REVIEW ARTICLE

The Benefits of Human Papillomavirus Vaccination on Men's Health: A Literature Review

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ABSTRACT

Human papillomavirus (HPV) is recognized globally as a major sexually transmitted infection that not only poses a significant health risk to women, but also causes diseases in men, such as genital warts, infertility, and oropharyngeal cancer. These conditions can reduce a man's quality of life and overall happiness. Although HPV vaccination has been a notable success in women's health, it also needs to be implemented in men. In recent years, experts have advocated the HPV vaccine for men because of its broad effectiveness and safety in preventing HPV infection and related diseases. Therefore, the purpose of this review is to comprehensively explore the diseases caused by HPV in men and the significance of HPV vaccination, in order to improve the awareness and absorption of HPV vaccination in men. The review highlights the critical importance of increasing HPV vaccine coverage in men to reduce the incidence of HPV-related diseases and improve public health outcomes.
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Keywords: Human papillomavirus (HPV), HPV related diseases in men, HPV vaccine, Sexually transmitted infections, Genital warts

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INTRODUCTION

Human papillomavirus (HPV) infection is a prevalent sexually transmitted infection that affects both males and females. Approximately 80% of sexually active individuals may acquire HPV, making it highly common (1). Young women are particularly susceptible to this infection, while men have a lower risk. HPV primarily targets the squamous epithelial cells found in the skin and mucous membranes, which lack sufficient protection from virus-specific antibodies (2). Although most cases of HPV infections resolve naturally, persistent infection with specific types of HPV can lead to various benign conditions such as condyloma acuminatum and male infertility (3). Moreover, these persistent infections are closely associated with the development of malignant tumors including cervical cancer, oropharyngeal cancer, and anogenital squamous cell carcinoma. HPV is responsible for approximately 630,000 cancer cases annually worldwide, accounting for about 5% of all cancers (4). People who are HIV-positive or engage in high-risk sexual behaviors face an elevated risk of acquiring HPV and developing associated illnesses.

To mitigate the potential harm caused by HPV, vaccination against this virus has proven to be a highly effective preventive measure (5). The incidence of HPV infection and cervical cancer associated with HPV has exhibited a decline over the past decade, owing to the successful implementation of screening and vaccination programs in most high-income nations. However, low-income countries in Asia and Africa continue to shoulder an unequal share of HPV infection and cancers caused by infectious diseases (6). The HPV vaccine demonstrates significant efficacy in prevention, with the potential to reduce approximately 90% of cervical cancer cases. Furthermore, it exhibits notable effectiveness against other types of cancers: vulvar cancer incidence can be reduced by 22.8%, penile cancer by 24.5%, vaginal cancer by up to 79.0%, and oropharyngeal cancer by 21.3%. Additionally, there is a modest decrease observed in oral cancers (4.0%) and laryngeal cancers (2.7%) (7).

Currently, there is a widespread recognition of the potential threat posed by HPV to women's well-being and the importance of a preventive vaccine. However, it is crucial to acknowledge that men are equally vulnerable to the detrimental effects of HPV. With evolving societal attitudes towards love and sexual behavior, there has been a gradual increase in the prevalence of HPV infections among men. This article aims to explore the profound impact that HPV can have on men while emphasizing the significance and benefits associated with vaccinating them against this virus, enhancing awareness and uptake of HPV vaccination among males.

METHODS

The literature search was conducted across four databases, namely Science Direct, Pub Med, CINAHL, and Google Scholar. The search terms "HPV" and "male" were combined with the keywords “HPV related diseases in men”, “HPV vaccine”, “sexually transmitted infections”. This study comprehensively reviewed over 70 papers published between 2014 and 2024, encompassing systematic reviews, experimental reports, surveys, and qualitative studies.

