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REVIEW ARTICLE

Vaccination in the setting of sexually transmitted infections consultation

Vacinação na consulta de infeções sexualmente transmissíveis

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Abstract

Sexually transmitted infections (STIs) are a significant public health concern across the globe. Vaccines have played a crucial role in mitigating the burden of infectious diseases and are the most effective candidates for preventing STIs. Currently, vaccines for hepatitis A, hepatitis B virus (HBV), and human papillomavirus (HPV) are available. More recently, the smallpox vaccine was approved for Mpox (MPX) prevention. Ongoing research efforts are focused on developing vaccines for other STIs. This paper reviews the current indications for available vaccines for use in the context of STIs and discusses some of the vaccines currently being researched.

Keywords: Hepatitis A. Hepatitis B. Human papillomavirus. Mpox. Sexually transmitted infections. Vaccine.

Resumo

As infeções sexualmente transmissíveis (ISTs) são um importante problema de saúde pública em todo o mundo. Historicamente, as vacinas têm desempenhado um papel fundamental na redução das doenças infeciosas, sendo as melhores candidatas para a prevenção eficaz das ISTs. Atualmente, existem disponíveis as vacinas para a hepatite A, hepatite B e papilomavírus humano. Mais recentemente, a vacina contra a varíola foi aprovada para a prevenção da infeção por mpox. Para as outras ISTs, a investigação está em progresso para desenvolver uma vacina eficaz. Este artigo visa fazer uma revisão das indicações atuais das vacinas disponíveis para uso no contexto das ISTs e discutir algumas ISTs cujas vacinas que estão em investigação.

Palavras-chave: Hepatite A. Hepatite B. Vírus do papiloma humano. Mpox. Infeções sexualmente transmissíveis. Vacinas.

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Introduction

The World Health Organization (WHO) reports that > 1 million STIs are acquired daily worldwide, with most individuals infected not experiencing any symptoms. STIs have a significant impact on sexual and reproductive health, leading to considerable health issues and economic costs globally. The highest incidence of STIs is associated with eight pathogens, of which four can be cured, namely syphilis, gonorrhea, chlamydia, and trichomoniasis, while the other four are incurable viral infections–HBV, herpes simplex virus (HSV), human immunodeficiency virus (HIV), and HPV[1].

Preventing and controlling STIs is a crucial public health priority. Common prevention strategies, such as comprehensive sex education and promoting condom use, may not be effective in the long-term due to the challenges of maintaining safe sexual behaviors. Vaccines have played a significant role in reducing the burden of infectious diseases, and they are now considered a crucial tool in STI prevention programs. The increasing rates of antimicrobial resistance, limited availability of new antibiotics, persistent viral STIs, and high rates of condomless sexual intercourse highlight the urgent need for effective STI vaccines. Currently, safe and effective vaccines are available for three viral STIs–HAV, HBV, and human HPV. More recently, the smallpox vaccine has also been approved for MPX prevention. Ongoing research is focused on developing vaccines against genital herpes and HIV, with several promising vaccine candidates in early clinical development. Further research is needed to develop vaccines for bacterial STIs such as chlamydia and gonorrhea[1].

This paper focuses on reviewing the current indications of the available vaccines to use in the setting of STIs and discussing some of the vaccine's ongoing research.

Hepatitis A

Hepatitis A virus (HAV) is responsible for causing approximately 1.4 million cases of infection globally each year. The primary mode of transmission is through the fecal-oral route, either through direct contact between individuals or through the consumption of contaminated food or water. HAV can also be transmitted through sexual activity, likely as a result of fecal-oral contact[2].

In low and middle-income countries, individuals are often exposed to the virus at an early age, resulting in a higher prevalence of immunization. Conversely, countries with higher levels of sanitation and socioeconomic conditions often have lower exposure to the virus, leading to a larger number of susceptible individuals. In developed countries, the number of infections is on the rise among high-risk groups, such as men who have sex with men (MSM). The main risk factors for HAV transmission in MSM include engaging in oral-anal and digital-anal intercourse, having multiple sexual partners, having current infections with other STIs, and visiting venues like gay saunas, dark rooms, and dating apps[3]. These factors increase the likelihood of exposure to the virus and subsequent infection.

