Optimizing Human Papillomavirus (HPV) Vaccination in Adolescents: A Consensus on Closing Practice Gaps for Enhanced Impact

Summary

Human papillomavirus (HPV) is a common sexually transmitted infection and a major cause of several cancers, including cervical, vulvar, vaginal, head and neck, anal, and penile cancers as well as genital warts. Despite vaccination recommendations starting at the age 9 years, challenges such as low uptake, financial constraints, and vaccine hesitancy remain in India. Addressing such practice gaps is essential as we strive to eliminate HPV -related cancers and diseases in India.

At the Adolescent Health Academy, we aim to close gaps in HPV vaccination by analyzing key epidemiological trends and vaccination practices. Our focus is on raising awareness about HPV diseases and enhance preventive efforts. We aim is to explore strategies such as school-based programs and gender-neutral vaccination. On our 25th anniversary and in line with our ***"Empower Yuva"*** initiative, this consensus document will serve as a call to action for pediatricians to improve HPV vaccination strategies and work towards the elimination of HPV-related cancers in India.

Background

HPV is a major cause of various cancers, including cervical, vulvar, vaginal, anal, penile, and head and neck cancers, as well as genital warts (Grandahl et al., 2021). In 2020, India accounted for 24% of global HPV-related cancer cases, with projections suggesting that by 2025, these cancers will represent 7.7% of all cancer cases in India—3.3% in men and 12.0% in women (Ramamoorthy et al., 2022). Annually, India reports around 132,000 new cervical cancer cases and 74,000 deaths, making it the second most common cancer among women, particularly those aged 15–44.

Early HPV vaccination is essential to reduce the risk of related cancers and diseases. As HPV is easily transmitted soon after sexual debut, adolescent vaccination provides optimal protection. Furthermore, early detection and prevention can lower transmission rates, safeguard reproductive health, and reduce long-term healthcare costs, helping to eliminate HPV-related diseases and cancers.

HPV Vaccination Guidelines in India for Pediatricians

The Indian Academy of Pediatrics (IAP) Advisory Committee on Vaccines and Immunization Practices recommends the following HPV vaccination schedule (Rao et al., 2024): a 2-dose series for individuals aged 9–14 years, (0, 6 months), and a 3-dose series (given at 0, 2, and 6 months) for those aged 15 years and older, as well as for immunocompromised individuals.

The National Technical Advisory Group for Immunization (NTAGI) in India proposed the inclusion of the HPV vaccine in the Universal Immunization Program (UIP) two years ago (Devnath et al., 2024). Vaccinating only girls/women will not provide protection for men.

Challenges in Optimizing Adolescent HPV Vaccination in India

Improving HPV vaccination coverage in adolescents is essential to reduce HPV-related diseases (Acampora *et al*., 2020). Although vaccinating older population may also provide protection, it may not be cost-effective. Through a series of question-answers we will now attempt to address the practice gaps with respect to HPV vaccination in pediatric practice.

1) ***What types of HPV cause diseases and cancers?***

HPV is a group of over 200 related viruses, some of which are known to cause diseases, including several types of cancer. The main categories of HPV include high-risk types, such as HPV 16, 18, 31, 33, 45, 52, and 58, which can cause cervical cancer and other cancers. In contrast, low-risk HPV types are not usually associated with cancer but can lead to genital warts and respiratory papillomatosis. Additionally, they may cause low-grade changes in cervical cells, a condition known as cervical intraepithelial neoplasia.

2) ***Is it possible for HPV to be transmitted through non-sexual transmission routes, such as clothing, undergarments, sex toys, or surfaces?***

While non-sexual transmission of HPV is theoretically possible, it has not been conclusively proven. This is primarily because HPV cannot be cultured, making it challenging to detect its DNA in the environment, and such detection is likely to produce false negative results.

3) ***The body effectively clears HPV infections, with the immune system handling about 90% of cases. Then why is the HPV vaccine needed?***

While the human body is generally effective at clearing HPV infections, it is important to recognize that HPV is extremely common. Despite a high clearance rate, there are still many individuals who struggle to eliminate the virus on their own. Since we cannot predict who will be able to clear HPV, the aim is to vaccinate all adolescents to ensure their protection. (Bednarczyk, 2019)

4) ***What HPV vaccines are available in India?***

In India, there are currently two HPV vaccines available: a) the quadrivalent HPV vaccine, which protects against HPV types 6 and 11, as well as types 16 and 18, that are known to cause a significant number of cervical cancer cases; and b) the nonavalent HPV vaccine, which offers protection against five additional HPV types (31, 33, 45, 52, and 58) in addition to those covered by the quadrivalent vaccine. The introduction of the gender-neutral 9-valent HPV vaccine in India is designed to protect both young women and men from nine HPV serotypes (Kaur et al., 2024).