RESULTS

Characteristic of Including Studies

Table I shows the research section including year of publication, aim of study, study location, sample selection, immunization programmes, outcomes and findings. Different countries have different HPV vaccination policies, such as the United States (8), Australia (9) and Canada (10), which have extended HPV vaccination programs to male students; Japan (11) and Malaysia (12) include the HPV vaccine in their national immunization programs and offer it to girls free of charge. The findings of the study showed that there were gender differences in cognitive attitudes towards HPV and its related knowledge, with women generally having higher levels of awareness and more positive attitudes towards HPV (13-15). In some countries that have not yet popularized HPV vaccination for men, men have a low level of awareness and lack of knowledge about HPV, and perform poorly in accepting HPV vaccine (16-18). However, in developed countries where the HPV vaccine is widely available to men, men also show a willingness to accept the benefits of HPV vaccination, even though they have a lower understanding of HPV and its associated health issues than women (19, 20). Overall, there is an urgent imperative to enhance men's comprehension of HPV and the HPV vaccine, as this can not only augment their awareness regarding their own health but also contribute to mitigating the transmission of HPV infections and associated ailments, thereby safeguarding the well-being of society at large.

Table II: The outcomes and findings within select articles of this literature review

Author	Aim of study	Sample	Study Country	Immunization Programmes	Outcomes	Findings
Du et al., (2022) (8)	This study aimed to characterize knowledge of HPV, HPV vaccine, and HPV-associated HNC among medical students, and determine demographic and educational factors associated with differences in knowledge.	Total: 247 Male: 108 Female: 139	United States	In the United States, the vaccine is usually included in childhood immunization programs, which are routinely given to boys and girls ages 11-12.	This research uncovered a lack of understanding regarding HPV and the HPV vaccine among male students. Notably, men exhibited significantly less knowledge about the HPV vaccine compared to women (β = -1.53; 95% CI: -2.53, -0.52). Male students demonstrated notably lower levels of familiarity with HPV.	Given the inadequate HPV vaccination rates across the United States and the rising incidence of HPV-related cancers, it is recommended that educational curricula across the United States be fully informed about HPV, the cancers associated with it, and the appropriate prevention measures.
Lockwood et al., (2024) (9)	The purpose of this study is to gain an understanding of the knowledge and awareness of HPV, the HPV vaccine, and HPV-related cancers.	Total: 763 Male: 243 Female: 520	Australia	In Australia, the vaccine is usually included in the childhood immunization program and is usually given to boys and girls at 12-13.	Participants with modest knowledge of HPV had higher vaccination rates than participants with little or no knowledge of HPV.	The participants had limited knowledge regarding HPV, its transmission, the HPV vaccine, and its potential to cause cancer. Insufficient information can contribute to hesitancy in receiving vaccination.
Steben et al., (2019) (10)	This Canadian survey aimed to assess current knowledge of, attitudes towards, and barriers to the HPV vaccine among the general public.	Total: 450 Male: 200 Female: 250	Canada	In Canada, the vaccine is usually included in the childhood immunization program and is usually given to boys and girls in grade 6.	Greater levels of HPV knowledge were observed among the younger population, including both vaccinated women and men. They exhibited a higher awareness regarding HPV information and the significance of vaccination, along with more favorable attitudes towards receiving the vaccine.	Numerous obstacles hinder men from receiving the HPV vaccine, such as inadequate guidance from medical professionals or healthcare providers, insufficient knowledge regarding the HPV vaccine, unfavorable perceptions towards both the HPV vaccine and other vaccines in general, and an excessive association of HPV solely with females.

CONTINUE

Table II: The outcomes and findings within select articles of this literature review. (CONT.)