Frequent outbreaks of HAV infection have been reported over the years. Between June 2016 and 2017, an unusual increase in cases of hepatitis A affecting mainly MSM has been reported in 22 countries of the European Union (EU)/European Economic Area (EEA), including Portugal.

In the United States (US), effective control of HAV among men who have MSM is achieved by including the HAV vaccine in childhood vaccination programs. However, in many other countries, such as Portugal, the HAV vaccine is not part of the routine vaccination schedule[4]. Vaccination is considered the most effective way to prevent HAV transmission among individuals at risk for infection who did not receive the HAV vaccine during childhood. Knowledge of HAV risks and prevention, including vaccination recommendations, is poor among affected MSM; indeed, there is still a low rate of vaccination among this population.

A study recently published in Lancet[5] suggests that, while reactive vaccination of MSM in England during future outbreaks could significantly reduce the outbreak's magnitude and be a cost-saving strategy, pre-emptive vaccination of MSM between outbreaks in sexual health services could save even more money and have a greater impact, if the preemptive vaccination rate is sufficiently high (9% vaccination rate per year among MSM attending Sexual Health Services for the 5 years prior to an outbreak) Thus, preemptive vaccination should be the preferred choice.

Since 1991, an inactivated HAV vaccine called Havrix has been licensed for use in Europe and approved for individuals aged 12 months and older. The vaccine is administered in two doses, given at 0 and 6–12 months apart (Table 1). Nearly all adults develop protective antibody levels within a month after the first dose, ranging from 94 to 100%, and 100% achieve protective levels after the second dose. Studies show that protective levels persist for over 40 years based on kinetic models of antibody decrease among adults. Additionally, a combined HAV and HBV vaccine called Twinrix has

been developed and licensed for use in adults aged 18 years and older who are at risk for HAV or HBV infections. The vaccine is given as a three-dose series on a 0, 1 and 6-month schedule and has equivalent immunogenicity to that of the monovalent hepatitis A vaccines[2].

The routine testing of prevaccination serologic for HAV immunity is not recommended. However, it is recommended to test for anti-HAV antibodies after vaccination for individuals whose clinical management depends on their immune status and those who may require revaccination, such as people with HIV infection and other immunocompromising conditions[2]. A protective antibody titer level is believed to be equal to or greater than 20 mIU/mL[3].

In case of recent exposure to HAV, individuals who have not been previously vaccinated should receive either a single dose of monovalent vaccine or immunoglobulin (IG) as soon as possible, preferably within 2 weeks after exposure. A monovalent vaccine is usually preferred over IG for postexposure prophylaxis (PEP) because it provides active immunity and longer-term protection, is easier to administer, and is more widely available and acceptable[2].

Hepatitis B

The number of newly diagnosed HBV infections reported from countries across Europe remains high, with most of these infections classified as chronic[4].

The primary way HBV is transmitted in Asia is perinatal, while in Africa, it is usually transmitted from one child to another. However, in industrialized countries such as Portugal, sexual activity is the most common mode of transmission for HBV. Engaging in unprotected sex with someone who is infected with HBV, having multiple sexual partners, being an MSM, having a history of other STIs, and using injection drugs are all factors that increase the risk of HBV infection in adolescents and adults. According to the 2020's report from the European Centre for Disease Prevention and Control (ECDC)[4], heterosexual transmission was the most common way that acute HBV infections were spread, followed by transmission among MSM.

