered to all girls and boys aged 11 to 12 years, and can also be given as early as age 9 and through 26 years of age.”

Do not Have Sex Too Young - the younger one is when one starts having sex, the greater one's risk for HPV transmission. That is because one is more likely to come in contact with a partner who has HPV. If one is going to have sex, it is important that one be honest with one's partner about one's sexual history and that one's partner be honest about his or her sexual history, too. If one knows one's partner's history, one can make wiser choices for HPV prevention.

Adopt a Healthy Lifestyle - eat a healthy diet, one that is low in fat and sugars and rich in fresh fruits and vegetables, vitamins, and minerals. Also, get regular exercise, do not smoke, and do not consume alcohol. Keeping one's body in good shape helps boost one's immune system and a healthy immune system is able to fight off infections, including some of the more than 100 types of HPV that are out there.

The American Society of Clinical Oncology (ASCO) New Guideline on Human Papillomavirus (HPV) Vaccination for the Prevention of Cervical Cancer

During March 2017, the American Society of Clinical Oncology (ASCO) issued a new guideline on Human Papillomavirus (HPV) vaccination for the prevention of cervical cancer:

The guideline recommendations are as follows:

- In all environments and independent of the resource settings, 2 doses of HPV vaccine are recommended for girls ages 9–14 years, with an interval of at least 6 months and up to 12–15 months between doses.
- Girls who are HIV positive should receive 3 doses.
- If girls are ≥ 15 years and have received their first dose before age 15, they may complete the 2-dose series (for maximal and enhanced resource settings)
- If they have not received the first dose before age 15, they should receive 3 doses (for maximal and enhanced resource settings)
- In both scenarios vaccination may be given through age 26 years (for maximal and enhanced resource settings)
- If sufficient resources remain after vaccinating girls 9–14 years, girls who received 1 dose may receive additional doses between ages 15–26 years (for limited and basic resource settings)
- In all settings, boys may be vaccinated, if there is $\geq 50\%$ coverage in priority female target population, sufficient resources, and such vaccination is cost effective.

HPV Vaccine and Cervical Cancer Screening

Women vaccinated with earlier versions of the human papillomavirus (HPV) vaccine may only need cervical cancer screening every five years starting at age 25 or 30, and women who've received the updated vaccine need screening even less often, according to a study published online in the *Journal of the National Cancer Institute*.

Harvard researchers developed a disease simulation model to estimate the risks and benefits of both the current and potential screening guidelines, taking into account the protection afforded by HPV vaccines.

The investigators concluded that less-intensive screening is needed among HPV-vaccinated women because their risk of developing cervical cancer is quite low. Too much screening opens these women up to false-positive results that require invasive follow-up tests, and can lead to unnecessary health costs. For women who have received the nonavalent vaccine (Gardasil 9), the researchers recommend testing these women every 10 years starting at age 30 to 35 and ending at age 65. The research team also concluded that doctors could screen women using just an HPV test.

"This model-based analysis suggests screening can be modified to start at later ages, occur at decreased frequency, and involve primary HPV testing in HPV-vaccinated women, providing more health benefit at lower harms and costs than current screening guidelines," the authors write. (Kim, et al., 2016).

Gardasil 9

The Gardasil 9 (nonavalent) vaccine is said to be effective against 9 of the Human Papilloma Viruses and can be used as follows:

Prevention of HPV in Boys & Men - demonstrated to protect against diseases/precancerous conditions caused by human papilloma virus (HPV) types 6, 11, 16, 18, 31, 33, 45, 52, and 58

Ages 15 through 26 years: 0.5 mL IM as a 3-dose series at 0, 2, and 6 months

Indications in boys and men

- Prevention of the following diseases
 - Anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58
 - Genital warts (condyloma acuminata) caused by HPV types 6 and 11
- Following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58
 - Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3