Author	Aim of study	Sample	Study Country	Immunization Programmes	Outcomes	Findings
Suzuki et al., (2019) (11)	This study requires comprehensive understanding of knowledge and attitudes regarding CC prevention, HPV infection and HPV vaccination among the population including laypersons and medical professions in Japan.	Total: 2784 Male: 1182 Female: 1602	Japan	Japan's national immunization program offers HPV vaccination to girls between the ages of 12 and 16.	This study reveals that close to 50% of participants lack awareness regarding the transmission of HPV by men, indicating a need for improved education among young males concerning HPV, its related illnesses, and the benefits of vaccination.	There is a lack of knowledge and awareness among Japanese men regarding the prevention of HPV-related diseases, highlighting the significance of increasing male engagement in HPV prevention as a crucial step towards achieving the objective.
Tusimin et al., (2019) (12)	The purpose of this study is to investigate the sociodemographic determinants of knowledge and attitude among students of Universiti Tunku Abdul Rahman (UTAR) towards the HPV vaccination programme.	Total: 369 Male: 131 Female: 238	Malaysia	A free vaccination programme for 13-year-old girls in public and private schools was introduced in 2010.	More than half (75.2%) of respondents with a positive attitude were women, due to the relative scarcity of information about the HPV vaccine and diseases associated with men. The majority of male respondents believed that the HPV vaccine is only for women and is only associated with cervical cancer.	The promotion and reinforcement of health awareness should be prioritized in the education curriculum, with particular emphasis on male students.
Liu et al., (2020) (13)	This cross-sectional study aimed to assess the knowledge, practice and attitude towards HPV vaccination among college students in Beijing, China.	Total: 827 Male: 361 Female: 466	China	Not included in the national immunization programme,	The majority of students were familiar with HPV and the HPV vaccine, possessing a moderate level of understanding. Female students exhibited greater knowledge regarding HPV and its associated vaccine compared to their male counterparts.	The HPV vaccine will not be integrated into the Chinese national immunization program for a long time because of the high financial burden. Pilot programs for HPV vaccines have begun in some regions, providing free or subsidized HPV vaccination services to specific populations.
Galvao et al., (2022) (14)	The purpose of this study is to analyze knowledge, attitudes, and practices of adolescent students from public schools in the municipality of Teresina, state of Piauн, regarding human papillomavirus (HPV).	Total: 472 Male: 185 Female: 287	Brazilian	Brazil included the HPV vaccine in its national immunization program in 2014, but only for women aged 9-13. In 2017, it became the seventh country in the world to vaccinate boys against HPV.	The proportion of adolescents with insufficient knowledge about HPV was 72.7%, while 65.9% had a negative attitude towards infection prevention. Women were more likely to be vaccinated (92.7%) than men (46.5%). Female adolescents are 15.62 times more likely to be vaccinated than males, with sufficient knowledge increasing this chance by 2.09 times and positive attitudes by 1.89 times.	The vaccine was initially offered only to women, and there was more information about female diseases such as cervical cancer, leading to a lack of awareness that it was available to both men and women, with low vaccination rates among male adolescents.
Dai et al., (2022) (15)	This study aimed to explore and compare the willingness to HPV vaccination, as well as influencing factors such as knowledge and attitude between male and female university students in China who have not been vaccinated against HPV.	Total: 7335 Male: 3570 Female: 3765	China	Not included in the national immunization programme	Female students had better knowledge and attitude to HPV in general. While male students exhibited a higher inclination towards receiving the HPV vaccine compared to their female counterparts (89.7% vs. 32.1%), it was observed that female students were more inclined to seek consultation regarding the vaccine and held stronger beliefs in its effectiveness.	In China, the prevalence of HPV infection among men is high, but most studies have focused on cervical cancer in women, and only a few studies have addressed the new prevalence of HPV-related cancers among men.

CONTINUE

Table II: The outcomes and findings within select articles of this literature review. (CONT.)

Author	Aim of study	Sample	Study Country	Immunization Programmes	Outcomes	Findings
Winarto et al., (2022) (16)	This study aimed to investigate the association between knowledge, attitudes, and practices (KAP) and socio-demographical influences related to HPV, CC, and vaccination among Indonesian urban citizens.	Total: 400 Male: 105 Female: 295	Indonesia	Indonesia, which first began offering the HPV vaccine to adolescent girls through schools in selected areas of the country in 2016, expanded HPV vaccination nationwide in 2023 to include the HPV vaccine in the national immunization program.	Both men and women exhibit limited knowledge about HPV, with women demonstrating higher scores and proportions in all aspects and overall compared to men ($p<0.01$). Additionally, women tend to have a higher proportion of positive attitudes across aspects and overall ($p<0.05$).	In the female group, the proportion of good knowledge awareness practice is obviously higher. In contrast, men have limited knowledge about HPV and HPV vaccination. This may be because of their lack of awareness, whereas women generally perceive the issue as more relevant to them.
Kiener et al., (2022) (19)	This study aimed to examine the association between vaccine hesitancy (VH) and HPV vaccine uptake among male and female youth in Switzerland.	Total: 674 Male: 415 Female: 259	Switzerland	The government has recommended the HPV vaccine as a routine vaccine for girls aged 11-14 since 2007. In 2015, HPV vaccination was extended to include boys.	The rate of HPV vaccine adoption was notably lower among males in comparison to females. Although vaccination rates were higher for younger males, the reduced rates observed among older male adolescents suggest a need for public health initiatives aimed at increasing awareness about catch-up vaccinations within this demographic.	Male adolescents face some additional challenges when receiving the HPV vaccine, such as poor awareness and understanding of the vaccine, difficult access to the vaccine, and low emphasis on male HPV vaccination by public health authorities and health care providers.