In Portugal, the HBV vaccine has been included in the National Vaccination Plan (PNV) for all children. It is given in three doses, with the first dose administered at birth, the second dose at 1 month, and the third dose at 6 months. The vaccine is also recommended for adults who are at high-risk of HBV infection, such as healthcare workers, people who inject drugs, MSM, and individuals with chronic liver disease. The hepatitis B vaccine is generally well-accepted in Portugal, and vaccination coverage rates have been high, especially among children and adolescents. However, there are still some gaps in vaccine coverage, particularly among certain high-risk groups, and efforts are ongoing to increase access and uptake of the vaccine in these populations. Healthcare settings that offer STI services to adults at high-risk for infection should provide the hepatitis B vaccine to individuals who have not been vaccinated[2]. Simultaneous education of MSM about hepatitis A and B and routine use of dual HAV/HBV vaccine may help address attitudinal barriers that interfere with acceptance of vaccination. As universal hepatitis B vaccination of newborns and children becomes increasingly successful in the coming decades, the need for vaccinating individuals with specific risk factors will be significantly reduced[5].

There are two approved products for preventing HBV–the hepatitis B vaccine and hepatitis B immune globulin (HBIG). HBIG can provide temporary protection from HBV infection for a period of 3-6 months and is often used as PEP along with the hepatitis B vaccine. This is especially important for individuals who have not been previously vaccinated or have not responded well to vaccination[2].

The HBV vaccine is made using recombinant deoxyribonucleic acid (DNA) technology to produce hepatitis B surface antigen (HBsAg) in yeast, and it is effective for both preexposure vaccination and PEP.[3] The vaccine is available in Europe under the brand name Engerix-B®[2].

A positive immune response to the vaccine is defined as the development of HBV anti-HBs at a titer of > 10 mIU/mL after a complete and adequate immunization schedule measured preferably 1-3 months after the last vaccine administration[3]. In adolescents and healthy adults below 40 years of age, the percentage of individuals who develop a protective antibody response after the first dose of the HBV vaccine is approximately 30-55%, which increases to 75% after the second dose and to > 90% after the third dose. Studies have shown that vaccine-induced immune memory remains intact for > 30 years, and long-term protection against HBV infection persists despite a gradual decrease in anti-HBs antibodies over time[2].

Routine testing to determine antibody levels after hepatitis B vaccination is not needed for healthy individuals with normal immune systems, and booster doses are not recommended[2,3]. However, individuals with HIV infection should be tested for the presence of anti-HBs 1-2 months

after the third vaccine dose due to the possibility of impaired vaccine response. Postvaccination testing is also recommended for certain high-risk groups such as healthcare workers, sex, and needle-sharing partners of HBsAg-positive persons, immunocompromised individuals and hemodialysis patients. Individuals who have anti-HBs levels of < 10 mIU/mL after completing the primary hepatitis B vaccine series should undergo a new three-dose vaccine series and get tested for anti-HBs 1-2 months after receiving the third dose. If they still don't have protective antibody levels, they should undergo HBsAg and Anti-HBc testing to determine their HBV infection status[2].

Human papillomavirus (HPV)

Human papillomavirus (HPV) infection is the most frequent STI and the second most common cause of cancer attributable to an infectious agent globally[6].

The HPV is transmitted through skin-to-skin contact, which can lead to infection in susceptible people. Several studies reported a higher prevalence of HPV infection in MSM than in heterosexual men, especially in anal region[7,8].

Human papillomavirus (HPV) vaccines are generally considered safe and effective in preventing HPV infections and related health problems, such as anogenital warts and precancerous lesions. They are most effective when given to individuals who have not been previously exposed to HPV. When vaccination coverage is above 50%, there is substantial evidence of indirect protection, known as herd immunity, which can further reduce the spread of HPV infections in the population[6].

Three vaccines have been available since 2006—a bivalent vaccine containing HPV 16 and 18 genotypes, a tetravalent vaccine also containing HPV six and 11 genotypes, and a nonavalent vaccine, which contains genotypes 6, 11, 16, 18, 31, 33, 45, 52, and 58[3]. Only the bivalent and nonavalent HPV vaccines are currently available on the market in Portugal.

