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Evaluating the Effectiveness of HPV Vaccination in Preventing Oral and Oropharyngeal Cancers Among Men: An Epidemiological Review

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INTRODUCTION

Concerns and observations have been expressed regarding the multifaceted nature of Human Papilloma Virus (HPV) infections and their implications for public health, particularly considering recent epidemiological trends and evolving vaccination strategies. HPVs are small double-stranded deoxyribonucleic acid (DNA) viruses approximately 8kb in length from the family Papillomaviridae1, long recognized as significant etiological agents for several sexually transmitted diseases, including genital warts. In recent years, however, its role in the pathogenesis of various malignancies, notably cervical and oropharyngeal cancers, has become increasingly evident. The virus primarily infects epithelial cells, residing on the mucosal surfaces—such as the rectum, sexual organs, and oral cavity—as well as on the skin, thereby establishing persistent infections that can culminate in neoplastic transformation[1].

The complexity of HPV is underscored by the diversity of its genotypes. To date, over 400 types of HPV have been identified with about 200 approved2. More than 40 varieties are transmitted through sexual contact, and they infect the anus and genitals. These genotypes are broadly classified into high-risk and low-risk categories. High-risk types, particularly HPV16 and HPV18, have been implicated in most HPV-associated cancers. For instance, HPV16 accounts for over 90% of HPV-positive oropharyngeal malignancies3 and, along with HPV18, is responsible for approximately two-thirds of cervical cancers3. A study further demonstrated that HPV was detected in 55% of oropharyngeal squamous cell carcinoma (OPSCC) cases, with HPV16 alone being implicated in nearly 90% of HPV-positive OPSCC2. These findings emphasize the oncogenic potential of certain HPV types and underscore the necessity for vigilant screening and prevention measures.

The epidemiological landscape of HPV-related cancers has undergone a marked transformation in recent decades. Historically, oropharyngeal cancers were predominantly associated with traditional risk factors such as tobacco and alcohol use. However, a growing body of evidence now implicates HPV infection as a primary driver of these malignancies, particularly in high-income nations where the decline in smoking rates has been offset by an increase in the incidence of HPV-positive oropharyngeal cancers4. In the United States alone, approximately 30,700 cases of HPV-induced cancers are reported annually5, with HPV being responsible for about 30% of oropharyngeal malignancies, translating to nearly 29,000 cases per year5. The shift in etiological patterns calls for a reassessment of public health strategies, placing greater emphasis on vaccination and early detection of HPV-associated lesions.

The global burden of HPV-related malignancies is substantial, with high-risk HPV types accounting for around 5% of all cancers worldwide. Annually, approximately 570,000 women and 60,000 men are hospitalized due to malignancies related to high-risk HPV infections6. Cervical cancer, in particular, remains one of the most prevalent cancers among women, representing the leading cause of cancer-related mortality in low- and middle-income countries where screening and early treatment are often unavailable7. This disproportionate impact underscores the urgency for effective HPV vaccination programs, which not only promise to reduce the incidence of cervical cancer but may also have broader implications for other HPV-associated malignancies.

The advent of HPV vaccination has marked a significant milestone in the prevention of HPV-related diseases. Two vaccines currently available in the United States—Gardasil (HPV4) and Cervarix—have revolutionized the approach to preventing cervical and other HPV-associated cancers. Gardasil, a quadrivalent vaccine targeting HPV strains 6, 11, 16, and 18, was first approved in 2006 for the prevention of cervical, vaginal, and vulvar

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cancers in girls aged 9 to 26 years5. Clinical studies subsequently demonstrated its efficacy in preventing genital warts, prompting an expansion of its approved use to include boys within the same age range in 20095. More recently, the vaccine's ability to prevent anal pre-cancers has further broadened its clinical indications. In contrast, Cervarix, a recombinant vaccine that targets HPV16 and HPV18, was approved in 2009 specifically for the prevention of cervical cancer5. While both vaccines have shown high efficacy in HPV-naïve individuals, their protective capabilities diminish when administered to individuals with prior exposure to the virus, particularly regarding the prevention of genital warts and other non-cervical malignancies[8].

Despite these advancements, significant disparities persist in the uptake of HPV vaccination. In many countries, particularly those utilizing the quadrivalent vaccine, inequalities in vaccination coverage between genders have been observed. Women are generally more likely to be vaccinated than men, a disparity reminiscent of earlier instances in vaccination history. For example, following the resurgence of rubella among men in 1996, immunization programs were revised to include both sexes to mitigate prior inequities9. Nevertheless, there remains a dearth of substantial data to justify the routine vaccination of men with conventional HPV vaccines in many settings10. Moreover, while substantial research has focused on cervical HPV infection, relatively little is known about the epidemiology and prevention of oral HPV infections10. This gap in knowledge is particularly concerning given the rising incidence of HPV-related oropharyngeal cancers, underscoring the need for expanded research and more inclusive vaccination strategies.