Types of HPV

HPV infection is one of the most common sexually transmitted diseases in the world (21). It is characterized by spherical, tiny, unenveloped circular double-stranded DNA viruses. HPV primarily affects genital and upper respiratory epithelial cells as well as skin, leading to proliferative lesions on human skin and mucosa. Notably, certain carcinogenic types such as HPV16 and HPV18 have been identified by the International Agency for Research on Cancer (IARC). These two types exhibit high detection rates among cervical cancer cases globally while also being implicated in other genital tumors like head and neck cancer. Particularly noteworthy is the significant detection rate of HPV16 in oropharyngeal cancer due to its ability to persistently infect oral tissues while effectively evading host immune responses. This prolonged infection creates favorable conditions for malignant transformation. The human papillomavirus (HPV) is a diverse group of viruses comprising over 200 different genotypes, which are associated with various skin and mucosal lesions (22). The HPV types can be classified into high-risk (HR) and low-risk (LR) groups based on their potential to cause cancer. Significantly, various cancers such as cervical cancer, vaginal cancer, vulvar cancer, anal cancer, penile cancer, and head and neck cancer (especially oropharyngeal cancer) have a strong association with high-risk HPV types like HPV 16 and 18. In fact, roughly 70% of cervical cancer cases worldwide can be attributed to HPV types 16 and 18 (23). Conversely, low-risk HPV types primarily cause benign lesions such as genital warts and some mild cervical abnormalities. Among these low-risk types, genital warts are most frequently linked to HPV types 6 and 11.

HPV transmission

Sexual contact is the primary route of HPV transmission, including vaginal, anal, and oral sex, which result in the transmission through direct contact with HPV particles carried by an infected person (24). Additionally, HPV can be spread through contact with lesions on the genitals or skin of an infected individual. Contact with an infected person's external genital warts or oral warts can also lead to infection (25). When a woman carries HPV, it can be transmitted to her newborn during labor and delivery (26). Furthermore, HPV can be transmitted through shared items such as bath towels and hand towels (27). If these items come into contact with the skin lesions of an infected person, the virus may be transmitted.

HPV related male diseases

Human papillomavirus (HPV) is a commonly transmitted sexually acquired infection linked to different types of genital warts. Although most HPV infections do not exhibit symptoms, this characteristic contributes to its widespread transmission. Women infected with HPV may be at risk of developing gynecological malignancies such as cervical, vaginal, and vulvar cancer (28). Men also experience a significant prevalence of HPV infections resembling those observed in women in terms of infection type and affected tissues. In fact, males globally exhibit a higher incidence rate of contracting HPV compared to females, particularly among

uncircumcised individuals, those living with HIV/AIDS, and homosexual males (29). HPV infection takes many forms in men and can lead to genital warts, anal cancer and other related diseases. While some men may show obvious symptoms, such as warty lesions in the genital area, many infected people may have no symptoms at all, making the virus more stealthy and widespread (30).

Genital warts

Genital warts, a commonly transmitted infection, are primarily caused by types 6 and 11 of the human papillomavirus (HPV) (31). Manifesting as fleshy protrusions in genital and anal areas, they can vary in appearance, from tiny, imperceptible bumps to larger cauliflower-like protrusions. Though often painless, some individuals may experience itching, burning, or even pain. The warts can affect areas like the vulva, penis, cervix, anus, and occasionally the mouth or larynx (32). Despite their benign nature, they can lead to psychological distress due to their appearance and the potential physical discomfort. The contagion rate is so high that around 64% of sexual partners of infected individuals might contract it. Throughout their lifetimes, about 50% of sexually active adults might contract some form of HPV, with types 6 and 11 being associated with 90% of genital warts cases (33). Despite this prevalence, detailed data is sparse since many countries don't mandate the reporting of genital warts. The overall infection rate stands at approximately 10%, affecting both genders (34). Other HPV types like 16 and 52 are also culprits behind genital warts (35).