The WHO reports that only 30% of the target population worldwide has received the HPV vaccine. In Portugal, the nonavalent vaccine is included in the PNV and is given to both boys and girls at 10 years of age. It's also recommended for all individuals between the ages of 11 and 26. For adults aged 27-45, shared clinical decision-making is recommended to determine if vaccination is appropriate[2]. Certain high-risk groups, such as MSM, sex workers, people with multiple sex partners, and immunocompromised individuals [e.g. people living with HIV/acquired immunodeficiency syndrome (AIDS) (PLWH)], may benefit from the vaccine (Table 1). MSM, in particular, are at a high-risk of HPV infection and associated diseases and may not benefit from the girls-only vaccination programme. In England, MSM up to and including 45 years of age have been eligible for free HPV vaccination when they visit specialist sexual health services and HIV clinics since April 2018[9]. A recent study suggested that all MSM with HIV would benefit from nonavalent HPV immunization, especially those who are younger and have had prior gonococcal infections[10].

For individuals who start HPV vaccination before their 15th birthday, a two-dose schedule is recommended, with doses given at 0 and 6-12-month intervals. However, people who are 15 years of age or older or are immunocompromised should receive a three-dose schedule, with doses given at 0, 1-2, and 6-month intervals[2].

It's important to note that HPV vaccines should not be given to pregnant women, as the safety of these vaccines during pregnancy has not been established. However, the vaccines can be given to individuals regardless of their history of anogenital warts, abnormal Papanicolaou test or HPV test or anogenital precancer[2] (Table 1).

An updated systematic review and meta-analysis, which included data from 60 million individuals and up to 8 years of postvaccination follow-up, showed compelling evidence of the substantial impact of three-dose girls-only HPV vaccination programs with the quadrivalent or bivalent vaccines on infections by HPV 16 and 18 and HPV 31, 33, and 45 as a group, anogenital wart diagnoses, and CIN2+ [SB3] among women. Furthermore, the study also found evidence of herd effects among boys and older women[11].

According to ECDC, the nonavalent HPV vaccine is efficacious in preventing persistent HPV infection and cervical high-grade or worse lesions in females 16-26 years and in preventing persistent HPV infections, genital warts, and high-grade anal intraepithelial lesions among males 16-26 years. The data also suggest stronger immunogenicity of the nonavalent HPV vaccine against vaccine serotypes in males and females 9-15 years compared to females 16-26 years[12].

Mpox (MPX)

Currently, officially starting from May 2022, an outbreak of MPX is ongoing, with 82,474 cases being notified as of December 9. Around > 100 countries and territories are affected, from all six WHO regions[13].

Cases in the current outbreak present a spectrum of symptoms and signs that differs from that described in past outbreaks of MPX in endemic countries[14]. Most frequently reported differences include-no prodromal symptoms or very mild; rash appearing before prodrome; rash presenting with very few lesions and/or limited only in genital or perianal areas; and lesions that do not evolve synchronously[15].

Human-to-human transmission of MPX occurs when an uninfected individual comes in close contact with the skin lesions of an infected person, through respiratory droplets during prolonged face-to-face interaction, and *via* contaminated objects or surfaces (fomites). It is still unclear whether MPX can be transmitted through genital secretions. During the current outbreak, MPX DNA was found in seminal fluid samples of young adult male patients in Italy who reported having unprotected sex. However, further studies are required to determine if MPX can indeed be sexually transmitted through genital fluids. It's important to note that the mere presence of MPX nucleic acid in bodily fluids is not enough to confirm infectivity[15].

In the current outbreak in nonendemic countries, most of the cases have been detected in males between 18 and 50 years, primarily among MSM. Particular sexual practices have facilitated the transmission of MPX among MSM groups with multiple partners. A significant percent of the cases detected to date have been PLWH (39%) undergoing antiretroviral treatment. The impact of MPX infection on PLHW who are not on appropriate antiretroviral treatment in the at-risk groups could be higher[15]. Based on the evidence from the cases reported in the current outbreak, the likelihood of MPX spreading further in networks of people with multiple sexual partners in the EU/EEA is considered high and the likelihood of spreading among the broader population is assessed as very low[15]. The Modified Vaccinia Ankara-Bavarian Nordic or MVA-BN (marketed as Imvanex in Europe, Jynneos in the USA, and Imvamune in Canada) is a third-generation attenuated smallpox vaccine that was approved in Europe on 22 July 2022 for use against MPX[15]. According to older studies, it is estimated to be up to 85% effective in preventing MPX infection[16].

