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COMPREHENSIVE REVIEW OF HUMAN PAPILLOMAVIRUS (HPV) VACCINATION RECOMMENDATIONS FOR BOYS AND YOUNG MEN

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ABSTRACT

Human papillomavirus (HPV), a most common infection transmitted sexually, has significant implications for both males and females. It includes genital warts and a range of anogenital and oropharyngeal cancers. While early vaccination efforts primarily targeted girls to reduce cervical cancer rates, increasing recognition of HPV-related diseases in boys and young men has prompted major changes in vaccination guidelines. This review provides a comprehensive overview of the importanceof and current recommendations regarding HPV vaccination in males. Boys and young men are at risk for disfiguring and psychologically distressing genital warts, as well as malignant outcomes including anal and penile cancers. Furthermore, males contribute a significantpart in the transmission of HPV to sexual partners, underscoring the population-level benefits of widespread immunization.Clinical studies demonstrate high efficacy of HPV vaccines when administered before exposure, and current recommendations from agencies such as the CDC, ACIP, and AAP endorse routine vaccination for boys starting at ages 11–12, with catch-up vaccination up to age 26, and special attention to individuals with HIV and men having sexual encounters with partners from their own gender. Vaccine schedules have recently been updated, with evidence supporting a one-dose regimen for individuals under 25 years of age. Available vaccines protect against the major oncogenic types (16 and 18) and those causing most genital warts (6 and 11), with broader protection offered by the nonavalent vaccine. The adoption of routine HPV vaccination in boys and young men promises to reduce disease burden and transmission, and ongoing research and educational initiatives remain key to optimizing public health impact.

Key words: Human papillomavirus (HPV), HPV vaccination, Adult male immunization, HPV-related cancers, Vaccine efficacy, Vaccination guidelines, Herd immunity, Public health prevention.

INTRODUCTION

Human papillomavirus (HPV), a most common infection transmitted sexually, is implicated in a spectrum of anogenital and oropharyngeal cancers, as well as benign lesions such as genital warts[1]. Although the burden of HPV-related morbidity has been associated in the past with women, leading to policy focus on preventing cervical cancer, substantial epidemiological evidence now demonstrates significant HPV prevalence and disease impact in males[2].

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In men, persistent infection with oncogenic HPV types—particularly 16 and 18—is linked to increased risks of oropharyngeal, penile and anal cancers, and more than ninety percent of genital warts—caused by types 6 and 11—affect both sexes[3]. In Canada, for example, the overall incidence of men with HPV infection is similar to the infection among women, with studies observing rates of prevalence as high as 70% in adult males for any HPV type and 35% for vaccine-preventable types[4].

Vaccination against HPV has revolutionized the approach to preventing HPV-associated disease. Originally targeted toward adolescent girls, the HPV vaccine's introduction reflected a strategy to reduce cervical cancer. However, accumulating evidence of disease incidence in males and the demonstrated efficacy of the quadrivalent and nonavalent vaccines in reducing persistent infection and associated lesions in males prompted many countries to expand recommendations to include boys and young men[5]. Clinical trials affirm the safety and immunogenicity of HPV vaccination in males[6,7]. The HPV acquisition's median ageis usually in the 1st decade following beginning sexual activity, underscoring the rationale for vaccination in preadolescence before HPV exposure[8,9].

Internationally, there has been heterogeneity in HPV vaccination recommendations for adults[10]. A recent review observed that among 152 jurisdictions, 62 provided adult vaccination recommendations, and 84% of these included both genders[11]. While guidelines frequently recommend routine immunization of females aged 9–14 or up to 26, growing numbers now advocate for comparable inclusion of males, particularly as evidence accumulates of vaccine effectiveness in reducing transmission and providing direct protection against malignancies[12]. Notably, many funded public programs for adults consider eligibility at ages 26 to 45 years, and often prioritize high-risk groups such as those with HIV or other immunocompromising conditions[11,13-16].

Cost-effectiveness remains a vital concern in public program implementation, as the incremental benefit of extending vaccination to boys and adults must be balanced against existing coverage in girls and population-level herd immunity effects[17,18]. Nevertheless, modeling studies and real-world data indicate that male vaccination can accelerate disease reductions, benefiting both sexes and narrowing gaps for populations with historically lower vaccine uptake[19,20]. The Canadian case exemplifies shifting policy: while only select provinces publicly fund male vaccination, all provinces recommend the vaccine for both sexes, anticipating broader coverage as cost and equity arguments evolve[14,21].

