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Toward global prevention of sexually transmitted infections (STIs): The need for STI vaccines

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Abstract

An estimated 499 million curable sexually transmitted infections (STIs; gonorrhea, chlamydia, syphilis, and trichomoniasis) occurred globally in 2008. In addition, well over 500 million people are estimated to have a viral STI such as herpes simplex virus type 2 (HSV-2) or human papillomavirus (HPV) at any point in time. STIs result in a large global burden of sexual, reproductive, and maternal-child health consequences, including genital symptoms, pregnancy complications, cancer, infertility, and enhanced HIV transmission, as well as important psychosocial consequences and financial costs. STI control strategies based primarily on behavioral primary prevention and STI case management have had clear successes, but gains have not been universal. Current STI control is hampered or threatened by several behavioral, biological, and implementation challenges, including a large proportion of asymptomatic infections, lack of feasible diagnostic tests globally, antimicrobial resistance, repeat infections, and barriers to intervention access, availability, and scale-up. Vaccines against HPV and hepatitis B virus offer a new paradigm for STI control. Challenges to existing STI prevention efforts provide important reasons for working toward additional STI vaccines. We summarize the global epidemiology of STIs and STI-associated complications, examine challenges to existing STI prevention efforts, and discuss the need for new STI vaccines for future prevention efforts.

Keywords

Sexually transmitted diseases; Vaccines; Prevention and control

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Conflicts of Interest

We report no conflicts of interest.

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1. Introduction

Sexually transmitted infections (STIs) have a major impact on sexual and reproductive health worldwide. Although more than 30 identified pathogens are known to be transmitted sexually, eight of these have been clearly linked to the greatest amount of morbidity. Three bacterial STIs, *Chlamydia trachomatis* (chlamydia), *Neisseria gonorrhoeae* (gonorrhea), and *Treponema pallidum* (syphilis), and one parasitic STI, *Trichomonas vaginalis* (trichomoniasis), are currently curable. Four viral STIs, HIV, human papillomavirus (HPV), herpes simplex virus (HSV), and hepatitis B virus (HBV), can be chronic or lifelong, although medications can modify disease course or symptoms. This article focuses on STIs other than HIV.

STIs can cause genital symptoms affecting quality of life, important psychosocial consequences, and serious morbidity and mortality, through pregnancy complications, cancer, infertility, and enhanced HIV transmission. Controlling STIs is a core aspect of the World Health Organization's (WHO's) Global Strategy on Reproductive Health [1], and essential for achieving Millennium Development Goals 4 (child health), 5 (maternal health), and 6 (HIV prevention) [2]. However, STI control remains challenging in most settings, particularly in low- and middle-income countries where the health system infrastructure is least developed and the burden of STI-related complications is highest.

Safe and effective vaccines against two STIs have been major advances in global health. The first STI vaccine was developed over 30 years ago against HBV infection, which can be transmitted perinatally and parenterally as well as sexually [3]. HBV vaccine has now been adopted into infant immunization programs in 93% of countries and has already prevented an estimated 1.3 million deaths [4,5]. The second STI vaccine, against HPV, was developed recently and found to be highly efficacious in preventing infection with HPV types causing 70% of cervical cancers [6]. Countries achieving good HPV vaccination coverage have already observed marked benefits against proximal HPV-related outcomes such as genital warts [7,8].

Limitations of available prevention interventions for other STIs provide important reasons for working toward additional STI vaccines as well. The goal of this article is to summarize the global epidemiology of STIs and STI-associated complications, to examine challenges to existing interventions for STI control, and to discuss the need for new STI vaccines for future prevention efforts.

2. STIs: a global snapshot

WHO estimates that 499 million new cases of curable STIs occurred in 2008 among 15–49 year-olds globally: 106 million cases of chlamydia, 106 million cases of gonorrhea, 11 million cases of syphilis, and 276 million cases of trichomoniasis [9]. The prevalence of these infections at any point during 2008 was 360 million cases. STI numbers were high across all world regions, but incidence rates were highest in the WHO Region of the Americas and the WHO African Region (Fig. 1) [9]. Men and women were similarly likely to acquire new STIs, with a male to female ratio of 1.14 [9]. The number of new curable

STIs does not appear to be decreasing; the 2005 WHO estimate was 448 million cases [9,10].