Preexposure phase III trials have demonstrated positive results for immunogenicity and indirect measures of efficacy; a favorable safety profile was confirmed for healthy population groups, as well as PLWH, people with atopic dermatitis and hematopoietic stem cell transplants[17]. The vaccine response among people with HIV with clusters of differentiation 4 cell count < 100 cells/m^3 has not been established[15].

Primary preventive vaccination is recommended for individuals at high-risk of exposure, including MSM or other individuals with multiple sexual partners and health workers at high-risk of exposure[17] (Table 1). PEP vaccination is recommended for close contacts of cases, prior to the onset of any symptoms, ideally within 4 days of first exposure (and up to 14 days in the absence of symptoms), to prevent the onset of disease or mitigate disease severity[17].

The MVA-BN is administered as a subcutaneous injection, preferably in the upper arm, with a two-dose regimen, with the second dose given at least 28 days after the first[15]. For adults who have been vaccinated against smallpox might only need one dose. Given the currently limited supply of the vaccine, intradermal injections, which only use one-fifth of the subcutaneous dose, were authorized by European Medicines Agency as a temporary measure to use while the supply of the vaccine remains limited[18].

The most common side effects (in more than one in 10 vaccinees) associated with the administration of MVA-BN were injection site reactions (pain, redness, swelling, induration, itching) and systemic reactions such as muscle pain, headache, fatigue, nausea, myalgia and chills. Persons with atopic dermatitis may experience more intense local skin reactions and other general symptoms, as well as a flare-up or worsening of their skin condition[17].

Some recent studies have shown the concrete efficacy of the MVA-BN vaccine in protecting against MPX. According to a study conducted in the US, males who had not received the Jynneos vaccine were found to have an MPX incidence rate that was 14 times higher than those who had received at least one dose of the vaccine ≥ 14 days earlier[19]. Another recent report by The UK Health Security Agency stated that after receiving a single dose of the MVA-BN smallpox vaccine, an individual could expect to have around 78% protection against MPX 14 days after vaccination[20].

Vaccines in development

Neisseria gonorrhoeae

Gonorrhea infections are common worldwide, with an estimated global burden of 87 million new cases in 2016. As multidrug-resistant strains of *Neisseria gonorrhoeae* (*N. gonorrhoeae*) become more prevalent and new antibiotics are in short supply, the need for an effective vaccine has become urgent[3]. Currently, there

is no vaccine available that targets *N. gonorrhoeae* directly. The development of a *N. gonorrhoeae* vaccine has been challenging, as the bacterium has a high degree of genetic variability, which allows it to evade the immune system. Moreover, *N. gonorrhoeae* lacks stable surface proteins, which are targets for most vaccines. Thus, efforts to develop a gonorrhoea vaccine have faced several obstacles. Despite the intense innate inflammatory response that is the hallmark of *N. gonorrhoeae*, there is no naturally acquired immunity to the bacteria, making it difficult to predict which types of response might be protective[21]. There are four current vaccine approaches—(1) meningococcal and gonococcal outer membrane vesicles (OMV) vaccines that are intrinsic self-adjuvants; (2) purified protein subunit vaccines; (3) mixed OMV and protein subunit vaccines and (4) immunotherapeutic vaccines that utilize adjuvants to stimulate Th1-specific immune responses[22].

Promising vaccine candidates are currently being evaluated in murine infection models with different adjuvants and antigen-delivery systems. The evaluation of vaccine candidates has been challenging because no correlates of protection have been identified against *N. gonorrhoeae* in humans[22].