Male sterility

In males, HPV has been extensively documented to be present in various areas such as the anus, perineum, scrotum, glans, penile shaft, urethra, and even semen. Moreover, its persistence of infection at these sites has been associated with both male infertility issues and the development of cancer in different genital and non-genital regions (36). Recent studies highlight the detectability of HPV on sperm cells, particularly on the sperm head (37). Its presence is correlated with decreased sperm motility, suggesting a significant role of HPV in male infertility. Other sperm irregularities include abnormal morphology, impacting overall semen quality. Decreased sperm motility stands out as a primary consequence of HPV infection (38). A study indicated 17.4% of 615 infertile men tested positive for HPV, marking it a risk factor for male infertility (39). Moreover, HPV-infected sperm might transfer viral DNA to egg cells during fertilization. This can lead to the expression of the viral DNA in the developing embryo, increasing apoptosis in trophoblastic cells, affecting implantation success, and raising miscarriage risks. Both genders face severe physical and psychological repercussions from this. Notably, HPV subtypes 45, 52, 18, 59, and 16 are most associated with male infertility (40).

Oropharyngeal carcinoma

Oropharyngeal cancer, which has a significantly high prevalence in Northern Europe, the U.S., and Australia, the incidence approximately 98,000 cases of the oropharynx in the world (41). Studies have revealed that HPV DNA is present in many patients diagnosed with this type of cancer. Approximately 23.5% of cases involving oral cancer and 24% of cases involving laryngeal cancer were identified as having HPV positivity (42). Notably, HPV-related oropharyngeal cancer primarily affects younger individuals and more men than women. In fact, its incidence is on the rise and may soon surpass that of cervical cancer (43). This increase is particularly prominent in Western countries where men experience two to three times higher rates compared to women. The main culprits behind HPV-positive oropharyngeal cancer are predominantly HPV types 16 and 18, with an emphasis on HPV 16 accounting for about 95% (44). Transmission of HPV occurs primarily through saliva or mucus exchange during oral contact with areas rich in the virus. While most people naturally clear HPV infections from their system without complications, certain subtypes can evade immune responses over time potentially leading to malignancies. It's important to note that only a small fraction of individuals harboring long-term presence of HPV in their mouth develop oropharyngeal cancer.

Carcinoma of penis

The global prevalence of penile cancer, a rare form of malignancy, reached 36,068 cases in the year 2020, ranking it as the 30th most common type of cancer (45). This particular cancer primarily affects males who are over the age of 60 and has a notably high fatality rate. It is predominantly found in regions with lower healthcare standards and income levels such as certain parts of Africa, Asia, and South America. Penile cancer accounts for up to 10% of all male malignant diseases. Interestingly, its occurrence patterns closely resemble those observed in cervical cancer (46). More than half (50%) of penile cancers are linked to Human Papilloma Virus (HPV), specifically HPV strains 16/18 which are responsible for approximately 73% of cases. Certain risk factors like phimosis and smoking significantly increase the risk by around eleven-fold and two-fold respectively (47).

The main factor contributing to the penile cancer is the human papillomavirus (HPV), which mainly affects the skin and mucous membranes' squamous epithelial cells. Squamous cell carcinoma of penis (PSCC) is the main form of penile cancer. The proportion can reach 90%. In 2016, WHO classified penile squamous cell carcinoma into non-HPV-related and HPV-related. Non-HPV-related PSCC typically arises from prolonged stimulation and inflammation, whereas the HPV-positive variant presents a lower risk of metastasis (47). Olesen

conducted a systematic review and meta-analysis in 2018, which found 1,836 non-duplicated records and included 73 articles, found that the prevalence of HPV DNA in penile cancer (52 studies) was 50.8% and the main carcinogenic type of penile carcinoma was HPV16 (68.3%), followed by HPV6 (8.1%) and HPV18 (6.9%) (48). Consequently, persistent HPV infection remains a significant contributing factor to penile cancer and has prompted global implementation of male HPV vaccination.

