

# Demystifying the human papillomavirus vaccine



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## Human papillomavirus and cancer

Human papillomavirus (HPV) is the most common sexually transmitted infection, with an 84.6% lifetime risk among women with at least 1 opposite sex partner and 91.3% for men (1). HPV transmission occurs through direct skin-to-skin contact during sexual activity. Most HPV infections clear up on their own, but some persist leading to a chronic infection that can cause cancer, especially cervical cancer, but also head and neck squamous cell carcinoma, as well as vulvar, vaginal, penile and anal cancer (2).

**HPV vaccination** is highly effective in preventing HPV infection, pre-cancerous cervical lesions, and invasive cervical cancer (3,4). Currently, three types of vaccines are available: the bivalent vaccines (Cervarix and Cecolin) that protects against HPVs 16 and 18, which cause 70% of cases of cervical cancer (5); the quadrivalent vaccine (Gardasil) which additionally protects against HPVs 6 and 11, responsible for genital warts (6); and the nonavalent vaccine (Gardasil-9) which adds protection against HPVs 31, 33, 45, 52, and 58, responsible for 90% of all cervical cancers (7).

These vaccines are recommended before the onset of sexual activity (i.e., before first potential exposure to HPV infection). As of 27 October 2020, 110 countries had included HPV vaccination in their national immunization program (8), with an average coverage rate of 67% for the first dose and 53% for the final second dose. High final second dose coverages (90% or higher) have been recommended by the World Health Organization; unfortunately, they have only been achieved in five countries, while the majority have a final dose coverage of 50% or less (9). These low coverage rates have been associated with fears and myths around the vaccine. We address herein some of these myths.



**Myth 1: "My daughter/son is going to start sexual activity earlier, be more promiscuous and adopt a riskier sexual behavior after receiving the vaccine"**

HPV vaccination has neither been associated with a younger sexual debut, nor with an increased number of sexual partners (10,11). Also, the number of pregnancies and sexually transmitted infections have remained the same in vaccinated women compared to non-vaccinated ones (11,12). Similarly, there has not been an increase in contraceptive use after the introduction of HPV vaccination (13).

## Myth 2: "My daughter/son is not sexually active, so she/he does not need the vaccine"

HPV vaccine is hypothesized to work by producing antibodies against the HPV. Antibodies are components of the immune system that remain in the blood several years after infection or immunization; they neutralize the virus once it appears again and prevent the development of disease. Studies have found that at a younger age of vaccination, there is a higher titer of antibodies secondary to a higher immune response (14). Also, there is evidence that when vaccination occurs at younger age, there is higher protection against cervical lesions (15). The reason why vaccination is recommended before the initiation of sexual debut is the aforementioned evidence, younger age means higher protection.

## Myth 3: "The vaccine is just for girls, not for my son"



In men, 33% of penile cancers and 90% of anal cancers are attributed to HPV infections, especially HPV16 (included in all three HPV vaccines). HPV is also responsible for 22.4% of cancers in the oral cavity, 4.4% in the oropharynx, and 3.5% in the larynx. Although studies are scarce, the ones available show efficacy as high as 46.9% against HPV anogenital infections and 88% for oral infections in males. Importantly, vaccinating boys reduces the risk of HPV infection in their future partner(s) through indirect protection, also called, herd immunity. Herd immunity is achieved when most of a population is immune to the virus (16).

## Myth 4: "The HPV vaccine is not safe"



The safety of HPV vaccines has been assessed in several studies, from clinical trials to active surveillance on reported cases, both in women and men. All agreed that HPV vaccines are safe. One of the most common side effects is injection site reactions, such as pain, redness and swelling. Other potential side effects include headache, fever, and nausea. However, these side effects are mild, transient and resolve spontaneously in 2-3 days. HPV vaccines do not increase the risk of death or the development of autoimmune diseases. The only serious adverse event reported is anaphylaxis, but it is rare. The bivalent vaccine should be avoided in people with anaphylactic allergy to latex since the tip cap can contain natural rubber latex, and the other two vaccines are contraindicated for anyone with a history of hypersensitivity to yeast. Although not recommended during pregnancy, inadvertent administration of the vaccine during this time has not been associated with health problems in neither the mother nor the child (17).

## Myth 5: "I heard of some countries where vaccinated girls started fainting"

Syncope (fainting or passing out) after HPV vaccination has been reported, similar to temporary loss of consciousness after receiving other vaccines or undergoing medical procedures involving injections which is mainly considered as an anxiety and stress-related reaction to the injection. There are practical measures to avoid this, such as lying down and resting for at least 15 minutes after vaccination, which is common practice with other vaccines (18-20).



## What events have been reported in other countries?

In some countries such as Australia, Brazil, Colombia, Denmark and Japan, episodes of “crises” after HPV vaccination have been reported. Specifically in Colombia, these “crisis” consisted in symptoms such as headache, shortness of breath, numbness of the limbs, chest pain and fainting. The belief that it was secondary to the HPV vaccine generated a massive drop in vaccination coverage (from 98% for the first dose in 2012, to 14% in 2016). The National Institute of Health of Colombia developed a field study and rule out a biological relationship of the symptoms with the HPV vaccine. Also, the institute concluded that it was secondary to an exaggerated perception of risk from the vaccine which generated the presentation of a mass psychogenic illness, which consists in a conversion of stress into physical symptoms. It is linked with long standing anxiety, probably present in the population affected. Similar episodes in other countries were also related to immunization anxiety (21,22).

**The bottom line is, international agencies such as the World Health Organization, Centers for Disease Control and Prevention and the European Medicines Agency consider HPV vaccines to be safe, based on the current large body of evidence.**

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