Prevention of HPV in Girls & Women - demonstrated to protect against diseases and/or precancerous conditions caused by human papilloma virus (HPV) types 6, 11, 16, 18, 31, 33, 45, 52, and 58

Ages 15 through 26 years: 0.5 mL IM as a 3-dose series at 0, 2, and 6 months

Indicated for prevention of the following diseases

- Cervical, vulvar, vaginal, and anal cancer caused by human papillomavirus (HPV) types 16, 18, 31, 33, 45, 52, and 58
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11

Precancerous or dysplastic lesions

Indicated for prevention of the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

- Cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma in situ (AIS)
- Cervical intraepithelial neoplasia (CIN) grade 1
- Vulvar intraepithelial neoplasia (VIN) grades 2 and 3
- Vaginal intraepithelial neoplasia (VaIN) grades 2 and 3
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3

Dosing Considerations

- Patient, parent, or guardian should be informed that vaccination does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening
- Recipients should not discontinue anal cancer screening
- Has not been demonstrated to provide protection against disease from vaccine HPV types to which a person has previously been exposed through sexual activity

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- Not a treatment for external genital lesions; cervical, vulvar, vaginal, and anal cancers; CIN; VIN; VaIN; or AIN
- Not all vulvar, vaginal, and anal cancers are caused by HPV
- May not result in protection in all vaccine recipients

Treatment for HPV

There is currently no medical treatment for HPV infection. Infection with some HPV types may cause changes to cells in the cervix which can lead to cervical cancer. These are classified as 'high-risk' HPV types.

If one is infected with a 'high-risk' type of HPV, one will usually have no symptoms whether man or woman.

In most women, infection with HPV causes no harm because the immune system clears up the initial infection. This is particularly the case for women who are under 30 and who tend to have many HPV infections. Most women with an HPV infection do not go on to develop cervical cancer.

In men, at present there is no reliable test to detect HPV infection and it is often very difficult to diagnose.

One important way to prevent cervical cancer is through regular screening with the Pap smear test. An HPV test can also be used at the same time as the Pap smear test for women 30 years and older. The Pap smear and HPV tests can find early problems that could lead to cervical cancer over time.

These tests do NOT:

- Check for early signs of other cancers
- Check your fertility (ability to get pregnant)
- Check for all HPV types –The HPV test only checks for specific HPV types that are linked to cervical cancer.
- Check for other sexually transmitted infections (STIs).

Experts recommend HPV testing for women who are:

- Age 30 or older - as part of regular screening, with a Pap test, or
- Age 21 or older - for follow-up of an abnormal Pap test result

One must request a HPV test.

A HPV test is normally not recommended as part of regular screening for younger women and teens. HPV is very common in women under age 30. It is not useful to test women under age 30 for HPV, since most HPV that is found in these women will never cause them health problems. Most young women will fight off HPV within a few years.

HPV is less common in women over the age of 30, who are at increasing risk for cervical cancer. HPV is also more likely to signal a health problem for these women, who may have had the virus for many years. Doctors may use the HPV test with the Pap smear test to tell if these women are more likely to get cervical cancer in the future and if they need to be screened more often.

Getting regular Pap smear tests, even without the HPV test, is still a good way to prevent cervical cancer - for both younger and older women (Centers for Disease Control and Prevention).

Please refer to CANSA's Fact Sheet on Cervical Cancer as well as to CANSA's Position Statement on Cervical Cancer.

Common Questions and Answers Regarding HPV Vaccination

Why are HPV vaccines needed?

Certain HPV types cause cancer, including cervical, vulvar, vaginal, penile, anal, and oropharyngeal (base of the tongue, tonsils and back of throat) cancers. Certain HPV types also cause most cases of genital warts in both men and women.

HPV is a common virus that is easily spread by skin-to-skin contact during sexual activity with another person. It is possible to have HPV without knowing it, so it is possible to unknowingly spread HPV to another person.