Because viral STIs can be chronic, they comprise a large proportion of prevalent STIs. Approximately 291 million women have an HPV infection at any point in time [11], and it is likely that the numbers of HPV-infected men are similar [12,13]. HSV-2 infection, which is lifelong, affects an estimated 536 million people aged 15–49 years globally [14]. Approximately 360 million people suffer from chronic HBV infections, although most of these were acquired perinatally or in early childhood [3].

It should be noted that global estimates, especially for the curable STIs, have relied on the few regions with systematic STI surveillance along with a relatively small number of prevalence studies among discrete populations (n = 180, WHO 2008 estimates) [9]. Fewer data exist from areas with limited laboratory infrastructure. However, despite data limitations, it is clear that the number of global STIs is large: available estimates suggest that well over a million people acquire an STI every day [9,11,14].

Adolescents and young adults often have the highest rates of incident STIs and account for a disproportionate number of new infections [15]. However, transmission of STIs within populations is affected by a complex interplay of factors, including STI prevalence, which can vary markedly among populations or geographic areas. For example, HSV-2 seroprevalence ranges from 21% among 14–49 year-old women in the United States [16] to more than 80% among young women in parts of sub-Saharan Africa [17]. Chlamydia prevalence among pregnant women attending antenatal care is approximately 7% in sub-Saharan Africa [18], but as high as 25–30% in several Pacific Island countries [19]. In China, syphilis seroprevalence is less than 1% in the general population, but more than 12% among incarcerated female sex workers and almost 15% among men who have sex with men (MSM) [20].

3. STI consequences

STIs can have both short-term and long-term consequences across a broad spectrum of sexual, reproductive, and maternal-child health. The vast majority of STIs are asymptomatic or unrecognized; however, adverse outcomes can occur regardless of the presence of symptoms.

3.1. Genital symptoms

Although most STIs are asymptomatic, some cause genital symptoms that have an important impact on quality of life. Chlamydia, gonorrhea, and trichomoniasis can cause vaginal discharge syndromes in women and urethritis in men. Trichomoniasis, the most common curable STI globally [9], can cause profuse vaginal discharge and irritation. Genital HSV and syphilis infections can cause ulceration. Even if only 10–20% of infections of genital HSV infections are symptomatic [16], more than 50–100 million people around the world may suffer from painful recurrent genital ulceration [14]. HPV infection can cause genital warts, which are not painful but can be distressing and disfiguring [21]. Approximately 7% of women in the United States general population and over 10% of women in Nordic

countries report a history of a genital wart diagnosis [22,23]. Genital herpes ulceration and genital warts are more frequent and more severe among HIV-positive persons [24,25].

3.2. Pregnancy complications

All of the curable STIs have been linked with preterm labor, with associated risks to the neonate of pre-term birth, low birth weight, and death [26,27]. Active syphilis during pregnancy results in an estimated 215,000 stillbirths and fetal deaths, 90,000 neonatal deaths, 65,000 infants at increased risk of dying from prematurity or low birth weight, and 150,000 infants with congenital syphilis disease each year, almost all in low-income countries [28]. Chlamydia and gonorrhea infections during pregnancy can lead to neonatal eye infection (ophthalmia neonatorum), which was an important cause of blindness before the use of ocular prophylaxis [29]. Pneumonia can also occur in up to 10–20% of infants born to a mother with untreated chlamydial infection [30].

Perinatal transmission of HSV-2 infection is associated with high morbidity, including long-term neurologic sequelae, and mortality. In the United States, estimates of neonatal herpes incidence range from 1 in 3000 to 1 in 25,000 births; global data are lacking [31,32]. In areas of high HBV endemicity (e.g., East Asia), HBV is most commonly transmitted from mother to child at birth [3]. These infections lead to chronic HBV infection in 80–90% of cases [33].

