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Breaking barriers: why including boys and men is key to HPV prevention

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Abstract

Despite the common belief that human papillomavirus (HPV) primarily affects women, it is imperative to recognize and address the impact of HPV on boys and men. Overlooking the health implications for males is a notable gap, as efforts have predominantly focused on preventing HPV-related infections in women. This commentary aims to emphasize the importance of HPV awareness and vaccination for boys and men by highlighting the prevalence and consequences of HPV infection, elaborating on the associated health risks, elucidating the benefits of vaccination, and urging readers to recognize the necessity of protecting males from HPV. In addition, the increase in HPV-related cancers in men underscores the urgent need for increased awareness and vaccination. Although specific testing for HPV in men is not available, the inclusion of men and boys in gender-neutral vaccination programs can help reduce the harmful effects of this virus in both genders.

Keywords Human papillomavirus, HPV-related disease, Immunization programs, Boys and men, HPV vaccination, Penile cancer, Anal cancer

Introduction

Human papillomavirus (HPV) is a common sexually transmitted infection (STI) among women and men globally, with an estimated 9–13% prevalence, affecting approximately 630 million individuals [1, 2]. In 2023, the World Health Organization (WHO) reported approximately 30 million newly acquired HPV infections [3]. HPV accounts for 4.5% of all cancer cases globally, resulting in approximately 630,000 new cancer cases annually among both women and men, underscoring its significant impact on public health [4].

Although women bear a disproportionate burden of HPV infection, men are also affected by the virus. A 2022 systematic review identified 657,317 cancer cases linked to HPV, with 264,019 (40.2%) occurring in men [5]. Another systematic review in 2023 indicated that nearly one in three men aged ≥ 15 years was infected with at least one type of HPV and one in five with one or more high-risk or oncogenic HPV types. The global pooled prevalence between 1995 and 2022 for any HPV among men was 31% and 21% for high-risk HPV [6]. HPV-16, the predominant type of HPV (accounting for 5% of cases), is known to infect the anogenital tract in men as well as the epithelium of the oral cavity, oropharynx, and larynx through skin-to-skin or vaginal, anal, or oral sex with an infected person [7, 8]. The virus can be transmitted, even when an infected person exhibits no signs or symptoms [9]. HPV is associated with penile, anal, and oropharyngeal cancers in men [10], and its prevalence has been rising, with approximately 69,400 men acquiring HPV-related cancers in 2018 [11]. HPV affects men

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across all age groups globally [10], peaking among young men aged 25–29. While HPV prevalence rates are similar across most regions (30–37%), they are lower in Eastern and Southeastern Asia (15%) [6]. The prevalence of HPV and associated cancers is higher among people living with HIV than among those not infected with HIV [12].

Men's role in eliminating cervical cancer

The growing body of epidemiological evidence noted above highlights the substantial role that men play in transmitting HPV to women. Anogenital warts in men contribute significantly to adverse health outcomes and increase the risk of genital HPV transmission to female sexual partners [6, 11]. Cervical cancer is caused by persistent infections with high-risk oncogenic HPV genotypes [13], and male sexual behavior is a crucial factor influencing the development of cervical disease in women [3, 4]. Cross-infection between partners often leads to persistent HPV infections, increasing the likelihood of developing high-grade cervical lesions, and ultimately, cervical cancer [4]. The link between heterosexual sexual behavior and HPV is supported by a recent study of 503 college-age women in Canada, which found that 40.4% acquired HPV infections within 2 years of initiating a relationship with a male partner [14].