HPV vaccine is a strong weapon in prevention. These vaccines are available to protect individuals against some of the most common HPV types and the health problems that the virus can cause.

How common are the health problems caused by HPV?

HPV is the main cause of cervical cancer. It is estimated that about 1 in 100 sexually active adults have genital warts at any given time. HPV infection is responsible for 80% of cases of penile cancer. It is also a major cause of anal cancer.

What HPV vaccines are available in the South Africa?

Two HPV vaccines are available in South Africa. These vaccines are:

- Cervarix, a bivalent vaccine made by GlaxoSmithKline
- Gardasil, a quadrivalent vaccine made by Merck.

What vaccine is used by the National Department of Health in South Africa?

The National Department of Health in South Africa makes use of the bivalent vaccine in its HPV vaccination programme for school girls.

How are the two HPV vaccines similar?

- Both vaccines are very effective against diseases caused by HPV types 16 and 18 - HPV 16 and 18 cause most cervical cancers, as well as other HPV associated cancers
- Both vaccines have been shown to prevent cervical pre-cancers in women
- Both vaccines are said to be safe following trials
- Both vaccines are made with a very small part (in this case, the protein outer coat) of the human papillomavirus (HPV) that cannot cause infection
- Both vaccines are given as injections and usually require 3 doses

It has since been established that two (2) doses of the bivalent vaccine is just as effective as the three (3) prescribed doses.

How are the two HPV vaccines different?

The quadrivalent vaccine protects against HPV types 6, 11, 16 and 18 - the types that cause most genital warts. Only the quadrivalent vaccine has been tested and licensed for use in males. The bivalent vaccine protects against HPV types 16 and 18. The vaccines have different adjuvants—a substance that is added to the vaccine to increase the body's immune response

Who should get HPV vaccine?

Please refer to the ASCO Guideline published on page 8 of this Fact Sheet.

Cervarix and Gardasil are licensed, and said to be safe, and effective for females ages 9 through 26 years. The Centers for Disease Control and Prevention (CDC) in the United States recommends that all 11 or 12 year old girls get the 3 doses (shots) of either brand of HPV vaccine to protect against cervical cancer. Gardasil also protects against most genital warts, as well as some cancers of the vulva, vagina and anus. It is further recommended that girls and young women ages 13 through 26 should get HPV vaccine if they have not received any or all doses when they were younger.

Gardasil is also licensed, and said to be safe, and effective for males ages 9 through 26 years. The Centers of Disease Control and Prevention (CDC) in the United States recommends Gardasil for all boys aged 11 or 12 years, and for males aged 13 through 21 years, who did not get any or all of the three recommended doses when they were younger.

All men may receive the vaccine through age 26, and should speak with their doctor to find out if getting vaccinated is right for them.

The vaccine is also recommended for gay and bisexual men (or any man who has sex with men) and men with compromised immune systems (including HIV) through age 26, if they did not get fully vaccinated when they were younger.

Why is HPV vaccine recommended at an early age?

For the HPV vaccine to work best, it is very important for preteens to be vaccinated long before any sexual activity begins. It is possible to be infected with HPV the very first time one has sexual contact with another person. Also, the vaccine produces higher antibody that fights infection when given at this age compared to older ages.

In South Africa the ideal age for administration of the HPV vaccine has been determined to be nine (9) years of age or older based on the onset of puberty among South African girls.

What is the recommended schedule (or timing) of the 3 HPV doses (shots)?

3 doses (shots) are recommended over six months. CDC recommends that the second dose be given one to two months after the first, and the third dose be given six months after the first dose.

It has since been established that two (2) doses of the bivalent vaccine is just as effective as three (3) doses of the vaccine.

Are the HPV vaccines safe and effective?

Both the vaccines as said to be safe and effective. Both vaccines were tested in thousands of people around the world. These studies showed no serious side effects. Common, mild side effects included

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pain where the shot was given, fever, headache, and nausea. As with all vaccines, CDC and FDA continue to monitor the safety of these vaccines very carefully.