Anal cancer

Anal cancer is a malignant tumor that originates in cells inside the anus, usually on the skin of the anal canal or anal margin. Although anal cancer is relatively rare, according to a study by Krzowska in 2019, there are approximately 27,000 new cases worldwide each year, with a ratio of up to 5:1 men to women, and more than 90% of anal cancer cases are closely related to HPV infection (49).

Although anal cancer is not a highly prevalent disease, its prevalence has increased significantly in both men and women in recent years. According to the study data, more than 90% of cases associated with anal cancer are linked to HPV infection, particularly with high-risk HPV subtypes, such as HPV-16; Anal HPV infection varies greatly between genders and sexual orientations. Annually, around 27,000 anal cancer cases are estimated globally, with a female to male ratio of 5:1 (50). Anal HPV infection is prevalent among HIV-positive or MSM individuals, and the infection rate is higher in HIV-positive MSM (51). The incidence of MSM in HIV-positive male population is higher than that in the general population (52). A study in both Sweden and Demark, that involved 386 anal cancer patients observed that HPV was positive in 83% and 95% of patients respectively. In a US study, anal cancer incidence rates were markedly higher amongst the cohort of 447,953 people coinfected with HIV infections, especially in men who have sex with men (MSM), those of increased age and AIDS sufferers, compared to the general population (49).

HPV causes psychological disorders in men

As public awareness of health and disease prevention has increased, men, especially men who have sex with men, have begun to express concern about whether they have HPV. Among them, many expressed deep concerns about potential genital warts, penile cancer and anal cancer. When men test positive for HPV antibodies, they are often deeply concerned about their health, their possible risk of transmission, and their relationships with their partners. This worry is often accompanied by a range of emotional changes, including anxiety, guilt, depression, anger, and fear. This constant emotional repression may not only have an impact on their mental health, it may also lead to physical disorders. For example, obvious HPV symptoms such as genital warts can damage their self-esteem, while concerns about possibly transmitting the virus to a partner can also have an impact on their sex life, causing them to be overly cautious or lose interest in sex. What's more, social misunderstanding and discrimination against HPV may make these men feel isolated and marginalized in society, thus further increasing their psychological burden.

HPV vaccine

An overview of the HPV vaccine

Safe and effective vaccines against HPV are available since 2006, and the World Health Organization (WHO) recommends countries to vaccinate adolescent girls (53). Three vaccines are WHO pre-qualified: bivalent against HPV 16 and 18, quadrivalent against HPV 6,11,16, and 18 and nine-valent (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58). Vaccine efficacy is a measure of how well the vaccine works at preventing disease at the individual level in a clinical trial. Large pre-licensure trials of bivalent and quadrivalent vaccines demonstrated high protection against HPV 16 and 18 persistent infection and associated cervical intraepithelial neoplasia (CIN) grade 2 or worse in women without infection at vaccination (vaccine efficacy >90%) (54-56). Nine-valent vaccine showed non-inferior HPV 6,11,16 and 18 antibody responses compared with quadrivalent vaccine and efficacy of 96.7% (95% CI 80.9–99.8) against HPV 31,33,45,52 and 58-related high-grade lesions (57).

The HPV 023 extension study of the classical bivalent vaccine was a double-blind, randomized, placebo-controlled study involving women aged 15 to 25 years with normal cytology prior to vaccination. At 9.4 years post-vaccination, no HPV-16 or HPV-18-related infections or cytopathological abnormalities were observed in the vaccine group (58). In the V501-018-11 trial, which targeted 9- to 15-year-olds, no cases of cervical intraepithelial neoplasia (CIN), penile intraepithelial neoplasia (PIN), or related diseases were observed during the 10-year follow-up period, confirming the protective efficacy of the quadrivalent vaccine against HPV infections and genital diseases in men (59). Another 8-year project, V503-002, conducted across the African, Asia-Pacific, European, Latin American, and North American regions, showed that approximately 8 years post-vaccination, no lesions associated with the nine-valent vaccine types were observed in women, and no cases of PIN or genital warts associated with the vaccine types were observed in men (60).