WHO has established a global strategy to eliminate cervical cancer as a public health problem by 2030, with specific measurable global targets referred to as the 90–70-90 targets for vaccination, screening, and treatment. Eliminating cervical cancer relies heavily on achieving high rates of continuous vaccination coverage. However, vaccination uptake remains inadequate in most countries, with coverage varying across and within countries. In 2022, only 21% of girls worldwide received at least one dose of the HPV vaccine [15], far behind the WHO's target of vaccinating 90% of 15-year-old girls by 2030. A more comprehensive approach is needed to reach the target of eradicating cervical cancer by 2030. Gender-neutral immunization, which aims to eliminate HPV infections and related cancers, is essential [16]. However, a female-focused approach overlooks the fact that HPV is primarily transmitted from male to female or male to male via sexual intercourse. Therefore, more resources should be directed toward administering the HPV vaccine to both men and women [16] rather than focusing solely on women, which has been the traditional approach. Addressing the sexual and reproductive health needs of men [17] can significantly improve the sexual and reproductive health outcomes of women and children.

Why focus on men?

HPV treatment and prevention efforts should extend beyond women to include men who are significantly affected by HPV infections [4]. In men, the immune response to HPV infection is poor (only 20–30%) and non-protective, leading to frequent re-infection and effective transmission of the virus. Unlike natural infections, HPV vaccination protects against infections in men [18]. The global prevalence of genital HPV infection in men closely mirrors that in women (3.5–44% vs. 2–44%), with similar transmission rates [19]. Men bear a significant burden of HPV-related diseases, including anogenital warts, with an incidence rate ranging from 103 to 168 per 100,000 males per year. Globally, there are an estimated 22,000 cases of penile cancer per year, with approximately 40% of these cases attributed to HPV infection, primarily driven by high-risk HPV-16 and HPV-18 strains [10]. Additionally, men experience a disproportionate burden of HPV-related oral infections and oropharyngeal cancers [20]. Alarmingly, the rates of HPV-positive oropharyngeal squamous cell carcinoma (OPSCC) are projected to increase over the next 20–30 years, with the UK alone forecasted to spend around £2 billion on OPSCC treatment in men by 2038 [21]. Evidence also suggests that HPV infections may affect sperm quality and contribute to infertility [4, 20]. Thus, HPV underscores the need to engage men in comprehensive HPV preventive strategies. This will reduce HPV-related morbidity in men, regardless of sexual orientation, and help lower the incidence of cervical cancer in women [22].

Currently, there are no approved screening tests for HPV in men [23]. However, healthcare providers may recommend anal pap smears for men at a higher risk of developing anal cancer, such as those who are immunocompromised or engage in anal intercourse [23]. Vaccination remains the most effective preventative measure against HPV infections and related health issues in men, yet global vaccination coverage for males remains low, standing at a mere 4% [10]. The WHO recommends targeting girls aged 9–14 for HPV vaccinations, but only for males and older women when feasible and affordable [24]. HPV vaccination has been recommended for females since 2006 and for males since 2011 [10]. The US Food and Drug Administration (FDA) approved the first prophylactic HPV vaccine in 2007 for the prevention of HPV-related cancers, and the US Centers for Disease Control and Prevention (CDC) soon recommended it for both females and males (up to age 26). In 2018, the FDA extended the HPV vaccine approval for use in adults aged 27–45 [25]. Currently, six prophylactic HPV vaccines are licensed: three bivalent, two quadrivalent, and one nonavalent [12]. The 9-valent HPV Gardasil-9® vaccine

is particularly effective, serving as a preventive measure against anogenital lesions and oropharyngeal and other head and neck cancers resulting from specific HPV types such as 16/18/31/33/45/52/58 [12].

Calling for the expansion of HPV immunization programs

As of November 2023, 140 countries have incorporated HPV vaccines in their national programs, and as of April 2023, 47 countries have offered vaccination to males [26]. High-income countries are more inclined to include males in their routine HPV immunization programs [27]. Some argue that focusing only on women in HPV vaccination campaigns is based on achieving herd immunity [28]; that is, high female vaccine coverage protects unvaccinated women and heterosexual males [3]. However, there is also evidence to suggest that vaccination of *only females* may not provide adequate protection for unvaccinated males or even unvaccinated females, as the prevalence of HPV types that cause cancer in both sexes remains high in the unvaccinated population [29, 30].