In summary, expanding HPV vaccination programs to include boys and selected adult populations addresses a significant and preventable health burden. Such policies are supported by strong immunogenicity, efficacy, and safety data, and align with global trends seeking to reduce the incidence of HPV-related cancers and sexually transmitted conditions for all individuals[22,23].

MATERIALS AND METHOD

This narrative review conducted from January to June 2025 was composed following extensive research using online research platforms including Web of Science ,Science Direct, PubMed ,Scopus ,and Google Scholar. The keywords used to perform the research included 'Human Papilloma Virus', 'HPV' ,'HPV vaccination', 'HPV vaccination in adult male', 'HPV vaccination in boys', 'HPV vaccine dosage'. Research manuscripts that were from before the year 2000 and not available in English were excluded from the study.

OVERVIEW OF HPV

HPV affects an estimated 50% to 80% of sexually active individuals at some point during their lifetime[24]. HPV comprises a diverse group of over 200 related viruses, of which more than 30 are known to infect the genital tract. These types are categorized as either low-risk, primarily causing benign lesions such as genital warts, or high-risk, with the potential to lead to malignant transformation and cancer development[25]. Transmission of the virus occurs through skin-to-skin or mucosal contact, most commonly via sexual activity, but infection can also be acquired through other forms of close contact[26].

HPV infections in majority are transient and asymptomatic, with past research suggesting that about 70%–90% are cleared naturally by the immune system of the host within two to three years, often without any clinical consequences[27]. This immune clearance is thought to confer some degree of immunity, although reinfection can occur, especially with different HPV types. In about 10%–30% of cases, however, the infection becomes persistent, particularly with high-risk types, and long-term viral persistence may result in the gradual accumulation of genetic and cellular alterations that predispose to pre-malignant lesions and ultimately invasive cancers[28,29].

Low-risk HPV types, notably types 6 and 11, are responsible for approximately 90% of all genital warts and can also cause benign growths in the respiratory tract, such as laryngeal papillomatosis. These types are not usually linked to cancer but may require medical management to prevent spread and discomfort[30]. the types of HPV with high risk, particularly types 18 and 16, account for roughly 70%–80% of cases of cervical cancer globally and aggravates the pathogenesis of other anogenital cancers (anal, vulvar, vaginal, penile) and a significant proportion of oropharyngeal malignancies[31]. Continuous infection with these oncogenic strains can disrupt vital regulatory pathways within host cells, notably through viral E6 and E7 proteins , which exhibits interference with p53 and retinoblastoma protein (tumor suppression genes), fostering an environment conducive to malignant transformation[32].

Despite its ubiquity, the HPV disease burden is not uniform. Most individuals will never develop clinical disease, but risk is amplified in high-risk HPV infection which is persistent and is further modulated by cofactors such as immunosuppression, smoking, co-infection with other sexually transmitted pathogens, and genetic susceptibility[33,34]. The HPV infection's natural history is such that there can be a prolonged latency period between the initial infection and the manifestation of precancerous or cancerous lesions—sometimes spanning decades[35].

Given the prevalence, oncogenic potential, and silent nature of most HPV infections, HPV represents a major global public health challenge. Universal vaccination, early detection, and education in regards to sexual practices which are safe are paramount in reducing transmission and the burden of HPV-associated disease worldwide[36].

Efficacy of HPV Vaccination in Males

Vaccination of HPV vaccination has exhibited high efficacy in males, particularly when administered before exposure to the virus, affirming its role as a critical public health intervention[5]. Clinical trial data consistently support the capacity of HPV vaccines to induce robust immune responses and substantially reduce the prevalence of infection, persistent viral carriage, and related clinical manifestations, including genital warts and anal intraepithelial neoplasia[5,6,37].

HPV VACCINATION GUIDELINES, VACCINES AVAILABLE, VACCINE SCHEDULE

The Centers for Disease Control and Prevention (CDC) 2024 guidelines now advised administering vaccine of HPV routinelyin boys starting at ages eleven to twelve years, with the possibility of initiating vaccination as early as age 9. This age recommendation aligns with the understanding that vaccination prior to the commencement of sexual activity ensures maximal defense against HPV acquisition[38]. Importantly, teens and young adults who have not begun or finished the dosage of the HPV vaccine series are also strongly encouraged to receive vaccination to confer protection against new HPV infections and reduce transmission[39].