HPV vaccine protection for men

Following WHO's guidance recommending men's inclusion in HPV vaccination after primary target groups have been addressed, the FDA approved the nine-valent HPV vaccine to prevent specific cancers in men. Countries like Australia, the US, and Canada have introduced male HPV vaccinations, leading to a decline in male HPV infections and associated diseases. Consequently, the importance and upward trend of

male HPV vaccination is evident (61).

Vaccination stands as a potent preventive measure against HPV-induced harm, with 65 nations globally integrating it into standard immunization schedules. A study suggest that the HPV vaccine significantly combats HPV infections, while antibody titers after the nine-valent HPV vaccine administration can differ among individuals, the vaccine demonstrates substantial preventive capabilities against various cancer types (62). Global adoption of the HPV vaccine into immunization programs has yielded positive outcomes. Both genders, despite distinct natural infection responses to HPV, acquire enduring immune protection post-vaccination. Research indicates the vaccine's comparable efficacy in men, substantially lowering the risk of HPV-related conditions (63). Australia's commendable reduction in HPV infection rates stems from its high vaccine coverage. Sole reliance on female vaccination may fall short in offering sufficient herd immunity for men, underlining the necessity for direct male HPV vaccination to further diminish HPV transmission risks (64).

Benefits of HPV vaccination for special populations

While the benefits of the HPV vaccine for women and the need for it are widely accepted, certain populations, such as gay men (MSM), people living with HIV, and non-infected partners with HPV-positive partners, are often overlooked despite being at high risk for HPV infection. Vaccination in these special groups is not widely available, so it is important to study these groups in depth to determine the need and potential benefits of HPV vaccination. In 2014, the Advisory Committee on Immunization Practices (ACIP) recommended that people with MSM and HIV before the age of 26 receive the vaccine. Studies have shown that it is necessary to vaccinate MSM, HIV-infected people, and non-infected partners with HPV-positive partners (65).

MSM

As the incidence of MSM continues to rise in different countries and regions, MSM has become a high risk group for HPV infection due to their unique sexual lifestyle, which mainly includes anal and oral sex. Some research data reveal that the HPV infection rate in healthy men in the general population is about 20%, while in MSM group, the rate is as high as more than 90% (66). More worryingly, the risk of HPV infection in MSM is increasing at an alarming rate, with an infection rate 20 times higher than that of men who have sex only with women (67). Unlike heterosexual men who have sex with women, MSM may not benefit from the so-called "herd immunity" from HPV vaccination in women, underscoring the urgency of achieving high HPV vaccination coverage among men. Rossi (2018) showed in a study that all men in developed countries, regardless of sexual orientation, face an increasing burden of HPV-related diseases year by year (68). Since 2011, HPV vaccination has been recommended in the United States for young adult men with MSM and is strongly recommended in early adolescence. Vaccination against HPV provides significant health protection for gay men. This not only effectively reduces their risk of developing HPV-related cancers, such as anal and oropharyngeal cancers, but also prevents genital warts caused by HPV. In addition, the vaccine also helps reduce the spread of the virus and provides additional protection for their partners. Taken together, the HPV vaccine provides an important health barrier for gay men and helps protect them from the long-term health risks of HPV.

HIV-infected person

People with HIV have a higher rate of HPV infection, a longer duration of infection, and a more rapid progression of HPV-related diseases compared with HIV-negative people. According to a study by Poljak in 2017, there is an interaction between HPV and HIV, and they can influence each other's risk of infection. Specifically, the risk of HIV infection increases significantly when HPV infection occurs in the genitals (69). A study has shown that the HPV vaccine is effective in HIV-positive patients, including those treated with HAART(70). Patients treated with HAART typically show a stronger response to the HPV vaccine than those who do not receive HAART, as HAART suppresses HIV viral load to undetectable levels, leading to a partial recovery of the immune system (71). This recovery enhances their response to the HPV vaccine and significantly improves their overall immune function. Therefore, promoting HPV vaccination, especially during early adolescence, is critical to preventing HPV-related diseases among HIV-positive patients.

