

SCCPS Scientific Committee Position Paper on HPV Vaccination

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Obstetrical & Gynaecological Society of Singapore (OGSS)
Society for Colposcopy and Cervical Pathology of Singapore (SCCPS)
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The aim of this guideline is to provide information, based on clinical evidence where available, on the use of the HPV vaccine.

In Singapore, the HPV vaccine is licensed for use in girls and women aged between 9 and 26 years. There is recent evidence that clinical utility is not limited to this age group. However, it must be emphasized that the use of the vaccine in such situations is not currently considered standard of care.

Introduction

Cervical Cancer is the 10th most common cancer among women in Singapore ¹. Almost 100% of cases have been attributed to oncogenic Human Papilloma Virus (HPV) infection, of which types 16 and 18 are found in up to 70% of all cervical cancers ². Oncogenic HPV is also implicated in the development of other cancers including tumors of the vulva, vagina, anus, penis as well as of the head and neck. HPV types 6 and 11 though non-oncogenic account for 90% of genital warts.

Types of Vaccines:

Currently 2 vaccines are available in Singapore: Gardasil® and Cervarix®.

Both the vaccines are prepared from HPV type-specific empty shells or virus-like particles (VLPs). VLPs do not contain any viral DNA and therefore are able confer immunity without infecting the host.

Gardasil® is a quadrivalent vaccine containing VLPs for 4 HPV types – 6,11,16 and 18. It is licensed in Singapore to be used in girls and boys aged 9 to 26 years of age.

Cervarix® is a bivalent vaccine containing VLPs of 2 HPV types – 16 and 18. It is licensed for girls aged 9 to 25 years of age ⁵.

Vaccination Schedule and recommendations:

Currently the National Childhood Immunization Schedule and the Health Promotion Board Singapore recommend the HPV vaccination

only for females age 9 to 26 years old on the following schedules: ^{6,7}

Gardasil:

- 3-dose schedule: 0, 2 and 6 months for individuals 9-26 years of age.
- OR
- 2-dose schedule: 0 and 6 months for individuals 9-13 years of age.

Cervarix:

- 3-dose schedule: 0, 1 and 6 months in females 9-25 years of age.
- OR
- 2-dose schedule: 0 and 6 months in females 9-14 years of age.

The need for boosters for either of the two vaccines has not been established.

Efficacy

The efficacy for both vaccines has been demonstrated in large Phase III randomized controlled trials involving healthy young women ^{3,4}. The vaccines are highly efficacious against HPV 16/18 related pre-cancerous lesions. The long term efficacy continues to be evaluated. All available data for seroconversion and seropositivity show non-inferiority of the 2-dose compared with the 3-dose schedule; no clinical outcome data are available yet for 2-dose schedule. ⁵

Safety

Both vaccines are generally safe and well tolerated and no serious adverse events have been documented. Local side effects such as pain, swelling, itching and redness at the site of injection are common. Post vaccination syncope has also been reported and can be avoided with appropriate care.

Frequently Asked Questions (FAQs)

Can sexually active women younger than 26 years of age be vaccinated?

Yes. They can be offered HPV vaccination.

Both HPV vaccines are prophylactic vaccines. For optimal benefit, the

vaccine should be given before the onset of sexual activity, as it does not protect against pre-existing HPV infections. However, sexually active women can be vaccinated.

Women who are sexually active risk HPV infection, hence these women should be advised that the vaccine may be less effective compared to women who have had no previous HPV exposure at the time of vaccination. ^{8,9,10,11}

Can women older than 26 years of age be vaccinated?

Yes. Women older than 26 years of age can be offered HPV vaccination.

The value of HPV vaccination beyond 26 years is unclear, however women can be provided with information to make an informed decision about the costs and benefits of vaccination.

Women up to 45 years of age have been shown to exhibit strong immune serological response to the Cervarix® vaccine ¹². Early data from randomised trials testing the Gardasil® vaccine in women between 24 years and 45 years have demonstrated a high vaccine efficacy against HPV related infection and have lower rates of CIN compared to placebo ¹³.

Women between the ages of 27 to 45 years of age who request HPV vaccination should be counseled that for vaccination in this age group does not fall within the standard of care for HPV vaccination.

The benefit received from HPV vaccination in women older than age 27 also may be limited compared to HPV naïve populations or if they have been exposed to HPV infection e.g sexually active, evidence of abnormal pap smear, previous treatment for CIN3.

Is HPV testing recommended before vaccination?

Testing for HPV DNA is not necessary prior to vaccination. Serologic tests for HPV are currently not available commercially ^{16,18}.

Should women who have been vaccinated be encouraged to have Pap smear screening?

The HPV vaccine is not a substitute for cervical cancer screening. It must be emphasized that women aged 25 years and above, who are

sexually active or who have ever had sex, must continue with pap smear screening once every 3 years regardless of their HPV vaccination history⁶.

Can women who have had an HPV infection or a history of CIN be vaccinated?

Women with current HPV infection, current CIN or previously treated CIN can be given the HPV vaccine.

However, these women must be informed that the HPV vaccine is not therapeutic and does not treat existing infection or CIN, and the benefits of the vaccination may be limited to the prevention of future HPV infection.

The role of HPV vaccination on the risk of recurrence of CIN after initial treatment is still a subject of research.

Clinical follow-up according to Cervical Screen Singapore guidelines must continue in these women.

Can women who are immunocompromised be vaccinated?

Vaccination can be given to women who are immunocompromised e.g. those who are on steroids, immunosuppressant medication or are HIV-infected.

However, these women should be informed that their immune response to the vaccine may be lower compared to immunocompetent women ^{14,15}.

Can pregnant or breastfeeding women be vaccinated?

The HPV vaccine is not recommended for use in pregnancy.

Women who become pregnant before completing the vaccination schedule should defer the subsequent doses until the pregnancy is completed ^{8,9,10,16}. There is no need to restart the entire vaccination schedule but there should not be a delay of more than 12 months between the 2nd and 3rd dose.

Lactating women can be vaccinated. The HPV vaccine is an inactivated vaccine which does not contain a whole virus, hence it does not affect the safety of breastfeeding for mothers or infants ^{8,17}.

Can males be vaccinated?

Males can be vaccinated on request.

Early data from a phase 3 double blind randomised study involving males aged 16 to 26 years show that the Gardasil® vaccine can protect men against genital warts. The possibility that this vaccine also protects men from Penile intraepithelial neoplasia or HPV-related cancers, like anal and penile cancers is still being evaluated^{19,20}.

Males who do not have clinical evidence of HPV infection may benefit the most from the vaccine.

Can the HPV vaccine be given together with other vaccines?

Both vaccines may be administered concomitantly with booster vaccine containing diphtheria (d), tetanus (T) and acellular pertussis with or without inactivated poliomyelitis (IPV, dTpa, dTpa-IPV vaccines), with no clinically relevant interference with antibody response to any of the components of either vaccine.

What about the 9-valent or nonavalent HPV vaccine?

A 9-valent HPV vaccine (Gardasil 9, Merck & Co., Inc) was licensed for use in females and males in the United States in December 2014. However, it is not available or approved for use in Singapore²¹.

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