ISSN: 2976-1077

Human papillomavirus vaccine

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http://doi.org/10.58196/jhswn.com-v16/1062519

Multidisciplinary- Peer-reviewed Journal

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Publishing Process
Received on: 15 Sept. 2025
Finalized to publish: 28 Oct 2025

Published 12 Nov 2025

Abstract: Human papillomavirus (HPV) is a common sexually transmitted infection (STI) in the world, and it causes many cancers, including cervical, vulvar, anal, penile, and oropharyngeal cancer. HPV16 and HPV18 together are responsible globally for 71% of cases of cervical cancer. A comprehensive literature review was conducted to gather relevant information about the HPV vaccine. All HPV vaccines are indicated for use in females aged 9 years or older, and are licensed for use up to 26 or 45 years of age. Some HPV vaccines are also licensed for use in males. The information and historical development of the HPV vaccine offer vital lessons for advancing public health strategies, guiding effective policies, research, and program development, and it helped to prevent life-threatening diseases

Keywords: Human, Papillomavirus, STI, Vaccine.

Declaration: There is no conflict of interest.

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Introduction

Human papillomavirus (HPV) is a common sexually transmitted infection (STI) in the world, and it causes many cancers, including cervical, vulvar, anal, penile, and oropharyngeal cancer. Almost all sexually active people will be infected at some point in their lives, usually without symptoms. (1). HPV16 and HPV18 together are responsible globally for 71% of cases of cervical cancer. The first vaccine for the prevention of HPV-related disease was licensed in 2006. Currently, 6 prophylactic HPV vaccines are licensed. All are intended to be administered, if possible, before the onset of sexual activity, i.e., before exposure to HPV. All HPV vaccines are indicated for use in females aged 9 years or older, and are licensed for use up to 26 or 45 years of age. Some HPV vaccines are also licensed for use in males (2). The WHO recommends HPV vaccination as a critical preventive measure (prevents 90% of cancers caused by HPV), especially when administered to girls before the onset of sexual activity, typically between the ages of 9 and 14 years (2). In line with these recommendations, Nepal has introduced the HPV vaccine for 9- to 14-year-old schoolgirls as part of its national immunization schedule (3).

Methodology

A comprehensive literature review was conducted to gather relevant information about the HPV vaccine. Targeted keyword searches were performed using terms such as “HPV vaccine history”, “HPV and cervical cancer”, etc. Information was collected from reputable online databases, such as PubMed and Google Scholar, as well as official websites, including the WHO and the Family Welfare Division (FWD).

History of the HPV vaccine:

- 1840s: First clues linking cervical cancer to sexual activity
- In the 1840s, researchers observed that nuns, with little sexual experience, seemed to have a lower incidence of cervical cancer compared to married women, who had more

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sexual exposure. This idea was revisited in the 1960s, focusing on the frequency of sexual intercourse and its potential link to cervical cancer (4).

- 1951 – HeLa cells are collected, becoming the first "immortal" cell line
- Henrietta Lacks, a 30-year-old mother of five, sought treatment for cervical cancer at Johns Hopkins Hospital. Without her consent, a cell biologist collected her cells, which turned out to be "immortal," doubling rapidly. Known as HeLa cells, they have played a vital role in major medical breakthroughs, including the link between HPV and cervical cancer, highlighting their significant yet unrecognized impact on science (5).
- 1970s: HPV suspected as cause of cervical cancer
- Before HPV, herpes simplex virus was suspected, but it couldn't explain cancer development. Harald zur Hausen proposed that certain human papillomaviruses could cause cervical cancer, inspired by evidence from animal papillomaviruses causing tumors (4).
- 1983: HPV DNA detected in cervical cancers
- Harald zur Hausen and Lutz Gissmann found HPV16 DNA in most cervical cancer tissue samples, proving a strong association (4).
- 1984–1989: Ian Frazer enters HPV research
- Frazer, a clinician-scientist in Melbourne, studied HPV in immunosuppressed HIV patients, linking HPV to anal dysplasia (a precursor to anal cancer). In 1989, he met Jian Zhou, a virologist from China, leading to a collaboration on making HPV virus-like particles (VLPs) (4).
- 1990–1991: Creation of HPV VLPs & patent
- Zhou and Frazer successfully expressed HPV16 capsid proteins (L1 and L2) in cultured cells, which self-assembled into empty viral shells (VLPs) that mimic HPV but contain no DNA. These VLPs could trigger immune responses without causing infection. A provisional patent was filed in 1991 for the VLP production method (4).
- 2001–2002: Clinical proof of HPV vaccine

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- Laura Koutsky's trials showed that a monovalent HPV16 vaccine was safe and provided strong protection against infection, proving that vaccination could prevent HPV-related disease (5).
- 2006: First HPV vaccine (Gardasil) licensed
- Gardasil (HPV4, covering types 6, 11, 16, 18) was approved in the US for girls aged 9–26. It targeted two high-risk types (16 & 18), causing ~70% of cervical cancers, and two low-risk types (6 & 11), causing 90% of genital warts (5).
- 2007: Global licensing of HPV vaccines
- Multiple countries, including Australia and the US, rolled out VLP-based HPV vaccines as part of cervical cancer prevention programs (5).
- 2008: Nobel Prize for HPV–cancer discovery
- Harald zur Hausen was awarded the Nobel Prize in Physiology or Medicine for proving that HPV16 and HPV18 cause cervical cancer (5).
- 2009: HPV vaccination for boys
- Gardasil approved in the US for boys aged 9–26 to prevent genital warts and reduce HPV transmission (5).
- 2014: Gardasil 9 approved
- Expanded protection to 9 HPV types (7 high-risk, causing ~90% of cervical cancers, and 2 low-risk wart-causing types). Clinical trials showed nearly 100% effectiveness in preventing HPV-related pre-cancers (5).
- 2016: Dosing schedule changes
- CDC recommended 2 doses (instead of 3) for 11–12-year-olds, given at least 6 months apart, improving compliance and coverage. For individuals older than 15, the recommendation remained the same (3 doses of the vaccine) (6).
- 2018: Expanded age approval
- US FDA approved Gardasil 9 for adults aged 27–45, extending prevention to a wider population (5).

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- 2030: WHO elimination strategy
- WHO launched the 90-70-90 targets to eliminate cervical cancer:
- 90% of girls are fully vaccinated with the HPV vaccine by age 15;
- 70% of women initially screened with high-performance testing by age 35 and a secondary test at age 45; and 90% of pre-cancers treated and 90% of invasive cancers managed (7)

Conclusion

Applying these insights can enhance vaccine uptake, prevent HPV-related diseases, and improve population health, emphasizing the profound impact of preventive medicine.

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Recommended Citation: Bista, S. (2025). Human papillomavirus vaccine, jhswn.com, vol16 (19)

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