HPV-positive spouse

Although the focus of the HPV vaccine is often on women, HPV infection in men both endangers their health and may increase the risk of their female partners becoming infected with the virus. Studies have shown that up to 83.5% of men who carry HPV antibodies or are in a relationship with a woman with cervical cancer have genital HPV infection, suggesting a fairly high rate of infection among male partners of female patients (72). Epidemiological data also reveal that among those infected with HPV, many have unsafe sex or multiple sexual partners. These partners often exhibit symptoms of genital warts, which are often associated with mixed HPV infection (36).

Sexual transmission is one of the main ways HPV is transmitted, and when either partner is infected with HPV, the other partner is also at a higher risk of infection. Therefore, the need to vaccinate both sides should be emphasized. Based on how HPV is transmitted, men who get the HPV vaccine not only protect themselves, but also provide protection against their sexual partners. Therefore, in the current situation, it is necessary to put special emphasis on HPV vaccination for men,

especially the male partners of infected women. Only in this way can we effectively prevent and protect this high-risk group and finally achieve herd immunity (73).

Adverse effects of HPV vaccination in men

The four-valent and nine-valent HPV vaccines have demonstrated remarkable immune effectiveness in men, offering robust protection. Yet, like many vaccinations, side effects can occur. Common side effects are pain and swelling where injected, systemic reactions such as nausea, appetite loss, and vomiting, which usually subside within a day. Additionally, some might experience mild headaches, dizziness, or a minor fever. A fever over 38.5°C necessitates medical intervention. People allergic to vaccine ingredients might develop skin reactions, warranting prompt medical attention. Research indicates that after receiving the nine-valent HPV vaccine, young men have a 76.2% adverse reaction rate, lower than the 86.4% observed in young women (63). Most of these reactions were mild to moderate and localized to the injection site. Another study involving 500 men found similar adverse effects between the nine-valent and quadrivalent vaccines, with few serious adverse events noted (64).

Future trends of HPV vaccines

After more than ten years of development, HPV vaccines have made breakthrough progress, especially the nine-valent vaccine, which prevents about 90% of cervical cancer, vulvar cancer, vaginal cancer and anal cancer. But current vaccines, while highly effective and focused primarily on prevention, do not cover the full range of HPV subtypes. On the other hand, the high price of vaccines limits their availability to the wider population. Therapeutic vaccines are being researched for those with HPV, which are designed to stimulate an immune response to eliminate precancerous lesions and persistent infections caused by HPV. In Malaysia, although women are still the main HPV vaccination group, due to changes in lifestyle and social culture, HPV infection rates and related diseases in men are also on the rise. Strategies should therefore shift to increasing overall vaccination rates, covering both men and women, to ensure full herd immunity.

With the increasing progress of scientific research technology and medical research, the development of HPV vaccines is ushering in an era of innovation. Future vaccines may cover more HPV subtypes and be optimized for cost reduction, making them more widely available globally. The possible direction is to move towards single-dose or long-acting vaccines to simplify the vaccination process, while strengthening public education to increase vaccine acceptance and penetration. In addition, taking into account individual differences, future vaccines may be more personalized, optimized for specific genetic or lifestyle risks. Digital health technologies, such as mobile apps and online platforms, can further promote vaccination, providing vaccination reminders and education.

In addition, transnational cooperation, policy development, financial support, and education will play a key role in HPV vaccine access and research. This will ensure that more people have access to this important preventive measure, especially in countries and regions with limited resources. Advances in biotechnology and gene editing may drive the effectiveness and efficiency of vaccines, leading to more efficient and durable protection against HPV.

Finally, the continued global focus on public health and strong support for the HPV vaccine indicate that we are moving toward eliminating HPV-related diseases and ensuring that everyone can live and grow in a healthy environment.

CONCLUSION

HPV infection in men can lead to genital warts, infertility, oropharyngeal cancer, anal cancer and penile cancer, which are not only harmful to physical health, but also cause great psychological stress. To prevent these diseases, HPV vaccination is particularly critical for men, as it not only provides direct protection for men, but also brings the benefits of cross-protection and herd immunity to the community. In view of this, the importance of universal HPV vaccine for men has become particularly urgent, and the health sector and relevant institutions should provide more resources and support to reduce the cost of the vaccine and improve its accessibility. In conclusion, in order to ensure public health, the government should pay more attention to the popularization and vaccination of HPV vaccine for men.

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