Do people faint after getting HPV vaccines?

People faint for many reasons. Some individuals may faint after any medical procedure, including receiving vaccines. It is possible for falls and injuries to occur after fainting. Sitting or lying down for about 15 minutes after a vaccination can help prevent fainting and related injuries.

Can HPV vaccines treat HPV infections, cancers, or warts?

HPV vaccines will not treat or get rid of existing HPV infections. Also, HPV vaccines do not treat or cure health problems (like cancer or warts) caused by an HPV infection that occurred before vaccination. It is important for adult women to still get cervical cancer screening even if they have completed the HPV vaccine series.

How important is it to get HPV vaccine?

The HPV vaccines are important tools to help prevent cervical cancer and other HPV related cancers and genital warts.

Why are HPV vaccines not recommended for people older than 26?

Both vaccines were studied in thousands of people from 9 through 26 years old and found to be safe and effective for these ages.

Should pregnant women be vaccinated?

HPV vaccine should only be administered to girls before they become sexually active – once infected with HPV, the vaccine has no role to play in preventing cervical cancer.

Pregnant women are not included in the recommendations for HPV vaccines. Studies show neither vaccine caused problems for babies born to women who got the HPV vaccine while they were pregnant. Getting the HPV vaccine when pregnant is not a reason to consider ending a pregnancy. Thus, to be on the safe side until even more is known, pregnant women should not be given HPV vaccines until their pregnancy is completed.

Is Parental/Legal Guardian Consent Required?

Parental/legal guardian consent is required before any child will be given a HPV vaccination in South Africa. This also applies to the HPV programme of the National Department of Health and National Department of Education in South African public schools.

FDA Approves First Human Papillomavirus Test for Primary Cervical Cancer Screening

The US Food and Drug Administration recently approved the first FDA-approved HPV DNA test for women 25 and older that can be used alone to help a health care professional assess the need for a woman to undergo additional diagnostic testing for cervical cancer. The test also can provide information about the patient's risk for developing cervical cancer in the future.

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Using a sample of cervical cells, the cobas HPV Test detects DNA from 14 high-risk HPV types. The test specifically identifies HPV 16 and HPV 18, while concurrently detecting 12 other types of high-risk HPVs.

Based on results of the cobas HPV Test, women who test positive for HPV 16 or HPV 18 should have a colposcopy, an exam using a device that illuminates and magnifies the cervix so a physician can directly observe the cervical cells. Women testing positive for one or more of the 12 other high-risk HPV types should have a Pap test to determine the need for a colposcopy. Health care professionals should use the cobas HPV Test results together with other information, such as the patient screening history and risk factors, and current professional guidelines.

“Today’s approval offers women and physicians a new option for cervical cancer screening,” said Alberto Gutierrez, Ph.D., director of the Office of In Vitro Diagnostics and Radiological Health at the FDA’s Center for Devices and Radiological Health. “Roche Diagnostics conducted a well-designed study that provided the FDA with a reasonable assurance of the safety and effectiveness when used as a primary screening tool for cervical cancer.”

The FDA first approved the test, called the cobas HPV Test in 2011 for use in conjunction with or as a follow-up to a Pap test (cell cytology), which examines cervical cells for changes that might become cervical cancer.

Today’s approval expands the use of the test to include use as either a co-test or as a primary cervical cancer screening test, however; it does not change current medical practice guidelines for cervical cancer screening. These guidelines are developed, reviewed and modified by groups other than the FDA.

Genital HPVs are a group of more than 40 related viruses and, according to the Centers for Disease Control and Prevention (CDC), are the most common sexually transmitted infections. Approximately 14 ‘high-risk’ HPV types are associated with cervical cancer.