3.3. Cancer

HPV and HBV are oncogenic. Infection with high-risk types of HPV is a necessary causal factor for cervical cancer [34], and can also cause anal, vulvar, vaginal, penile, and some oropharyngeal cancers. Worldwide, HPV infection results in 530,000 cases of cervical cancer and 275,000 cervical cancer deaths each year, with the vast majority of deaths (88%) occurring in resource-poor settings [35]. In some areas of the world, cervical cancer is the most common cancer and the main cause of cancer death among women. Among women in Eastern Africa, cervical cancer leads to more than twice as many deaths as the next most common cause, breast cancer [35].

Chronic infection with HBV can lead to liver cirrhosis and hepatocellular carcinoma, especially if acquired at birth. Mathematical models have estimated that approximately 600,000 people die from these adverse outcomes of HBV infection annually [36].

3.4. Upper genital tract disease

Chlamydia and gonorrhea can ascend to the upper genital tract in women and cause acute pelvic inflammatory disease (PID), tubal factor infertility, potentially fatal ectopic pregnancy, and chronic pelvic pain. Data on the global STI-related burden of these outcomes are limited. Based on prospective studies in high-income countries, about 10–15% of untreated chlamydia infections lead to clinical PID [37,38], and about 10–15% of clinical PID cases lead to tubal factor infertility [37,39]. Chlamydia can also lead to asymptomatic tubal infection and infertility, but the extent of this is unknown. The proportion of gonorrhea infections leading to PID and infertility may be even higher, especially in areas without access to early treatment [40]. As an estimated 95.5 million cases of chlamydia and

gonorrhea occurred among women in 2008 [9], the numbers of women with adverse reproductive outcomes could be sizable. Estimates of global infertility have ranged from 45 million to 186 million couples unable to have a child over 5 years [41,42]. The proportion of infertility that is primarily caused by scarring from genital infection varies by population. In the United States, the proportion of infertility that is tubal factor ranges from 10–40% [43,44]. However, in sub-Saharan Africa, tubal infertility may be the cause of up to 85% of infertility [45].

3.5. Increased HIV risk

Several STIs increase the risk of both acquiring and transmitting HIV. A large body of literature demonstrates that people with HSV-2 infection have a three-fold increased risk of acquiring HIV infection [46]. Further, HIV- and HSV-2-co-infected persons have higher HIV viral loads and are more likely to transmit HIV infection [47,48]. Both ulcerative (syphilis) and inflammatory (chlamydia, gonorrhea, trichomoniasis) curable STIs may also be associated with an increased risk of HIV acquisition, by up to two- to threefold [49,50]. These infections are linked to increased infectiousness among HIV-infected persons; urethritis and cervicitis substantially increase genital HIV shedding [51,52]. HPV might also increase the risk of HIV acquisition [53].

3.6. Psychosocial consequences

In addition to their physical consequences, STIs can have a profound psychosocial impact that is often difficult to quantify. Studies have shown that an STI diagnosis can lead to feelings of stigma, shame, and diminished self-worth, as well as anxiety about sexual relationships and future reproductive health [54–56]. STIs also have an effect on sexual relationships, and can lead to disruption of partnerships and intimate partner violence [55,57].

3.7. Human and financial costs

In the recent Global Burden of Disease Study, curable STIs accounted for almost 11 million disability-adjusted life years (DALYs) lost in 2010: syphilis, 9.6 million DALYs; chlamydia, 714,000 DALYs; gonorrhea, 282,000 DALYS; and trichomoniasis, 167,000 DALYs [58]. HPV-related cervical cancer accounted for another 6.4 million DALYs lost. The 2010 disease burden study did not calculate DALY estimates for HSV-2, which could be substantial given the role of HSV-2 in HIV transmission. Further, study authors have not yet published the specific methods used to calculate DALYs for STIs; global burden estimates have been limited by a paucity of precise data on STI-related complications, especially from low-income settings [59].

STIs also pose a substantial economic burden. In the United States, approximately $3 billion in direct medical costs were spent in 2008 to diagnose and treat 19.7 million cases of STIs and their complications, excluding HIV and pregnancy-related outcomes like stillbirth [60]. The costs associated with adverse STI outcomes are less well documented in resource-poor settings.