Optimism about the feasibility of gonococcal vaccine development has been recently revived because of accumulating observational data related to vaccines developed for preventing the disease from *N. meningitidis* group B (MenB). There is mounting evidence suggesting that the vaccine to prevent MenB provides some cross-protection against *N. gonorrhoeae*[1]. During a meningococcal outbreak between 2004 and 2006 in New Zealand, MeNZBTM was used, and there was a simultaneous decline in reported cases of gonorrhoea observed during and after its use. Fully vaccinated individuals aged 15–30 years had an adjusted vaccine effectiveness of 31% against *N. gonorrhoeae*[3,23]. The development of the recombinant protein-based 4CMenB (Bexsero®) vaccine is one of the more recent advances in the prevention of invasive meningococcal disease. In a retrospective study in Canada, after a group of individuals from 2 months to 20 years of age were vaccinated in 2014, there was a 59% decline in gonorrhea notifications among people aged 14-20 years was observed during the postvaccination period, suggesting the cross-protection of Bexsero® against *N. gonorrhoeae*[22].

Chlamydia trachomatis

Chlamydia is the most common bacterial STI worldwide[3]. The infections are caused by a range of serovars separated into two major and two minor complexes. Serovars A–C and Ba are major causes of trachoma, D–K, Da, Ia, Ja are linked to genital sexually transmitted diseases and L1–L3 are commonly associated with lymphogranuloma venereum. Vaccine development is ongoing, and the ultimate goal is to design vaccines that cover all of the most prevalent serovars[24].

The prospects for a chlamydia trachomatis (CT) vaccine are increasingly promising, primarily because the last years have seen the rapid development of new tools for Chlamydia research that will accelerate vaccine development. One of the major developments has been the long-awaited technology to genetically manipulate Chlamydia[21]. The major outer membrane protein (MOMP) has been identified as the ideal substitute for whole-cell antigenic targets. The first CT vaccine in clinical development (CTH522/CAF®01) induced neutralizing antibodies directed to the variable domain 4 regions of MOMP, covering predominantly B and intermediate groups of serovars[24]. Although intramuscular immunization has worked effectively for preventing cervical HPV infection, it is unclear whether a CT vaccine can be similarly administered to achieve protection, given the need for robust local T cell immunity. An effective CT vaccine may need to induce strong transmucosal immunity with resident memory T cells in the genital tract[23]. Several new candidate antigens (e.g., polymorphic membrane proteins) are emerging and are showing great promise in both mouse and primate models. It is likely that several candidate vaccines will enter phase I clinical trials in the next few years[21].

Human immunodeficiency virus (HIV)

Globally there were estimated to be 37.9 million PLWH at the end of 2018[23]. In addition, there were 1.7 million new infections with approximately 770,000 AIDS-related deaths in the same year despite the widespread rollout of antiretroviral therapy. The development of potent antiretroviral therapies has transformed HIV infection into a clinically manageable chronic disease. Globally, over 19 million people are now on life-long treatment, and test and treat strategies and oral preexposure prophylaxis (PrEP) could further reduce HIV transmission. However, despite these remarkable advances, prolonged combined antiretroviral therapy (cART) does not eradicate the virus, which often rapidly rebounds upon treatment interruption. In addition, while cART has decreased mortality and morbidity among PLWH, long-term cART treatment is associated with increased occurrence of