5) ***Why is it crucial to vaccinate children aged between 9 and 14 years against HPV?***

Administering HPV vaccination at ages 9–10 enhances immune response and increases the likelihood of completing the series by age 14, providing early and effective protection against HPV (Saxena et al., 2023). Studies show that girls aged 10–15 years generate geometric mean titers that are twice as high as those of women aged 16–26). Additionally, completing the HPV vaccine series by age 13 offers better immunity and broader pre-

exposure protection compared to completion by age 15 (Drolet et al., 2019; Saxena et al., 2023).

6) ***How effective is the HPV vaccine if a child starts the vaccination series later (e.g., at age 15 or 16 years)?***

The HPV vaccine is most effective when given between the ages of 9 and 14 years (0 and 6 months), offering the best protection before potential exposure. A review of 21 studies showed that HPV vaccine effectiveness was highest in adolescents aged 9–14 years (74%–93%) when compared to those aged 15–18 years (12% to 90%), emphasizing the importance of timely vaccination (Ellingson *et al.*, 2023). However, starting at ages 15–16 years may require a full 3-dose series (0, 2 and 6 months).

7) ***Some parents oppose HPV vaccination for their 9 to 14-year-olds on the grounds that they are not sexually active. How can this concern be addressed?***

Parents should be informed that starting vaccination at ages 11 or 12 provides optimal protection before any potential sexual activity. Vaccinating prior to exposure to infections is standard practice, as seen with other childhood vaccines. Younger adolescents respond better to the HPV vaccine than older teens and adults, and those vaccinated at this age will need only two doses, compared to three doses if vaccinated later.

8) ***What should be done if an individual misses a dose of the HPV vaccine?***

It should be noted that vaccine series need not be restarted due to an extended interval between doses (Immunize.org). If a dose is missed, individuals should continue with the remaining doses based on their age, without restarting the vaccination series. However, studies have demonstrated the impact of missing doses, such as a United States longitudinal study showing that adolescents immunized at ≥15 years with a longer time to complete the 3-dose schedule had a higher risk of anogenital HPV infection and increased cervical cytological abnormalities (Schlecht *et al.,* 2016).

9) ***If a dose of the HPV vaccine is considerably delayed, do I need to restart the series?***

One should not restart the series; instead, continue from where the patient left off and complete the vaccination series.

10) ***What are the recommendations for catch-up HPV vaccination in adolescents and young adults?***

Catch-up HPV vaccination is recommended up to age 45 years.

11) ***What are the guidelines and best practices for switching from one HPV vaccine to another?***

Individuals vaccinated with a different HPV vaccine may consider an additional 9vHPV dose for broader protection against more HPV types, in consultation with their healthcare provider (Canadian guidelines, 2023).

11) Are additional doses of 9vHPV vaccine recommended for someone who started with quadrivalent HPV vaccine?

If the decision is made to give the 9vHPV vaccine after completing three doses of the quadrivalent HPV vaccine, there should be a minimum interval of 12 months between the completion of the quadrivalent vaccination and the initiation of the 9vHPV vaccine.

12) Can the HPV vaccine be administered alongside other vaccines?

Yes, it is acceptable to administer a different inactivated or live vaccine either during the same visit or at any time before or after receiving the HPV vaccine, as HPV is not a live vaccine.

13) A 17-year-old received the third dose of the HPV vaccine 3 months after the second dose, but only 4 months after the first dose. Should the third dose be administered again?

Yes, if an HPV vaccine dose is given with less than the recommended minimum interval, it should be repeated. The repeat of the third dose should occur either five months after the first dose or 12 weeks after the invalid third dose, whichever is later.

14) Will patients who have previously had genital warts benefit from receiving the HPV vaccine?

The history of genital warts indicates prior infection with HPV types 6 or 11, which account for 90% of cases. However, individuals may be infected with other HPV types included in the vaccine. Vaccination can protect against these uncontracted types but will not treat genital warts. It is important for patients to complete the full age-appropriate HPV vaccine series for protection against both genital warts and cancer-causing HPV types.

15) What side effects can occur after receiving the HPV vaccine?

Both the quadrivalent HPV and nonavalent HPV vaccines are safe, with common (mild and temporary) side effects including local reactions such as pain, swelling, redness, and itching; systemic reactions like fever, fatigue, headache, nausea, and dizziness; and musculoskeletal issues such as muscle and/or joint pains.

16) HPV vaccines can lead to autoimmune diseases – is this true?

There have been studies ranging from hundreds of thousands to over 3 million people that have failed to find any consistent relationship between HPV vaccination and autoimmune diseases (Bednarczyk, 2019)

17) Does ovarian failure occur with the use of HPV vaccines?