4. Challenges to available interventions for STI prevention and control

The public health approach to STI control revolves around two main strategies: behavioral and biomedical primary prevention, to prevent STI acquisition among uninfected people, and STI case management, to diagnose and manage infected people to prevent STI complications (secondary prevention) and ongoing transmission (Fig. 2) [61]. Behavioral primary prevention includes comprehensive sex education, risk-reduction counseling, and condom promotion and provision. The main biomedical STI primary prevention interventions are HPV and HBV vaccines. STI case management involves STI diagnosis, provision of effective treatment, notification and treatment of sex partners, and safer sex counseling and condom provision [61]. STI case management can apply to both symptomatic and asymptomatic people. However, in most settings, STI case management is limited to symptomatic people seeking STI care. In addition, because of a lack of laboratory infrastructure, most low- and middle-income countries rely on syndromic management: the use of genital symptom algorithms to guide treatment, without diagnostic tests [61,62]. Where tests are available, affordable, and feasible, they may be used to diagnose symptomatic infections or screen for asymptomatic infections. Several high-income countries recommend screening young women annually for chlamydia, based on evidence that screening reduces the risk of PID [38,63]. Screening pregnant women for syphilis is recommended in virtually all countries [64].

Several reviews have summarized the efficacy of individual STI prevention interventions [65–68]. Implementation of STI control programs requires not only providing availability and access to these interventions, but also ensuring effective scale-up and sustainability for maximal population impact. The public health approach to STI control has had clear successes, for example, syphilis and gonorrhea infections have decreased dramatically among general populations of several countries with ample resources for STI control [69,70]. However, the gains have not been universal across all infections and all settings. Several important behavioral, biological, and implementation factors influence the potential prevention impact of available interventions (Fig. 2), and are discussed below.

4.1. Behavioral and sexual network factors

Several factors can influence the effectiveness of behavioral primary prevention efforts. Consistent and correct condom use reduces the transmission risk of virtually every STI [65], and some countries have documented declines in STI incidence in concert with implementation of counseling promoting condom use [71]. However, there have been limits to how much progress has been made with condom promotion as the main primary prevention measure for most STIs, especially among young people. Cultural factors impact not only the acceptability of condom use, but also the comfort level with discussing sexual practices and the gender and number of partners and providing STI-related education. In addition, although several randomized trials have demonstrated that behavioral interventions can reduce STI acquisition, none of these assessed sustainability of behavior change past one year [68], which is a key factor in determining long-term impact [72]. Finally, sexual networks reflect how individuals in a population are linked through sexual relationships and thus the pathways through which STIs can be transmitted. In many populations, individual

behavior may be less important than network risk, that is, the risk of the individual's sex partner or STI prevalence in the community [16,72].

4.2. Asymptomatic and long-lasting infection

The vast majority of STIs cause few or no symptoms but can still lead to harmful reproductive sequelae, especially among women. Thus, the standard STI control approach based on symptomatic case management misses the greatest burden of STIs from the outset. Even when STI symptoms occur, they may be nonspecific, which affects syndromic diagnosis. While syndromic management can be more accurate for syndromes such as urethral discharge in men, it performs poorly for nonspecific syndromes like vaginal discharge [73].

STIs that are likely to be symptomatic soon after acquisition, e.g., gonorrhea in men, tend to be treated quickly in areas with quality health services. These infections are removed from the population and transmission is sustained only among groups in which high-risk sexual behaviors are common [69,70]. Infections that are more likely to be asymptomatic and of longer duration may spread more generally through the population, e.g., chlamydia and HPV infections, which can persist without symptoms for a year or more [74,75], and HSV-2 infections, which are lifelong and mostly unrecognized [76]. For these infections, prevention strategies that only partially reduce transmission may have more limited impact at the population level.

4.3. Antimicrobial resistance and treatment barriers

Several efficacious medications exist to treat STIs [65]. However, drug resistance, especially for gonorrhea, is a major threat to STI control globally. Third-generation cephalosporins are the last class of antimicrobials to which <5% of gonorrheal isolates are resistant worldwide, but resistant strains are being increasingly reported [77–79]. Nitroimidazoles are the only class of antimicrobials active against trichomoniasis, and low-level resistance is also on the rise [80,81]. Tetracyclines and macrolides can be used to treat chlamydia, but treatment failures with both have been observed in approximately 10% of cases [82]. In low-income countries, insecure supplies of essential drugs, use of ineffective alternative medications, and treatment in informal settings, such as by drug vendors or traditional healers, all contribute to antimicrobial resistance and hamper STI control efforts.