The relationship between sexual behaviour and HPV infection is well established. Factors such as multiple sexual partners, early onset of sexual activity, a history of oral-genital or anal–oral sexual contact, and persistent periodontitis have been associated with an increased risk of HPV-related cancers2. Notably, individuals with a sexual partner who has an atypical Pap smear or cervical dysplasia are also at heightened risk. Epidemiological studies have further indicated that patients with HPV-positive squamous cell carcinoma of the oropharynx tend to be younger, of higher socioeconomic status, and less likely to be smokers3. This demographic shift further emphasizes the need for targeted educational and preventive measures, as the traditional risk profile for head and neck cancers no longer applies universally.

A systematic review exploring the association between oral sexual partners and oropharyngeal cancer has provided valuable insights into the complex interplay of behavioural and biological factors that contribute to HPV transmission and carcinogenesis11. Although this review did not propose specific interventions to reduce mortality and morbidity associated with these cancers, it underscored the importance of considering both behavioural and immunological factors in the development of comprehensive prevention strategies. In addition, economic evaluations using models such as the Papilloma Rapid Interaction for Modelling and Economies (PRIME) have demonstrated that HPV vaccination is cost-effective in virtually all countries12. The potential for one-dose vaccination regimens, in particular, offers a promising avenue to simplify vaccine delivery and reduce costs, thereby enhancing the feasibility of universal immunization programs in resource-constrained settings[12].

In regions such as Sub-Saharan Africa, where healthcare resources are limited, the acceptability and uptake of HPV vaccines have been a subject of intense investigation. A systematic review conducted in several Sub-Saharan African countries assessed vaccine acceptability through the lens of the Health Belief Model, focusing on perceived risks, barriers, and effectiveness of the vaccine13. The review concluded that, despite cultural and logistical challenges, vaccine acceptability was generally high. However, it is important to note that most of the available research in this area has primarily focused on cervical cancer, with comparatively little attention given to the prevention of oral cancers13. Complementing this perspective, a survey examining the knowledge and perceptions of HPV among both men and women found that men had a lower level of awareness compared to women. This disparity in knowledge has significant implications for vaccination decision-making, as evidence

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suggests that women are often the primary decision-makers regarding the vaccination of their children, with as many as 22% of women including their husbands or partners in these decisions14. Such findings advocate for a more inclusive public health dialogue that actively involves both sexes in HPV-related educational initiatives.

The clinical efficacy of HPV vaccines in preventing malignancies extends beyond the cervix. A community randomized trial investigating the AS04-HPV-16/18 vaccine reported a high success rate in preventing oropharyngeal infections caused by HPV types 16 and 18, with an acceptable level of efficacy against a predefined mixture of other oncogenic types, including types 31, 33, and 4515. Moreover, a case-control study evaluating serum markers found that among individuals seropositive for HPV16, the likelihood of developing head and neck cancers containing HPV16 DNA was significantly increased16. These studies highlight the critical need for comprehensive evaluations of HPV vaccination outcomes, particularly in relation to the prevention of oropharyngeal and other non-cervical cancers. The evidence collectively emphasizes that while current vaccination strategies have made significant strides in reducing the incidence of cervical cancer, there remains an urgent need to extend these benefits to other HPV-related malignancies.

The justification for continued and expanded research in this field is clear. While existing literature provides substantial evidence regarding the efficacy and cost-effectiveness of HPV vaccination, there are still critical gaps in our understanding of the virus's role in oropharyngeal cancers and the factors influencing vaccine uptake among different populations. It is imperative that future research endeavours address these gaps by incorporating comprehensive systematic reviews and robust epidemiological studies that evaluate the full spectrum of HPV-associated diseases. Such research should not only assess the clinical efficacy of current vaccines but also explore potential modifications to vaccination strategies that may enhance protection against a broader range of HPV-related malignancies. Only through such comprehensive investigations can we ensure that public health policies are fully informed by the best available evidence.

Thus, the evolving epidemiological profile of HPV and its associated malignancies necessitates a re-examination of current prevention strategies. The transition from traditional risk factors such as tobacco and alcohol use to viral aetiology in the context of oropharyngeal cancers has significant implications for both clinical practice and public health policy. The widespread availability of effective HPV vaccines, such as Gardasil and Cervarix, represents a major advancement in our ability to combat HPV-related diseases. However, persistent disparities in vaccination coverage and the emerging evidence linking HPV to a broader spectrum of malignancies underscore the need for more inclusive and comprehensive approaches. It is essential that vaccination programs be expanded to address the needs of both genders and that educational efforts be intensified to ensure that all individuals are adequately informed about the risks associated with HPV infection. Considering the substantial global burden of HPV-related cancers and the demonstrated cost-effectiveness of vaccination programs, we urge policymakers, clinicians, and researchers alike to prioritize the development of integrated prevention strategies that are responsive to current epidemiological trends and tailored to the diverse needs of populations across different socioeconomic contexts.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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