Furthermore, global vaccination rates remain inadequate for achieving the necessary level of immune protection. The herd immunity argument also assumes that sexual encounters occur within this cohort [12]. In all likelihood, men who have sex with men (MSM) will not receive this protection. Therefore, vaccination models should be carefully factored in. MSM are at an increased risk of developing HPV-related anal disease [10]. Over the past three decades, there has been a significant increase in the incidence of anal cancer among MSM globally [31]. MSM have high rates of STIs, especially among those who engage in receptive anal sex and are highly vulnerable to HPV-related anal cancers [32]. The risk of anal cancer is exceptionally high among MSM living with HIV. This heightened risk is due to frequent exposure to anal HPV and the exacerbating effect of immunosuppression on HPV-related outcomes [33].

Multiple models suggest that vaccinating both males and females is more effective in reducing HPV infections and diseases than vaccinating only females, although male vaccination is less cost-effective [3]. Vaccinating males is anticipated to provide indirect benefits to females through the establishment of population-level immunity, a decline in viral load within the general population, and reducing anogenital diseases among males [12]. A recent study in Finland found that in towns where both boys and girls received the HPV vaccine, there was a significant reduction in cancer-related HPV strains [34]. Eight years after implementing HPV vaccination, researchers observed comparable reductions in high-oncogenicity vaccine-targeted HPV types 16/18/31/45 in gender-neutral communities (arms A–C, LRT = 172.7, $p = 0.001$) and types 16/18/31 compared with girls-only communities (arms B and C, LRT 182.8, $p = 0.001$). These findings suggest that vaccinating both boys and girls against HPV can achieve the same effects in 8 years as vaccinating only females would be over 20 years old. Similarly, an Australian study with 400 MSM revealed a 70% reduction in vaccine-preventable HPV genotypes among those aged 16–20 years following the implementation of an HPV vaccination program in 2013 [31]. These findings indicate that gender-neutral vaccination programs can effectively reduce the prevalence of high-risk anal HPV strains and potentially decrease the incidence of anal cancer among MSM.

Including boys and men in HPV vaccination does not undermine cervical cancer prevention efforts. Instead, it acknowledges that both genders play a role in transmitting and acquiring this common sexually transmitted infection. Prioritizing education and expanding HPV vaccination programs to include males are critical steps toward achieving public health goals and effectively combatting the spread of the virus and associated diseases among all individuals, regardless of gender identity or sexual orientation. Further modeling and implementation science research is needed to evaluate whether including boys and men in a vaccination approach will enhance protection for both men and women and reduce the risk of associated cancers. Policymakers can use modeling predictions to assess the potential impact of varying levels of gender-neutral vaccination coverage on HPV infections and associated cancers, aiding in informed decision-making regarding the allocation of limited resources for HPV vaccination roll-out.

We must not let the cost of the HPV vaccine stand in the way of protecting boys and men, given its proven effectiveness in preventing genital warts, cancers, and other HPV-related illnesses [35]. With increased vaccine production, new options entering the market, and the potential of single-dose vaccines for young girls, future vaccine shortages will unlikely hinder gender-neutral HPV vaccination programs [36]. While cost is an important consideration in allocating resources, limiting HPV vaccination to girls and women means missing the benefits of including men and boys in the vaccination approach. Expanding these programs to the latter not only maximizes public health outcomes but also challenges harmful stereotypes and misconceptions about sexuality that often unfairly target women. Discussions on HPV and prevention should move beyond focusing solely on female responsibility to acknowledge that HPV transmission is a shared issue. We should not perpetuate gender disparities by ignoring the importance of shared responsibility for the prevention and protection of both genders from the detrimental effects of HPV infection.

Together, we can work toward a future free from HPV and the diseases it causes.

Abbreviations

HPV	Human papillomavirus
STI	Sexually transmitted infection
WHO	World Health Organization
OPSCC	Oropharyngeal squamous cell carcinoma
FDA	Food and Drug Administration
CDC	Centers for Disease Control and Prevention
MSM	Men who have sex with men

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Data availability
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Declarations

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