Summary of WHO Position Paper on Human Papillomavirus (HPV) Vaccines, December 2022

This position paper, published in December 2022, replaces the corresponding WHO position paper on HPV vaccines published in the Weekly Epidemiological Record in 2017.

Background

Human papillomavirus (HPV) is the most common viral infection of the reproductive tract, causing a range of conditions in men and women, including precancerous lesions that can progress to cancer. While most HPV infections are asymptomatic and resolve spontaneously, persistent infection can result in disease. In women, persistent infection with oncogenic HPV types may lead to cervical intraepithelial neoplasia (CIN), which can progress to cervical cancer.

HPV vaccination is a key strategy in the WHO Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem. Implementation of this strategy could prevent 60 million cervical cancer cases and 45 million deaths over the next 100 years. HPV vaccines also prevent other cancers and diseases caused by HPV, including anogenital warts.

Vaccines

Six prophylactic HPV vaccines are currently licensed. These vaccines use recombinant DNA and cell-culture technology to produce virus-like particles (VLPs) that do not contain live biological products or viral DNA, making them non-infectious.

The vaccines are:

- 1. "Bivalent HPV vaccines": Cervarix, Cecolin, Walrinvax
- 2. "Quadrivalent HPV vaccines": Gardasil, Cervavax
- 3. "Nonavalent HPV vaccine": Gardasil 9

All HPV vaccines contain VLPs against high-risk HPV types 16 and 18. The nonavalent vaccine also includes VLPs against HPV types 31, 33, 45, 52, and 58. The quadrivalent and nonavalent vaccines also protect against HPV types 6 and 11, which cause anogenital warts.

Administration and Schedules

HPV vaccines are administered intramuscularly in the deltoid region. The standard dose is 0.5 ml. The vaccination schedule for which the vaccines are licensed depends on the age of the recipient: two doses for ages 9-14 years and three doses if the first dose is given at age 15 or older.

Immunogenicity, efficacy, and effectiveness

HPV vaccines are highly immunogenic and effective. Administered intramuscularly, they prompt a strong antibody response, peaking 4 weeks after the last dose and stabilizing after 12–18 months. This response is much stronger than following natural infection.

Clinical trials have shown high efficacy in preventing high-grade cervical, vulvar, and vaginal lesions, especially when administered before HPV exposure. Randomized control trials, meta-analyses and systematic reviews confirm high levels of protection against HPV16- and HPV18-associated conditions.

Additionally, HPV vaccination programmes have led to substantial reductions in HPV prevalence and related diseases, with herd immunity benefits observed in unvaccinated populations.

Evidence of single-dose schedule

Recent data suggest that a single dose of HPV vaccine may offer similar protection as multidose regimens. Trials and observational studies report high seropositivity and significant protection against HPV infections with one dose, even though antibody titres are lower compared to multiple doses. No published data are available on immunogenicity or effectiveness of 1- or 2-dose schedules among people living with HIV.

Duration of protection

HPV vaccines provide long-lasting protection with multidose schedules. Antibody titres remain high for at least 12 years for the bivalent (Cervarix) and quadrivalent (Gardasil) vaccines. Antibody levels remain significantly above those from natural infection for up to 11 years, including when single dose schedule is used.

Safety

HPV vaccines are safe and well-tolerated. Local reactions, such as pain at the injection site, and mild systemic reactions, such as headache and myalgia, are common. Severe adverse events are rare. Vaccination is not recommended during pregnancy, but data on the safety of vaccination in pregnancy are reassuring.

WHO Position

WHO recommends HPV vaccination as part of a comprehensive strategy to eliminate cervical cancer. HPV vaccines should be included in national immunization programmes, and the primary target are girls aged 9-14 years. Priority groups include immunocompromised individuals, and those who have faced sexual abuse. Vaccination can also be extended to secondary targets such older females, boys and men, only if this is feasible and affordable.

HPV vaccines can be used in the following schedules:

- Two doses, at least six months apart, at all ages for which the vaccine is licensed.
- Alternatively, a single-dose schedule¹ for individuals 9 to 20 years old
- For individuals known to be immunocompromised or HIV-infected, at least two HPV vaccine doses and, where possible, three doses.

Conclusion

HPV vaccination is crucial in preventing HPV-related diseases, especially cervical cancer. The vaccines are highly effective and safe, making them an essential component of public health strategies to control HPV infections and the elimination of cervical cancer.

For more detailed information, please refer to the full WHO position paper on HPV vaccines from <u>December 2022</u>.

¹ For vaccines products for which 1-dose efficacy data is available, including through immunobridging.