The concern came out of a few small case reports that did not actually show a connection between HPV vaccination and ovarian failure. In fact, early ovarian insufficiency is more common than one might expect, affecting about 1 in 10,000 young women. In a study of 200,000 young women, 46 developed ovarian

insufficiency but none of these cases were associated with HPV or other routine adolescent vaccines. (Bednarczyk, 2019)

18) If Pap smears can help detect cervical cancers why are HPV vaccines needed?

Pap smears are screening tests that detect abnormal cervical cells but do not prevent HPV infections. In contrast, HPV vaccines actively protect against the most common cancer-causing HPV types. Vaccination can reduce the incidence of cervical cancer and dysplasia, potentially lowering the need for frequent Pap smears and follow-ups. HPV vaccines also protect against other HPV-related cancers, such as anal, vulvar, vaginal, and oropharyngeal cancers, while Pap smears mainly target cervical cancer. Together, vaccination and regular screening create a more effective strategy for preventing and managing cervical cancer. Importantly, screening is not required before administering the HPV vaccine.

19) Why is shared clinical decision-making recommended to decide whether the HPV vaccine should be given to adolescents?

HPV infections are common during adolescence and young adulthood, but new sex partners at any age increase the risk. Shared clinical decision-making emphasizes that vaccine providers should discuss the risks and benefits of vaccination based on the patient's age, underlying conditions, and other risk factors, allowing both the patient and provider to make a shared decision in the patient's best interest (Hogue *et al*., 2020).

20) ***Could a single-dose HPV vaccine improve vaccination efforts?***

Adopting an alternate single-dose HPV vaccine schedule could enhance affordability, simplify logistics, and alleviate supply issues (Basu et al., 2021). This approach is most effective when integrated into the National Immunization Program rather than private practice. A recent modelling study suggests that implementing single-dose HPV vaccination could significantly decrease cervical cancer rates in India (Man et al., 2022).

21) What are the key strategies to improve HPV vaccination in India?

A recent review from India outlines strategies to improve HPV vaccination: scale up vaccination using the corona virus disease (COVID)-19 model with artificial intelligence (AI)-driven surveillance and resource allocation in rural areas (proactive immunization program); implement mandatory HPV vaccination in schools and colleges, modeled after successful programs such as in Sikkim (school and college vaccination); overcome sociocultural barriers by engaging community leaders and creating culturally sensitive education campaigns (cultural engagement); advocate for HPV vaccination in national programs to ensure broader access and reduced financial barriers (advocacy for policy change) (Kaur *et al*., 2024).

22) What strategies can be used to address vaccine hesitancy through counseling and school-based education to encourage adolescents to attend vaccination clinics?

Pediatricians are a key source of vaccine information, and in-depth consultations with patients are recommended. Improved HPV education in medical curricula is also

essential (Shetty et al., 2019). To address misconceptions about HPV vaccination, especially concerning side effects and efficacy, increased awareness is crucial (Kaur et al., 2024). While schools are ideal for administering HPV vaccines, teacher training is often insufficient. To enhance sustainability, timely planning, regular training, equity-focused strategies, and efficient resource distribution are needed (Waheed et al., 2023).

23) What is the current level of knowledge, attitude, and practice (KAP) regarding HPV vaccination and sexual health among adolescents in India?

Despite the potential of HPV vaccines to prevent related illnesses, the rise in HPV-associated diseases is largely due to limited awareness among adolescents and healthcare professionals (Ramesh et al., 2021). A systematic review in India found that only 22% had knowledge of the HPV vaccine, 45% held positive attitudes, and coverage was merely 4%. Significant knowledge gaps were particularly evident among government and paramedical staff, underscoring the need for ongoing medical and public education (Chawla et al., 2016). While awareness is low, many participants showed positive attitudes toward HPV vaccination, and acceptance is likely to increase if the vaccine is included in the National Immunization Program (Kumari et al., 2021).

24) What are the HPV vaccination considerations for adolescents studying abroad?

Adolescents traveling abroad for college should ensure they meet destination-specific HPV vaccination requirements to comply with immigration, university policies, and public health guidelines. A pretravel health check-up helps confirm vaccination status, prevent disease spread, and facilitate access to healthcare abroad. Studies have shown that allowing adolescents to self-consent for HPV vaccination could improve access and coverage.

Conclusions

Widespread HPV vaccination is essential for reducing the burden of HPV-related cancers, particularly in India. Routine vaccination for individuals aged 9–14 years (2-doses), with catch-up options for those aged 15 years onwards (3-doses) is essential for maximizing coverage and addressing immunization gaps. Achieving widespread coverage requires a comprehensive approach that includes standardized education for paediatricians and parents, school-based immunization programs, and gender-neutral vaccination policies. Furthermore, integrating HPV education into school curricula and engaging local stakeholders will be vital for enhancing vaccine accessibility and acceptance.

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