The available vaccines include the quadrivalent HPV vaccine (HPV4, Gardasil), initially approved in 2006 for females aged 9 to 26 years, which targets high-risk HPV types 18 and 16 that cause the majority of HPV-related cancers, in addition to low-risk types 11 and 6, responsible for around 90% of genital warts. Another vaccine, the bivalent HPV2 (Cervarix), protects against HPV types 16 and 18 and was approved in 2009 for females aged 10 to 25 years. More recently, Gardasil 9 has offered extended protection by including 5 other oncogenic HPV types (31, 33, 45, 52, and 58), thereby broadening the scope of cancer prevention[40-42].

Randomized controlled trials and longitudinal cohort studies reveal vaccine efficacy rates ranging from 90% to nearly 100% in preventing persistent HPV infections caused by vaccine-type HPV and associated precancerous lesions in males[43]. These outcomes extend to reductions in genital warts and anal intraepithelial neoplasia among vaccinated males, effects particularly pronounced when vaccination occurred before sexual debut. Moreover, post-licensure surveillance has corroborated durable protection, with immunogenicity sustained for over a decade in many individuals[44].

Regarding vaccination schedule, the American Academy of Pediatrics (AAP) mirrors CDC recommendations in vaccinating boys aged 11 to 12 years, administering two doses of HPV vaccine (such as Gardasil 9) separated by 6 to 12 months. Children starting vaccination before 15 years of age generally require the two-dose schedule, whereas those initiating vaccination at older ages (15–26 years) require a three-dose regimen spaced over six months. The guidelines extend special attention to bisexual, gay,and other men who have intercourse with men, as well as immunocompromised populations. This is including those living with HIV, recommending vaccination through age 26 if not previously immunized[45,46].

A notable update from September 2023 by the Joint Committee on Vaccination and Immunization (JCVI) endorses a one-dose vaccine schedule for individuals under 25 years of age, based on accumulating trial and observational evidence indicating comparable efficacy and immunogenicity to the traditional two-dose or three-dose regimens. This shift aims to simplify immunization logistics, improve vaccine uptake, and reduce costs while maintaining effective prevention. Nonetheless, persons older than 25 and immunocompromised individuals are advised to follow a multi-dose schedule to ensure optimal immunity[47].

Extensive evidence from the Costa Rica Vaccine Trial (CVT) and International Agency for Research on Cancer (IARC) studies supports the durability of a single dose, with stable antibody titers and sustained protection up to 10 to 11 years post-vaccination. This evidence has meaningful implications for expanding vaccination coverage globally, especially in resource-limited settings where the logistics of multi-dose administration present challenges[48].

SAFETY PROFILE OF HPV VACCINE

Safety profiles of HPV vaccines remain excellent, with common adverse events limited to mild injection site reactions and transient systemic symptoms such as headache and fatigue[49]. Contraindications include known hypersensitivity to vaccine components and pregnancy, with vaccination deferred until after pregnancy[50]. Despite effective vaccination, healthcare providers are urged to continue recommending barrier methods to prevent HPV and other sexually transmitted infections, as vaccines do not protect against all HPV types or other pathogens[51].

As anal and other HPV-associated cancers rise in incidence among men, the implementation of effective vaccination programs targeting boys and young men is expected to have a profound impact on reducing these outcomes[52]. The combination of proven vaccine efficacy, updated dosing recommendations, and expanding vaccination coverage underscores the importance of routine HPV immunization in males[53,54]. Continued efforts in public health messaging, vaccine delivery, and research are essential to optimize the benefit of HPV vaccination and ultimately control HPV-related diseases[55].

CONCLUSION

HPV vaccination is vital for reducing infection and preventing HPV-related cancers in both sexes. Initially focused on females, current evidence strongly supports inclusion of boys and men, given the demonstrated efficacy, durable protection, and excellent safety profile. Updated guidelines, including simplified one-dose schedules, expand access and cost-effectiveness, especially in resource-limited settings. Broader male vaccination not only ensures direct protection but also enhances herd immunity, making it a key strategy in controlling and ultimately eliminating HPV-associated diseases globally.

CONFLICT OF INTEREST

There is no conflict of interest.

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