Table 1. Vaccines recommendations and dose schedules in the setting of STIs

Vaccine	Recommendations in the context of STIs	Vaccine schedule	References
HAV (Havrix®)	– MSM – Postexposure prophylaxis	Two doses (0 and 6 months-1 year)	28
HBV (Engerix-B®)	– Unvaccinated persons with a high-risk of infection • Multiple sex partners, MSM, HIV+, sex partner of infected person • Postexposure prophylaxis – Anti-Hbs < 10mIU/mL in vaccinated adults • HIV+; sex partners of HBsAg-positive persons	Three doses (0, 1, and 6 months)	2, 29
HPV (Gardasil®9)	– Recommended to all individuals ≤ 26 years-old – Shared clinical decision-making in adults 27-45 years old (e.g. MSM, HIV+, multiple sex partners)	9-14 years old-two doses (0 and 6-12 months) ≥ 15 years old-three doses (0, 2, and 6 months)	2, 29, 30
MPX (Imvanex®)	– MSM, women and transgenders that are on PrEP for HIV and diagnosis of ≥ 1 IST in the last 12 months – MSM living with HIV and diagnosis of ≥ 1 IST in the last 12 months – MSM and transgenders that are sex workers – MSM with severe immunosuppression – Postexposure prophylaxis	2 doses (0, > 28 days) If have been vaccinated against smallpox-one dose	31

a range of serious non-AIDS events. There is a broad scientific consensus that developing a preventive AIDS vaccine that is safe, effective, affordable, and globally accessible is the most effective strategy to control and ultimately eliminate the HIV epidemic. However, despite over three decades of rigorous HIV research and numerous vaccine trials, there is currently no licensed HIV vaccine available on the market[25]. The RV144 trial provided some hope by demonstrating modest but significant vaccine-induced protection (31.2% by 42 months) against HIV acquisition[26]. In the past 30 years, only a few HIV vaccine regimens have been tested in phase 2b clinical trials. Recently, there has been increasing support for adaptive clinical trials aimed at accelerating vaccine development by rapidly evaluating vaccine candidates in small human studies and swiftly advancing promising candidates to efficacy trials. This new accelerated approach has resulted in > 100 HIV vaccine concepts being clinically tested[25].

Herpes simplex virus

Genital herpes is the leading cause of genital ulcers in developed countries. Most cases of recurrent genital herpes are caused by HSV-2; however, an increasing proportion of anogenital herpetic infections have been attributed to HSV-1, which is especially prominent among young women and MSM[2]. HSV is known to establish latency, which makes vaccine development more challenging as an effective vaccine needs to not only prevent active clinical disease but also ideally prevent the virus from entering a latent state. Although there are no currently available vaccines for HSV-1 and 2, there are various candidates in both the preclinical and clinical phases currently in development. The development of the Shingrix® vaccine for herpes zoster and a vaccine for varicella zoster virus has stimulated efforts to develop a vaccine for HSV due to similarities between the two viruses, particularly with regard to their ability to establish latency. Vaccine development efforts are focused on two broad goals—preventative and therapeutic[27]. In recent years, five vaccine candidates have entered phase I/II testing, and several other candidates are currently in development. Most vaccines being tested in clinical trials are aimed at reducing genital herpes recurrences and shedding among individuals who are already infected with HSV-2, known as 'therapeutic vaccination', rather than preventing infection among those who are HSV seronegative[21]. A vaccine that could prevent genital HSV infection and work for both HSV-1 positive and negative individuals, given in adolescence or childhood, would be ideal. The most recent phase III trial for a prophylactic HSV vaccine tested a subunit glycoprotein D2 vaccine on 8,323 North American women who were seronegative for HSV-1 and HSV-2. The trial did not show efficacy against HSV-2 disease, but higher antibody levels of GD-2 were associated with increased efficacy against HSV-1 infection and disease, indicating the first immune correlates of protection against HSV[21,27].

Conclusion

The development of vaccines against STIs is a crucial priority for achieving sustainable global control of these diseases. Currently, effective vaccines are only available for four viral STIs, which include HAV, HBV, HPV and MPX. However, research efforts are ongoing to develop vaccines for other STIs, as they are considered the ultimate solution to the growing epidemic of STIs. The development of HSV vaccines has made significant progress, with multiple promising vaccine candidates in early clinical trials offering hope that an HSV vaccine is on the horizon. However, research on bacterial STIs must also be quickly implemented due to the increased risk of untreatable infections caused by drug resistance. Ensuring vaccine adherence is another important aspect that needs to be emphasized. Healthcare settings, especially those that provide services for STIs, should regularly advise and encourage adults who are at high-risk for STI infection to get vaccinated.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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