In most cases, a high-risk HPV infection goes away on its own and does not cause any health problems. However, about 10 percent of women infected with high-risk HPV develop a persistent infection which may put them at risk of cancer. Virtually all cervical cancers are caused by HPV infections, with just two types, HPV 16 and HPV 18, responsible for approximately 70 percent of cervical cancers.

Data supporting the use of the cobas HPV Test as a primary screening test for cervical cancer included a study of more than 40,000 women 25 years and older undergoing routine cervical exams. Women who had a positive Pap test or whose cervical cells screened positive for HPV, as well as a subset of women whose Pap and HPV tests were both negative, underwent a colposcopy and cervical tissue biopsy. All biopsy results were compared to the Pap and cobas HPV Test results. Data from this study, which included three years of follow-up on women who went to colposcopy, showed that the cobas HPV Test is safe and effective for the new indication for use.

The cobas HPV Test is manufactured by Roche Molecular Systems, Incorporated, Pleasanton, Calif.

The Anti-HPV Vaccine Lobby

There are numerous anti-HPV lobbyists who claim that giving the HPV vaccine to girls is dangerous and irresponsible. Many claims are made as to the side effects of the HPV vaccine.

A typical example of claims made against HPV vaccines - Gardasil is the HPV vaccine, touted to fight cervical cancer. What they are not telling is that thousands of girls are having adverse reactions to the HPV Vaccines, some have even died - at last count, over one hundred lives have been lost. We have got to do something about this. These girls need our help!

These girls are having reactions such as; seizures, strokes, dizziness, fatigue, weakness, headaches, stomach pains, muscle pain and weakness, joint pain, auto-immune problems, chest pains, hair loss, appetite loss, personality changes, insomnia, hand/leg tremors, arm/leg weakness, shortness of breath, heart problems, paralysis, itching, rashes, swelling, aching muscles, menstrual cycle changes, fainting, swollen lymph nodes, night sweats, nausea, temporary vision/hearing loss just to name some of them!



Anti-HPV Lobbyist Dr Sin Hang Lee

Dr. Sin Hang Lee (pictured on the right), director of the Milford Molecular Diagnostics Laboratory in Connecticut, recently published a letter sent to the U.S. CDC, the World Health Organization, the Ministry of Health in Japan, and others, documenting “scientific misconduct” among the world’s leading health organisations tasked with providing vaccine safety, by deliberately misleading Japanese health authorities on the safety of the HPV vaccine.

Japanese health authorities had apparently halted their recommendation of the HPV vaccines in 2013 due to safety concerns. Japanese officials began a full investigation into the HPV vaccines at that time.

Dr. Sin Hang Lee has allegedly discovered that at a public hearing on HPV vaccine safety which was held in Tokyo, Japan on February 26, 2014, members of the Global Advisory Committee on Vaccine Safety (GACVS), the World Health Organization, the CDC and other scientific/health professionals: deliberately set out to mislead Japanese authorities regarding the safety of the human papillomavirus (HPV) vaccines, Gardasil® and Cervarix®, which were being promoted at that time.

The World Health Organization and Safety of HPV Vaccines

The following is an extract from report of the Global Advisory Committee on Vaccine Safety (GACVS) meeting of 2-3 December 2015, published in the WHO Weekly Epidemiological Record of 22 January 2016.

Since first being licensed at the beginning of 2006, >200 million doses of HPV vaccines have been distributed globally. WHO recommends that HPV vaccines be introduced into national immunisation programmes provided that:

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- prevention of cervical cancer and/or other HPV-related diseases constitute a public health priority
- vaccine introduction is programmatically feasible
- sustainable financing can be secured
- the cost-effectiveness of vaccination strategies in the country or region is considered.

The GACVS has systematically investigated safety concerns raised about HPV vaccines and has issued several reports in this regard. To date, GACVS has not found any safety issue that would alter its recommendations for the use of the vaccine.

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This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

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Dr Sin Hang Lee

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HPV-16

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Laryngeal Papilloma

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