4.4. Repeat infections

Curable STIs do not result in strong, lasting protective immunity after natural infection. While protective immunity may exist for some infections [83,84], it is easily overcome, and repeat infections are common [85,86]. Repeat infection rates for chlamydia, gonorrhea, and trichomoniasis range from 10–20% after treatment of an initial infection [85,86]. Repeat infection is even more common when little attention is paid to notification and treatment of sex partners of infected patients. Partner management strategies have proven challenging in most settings, especially if resources are limited or partner information is unknown. Data are particularly limited on ways to improve the numbers of partners treated in resource-poor settings [66].

4.5. Health system and implementation factors

Some key challenges exist related to effective implementation of STI control strategies. STIs are often stigmatizing and, in the setting of competing priorities, have often received little public policy attention [66]. These issues are compounded by the fact that many existing STI interventions are either not fully effective by themselves or it has been difficult to directly quantify their impact, making it harder to garner support.

Lack of availability and access to effective interventions hinders STI control in much of the world. Without an effective primary prevention tool such as a vaccine, or a feasible point-of-care diagnostic test with on-site curative treatment and a platform to access large numbers of infected persons, implementation of STI prevention remains challenging. This is especially true in resource-poor settings, where both health infrastructure and care-seeking may be sub-optimal. For example, prior to HPV vaccine, the use of Pap test screening with treatment of cervical cancer precursors dramatically reduced cervical cancer cases and deaths in high-income countries. However, in lower-income countries, without the infrastructure needed for Pap screening, HPV-related cervical cancer remains a major public health problem [35].

For STI case management, availability and access to feasible, affordable diagnostic tests is crucial. New accurate point-of-care diagnostic tests for syphilis are now available and are cheap, easy to use, and make syphilis screening of antenatal and high-risk populations possible even in remote settings [87]. Rapid diagnostic tests for chlamydia, gonorrhea, and trichomoniasis may also be on the horizon [87]. However, availability of accurate tests and other interventions alone does not ensure effective implementation and control [61,88,89]. In addition to needing a platform to access infected persons, it takes commitment, resources, and mechanisms for scale-up, to ensure broad intervention coverage and uptake, steady procurement of supplies, and ongoing sustainability of implementation efforts [61].

5. Needs for the future: working toward new STI vaccines

Vaccines have the potential to overcome many behavioral, biological, and implementation barriers to reducing global STI burden. Here we outline the case for the major new targets for STI vaccine development.

5.1. HSV-2

The large numbers of HSV-2 infections globally [14] are extremely important because of the marked synergy between HSV-2 and HIV infections. In some areas, HSV-2 infection may account for up to 30–50% of new HIV infections [46,90]. Antiviral medications treat HSV-2 symptoms and decrease HSV and HIV genital shedding; however, current regimens do not prevent HIV acquisition or transmission [47,91]. Thus, primary prevention of HSV-2 infection is currently the only way to reduce the excess risk of HIV infection related to HSV-2.

Available primary prevention strategies for HSV-2, such as condom use, use of daily suppressive therapy by symptomatic partners, and medical male circumcision may be useful for individuals. However, efficacy of these interventions ranges from only 30–50% [16,92,93], and interventions like widespread serologic testing and suppressive antiviral

therapy are costly and unlikely to be feasible on a large scale. Given mostly asymptomatic, lifelong HSV infection, with widespread transmission in the general population and lack of curative therapy, existing interventions are unlikely to provide broad population impact, and vaccines may be the only option for effective HSV control [76].

Recently, a tenofovir-containing microbicide gel halved the risk of HSV-2 acquisition in one clinical trial; additional trials are ongoing [94]. However, issues related to compliance and acceptability [95], and concerns about HIV resistance with antiretroviral-containing microbicides, remain barriers. A vaccine against HSV-2 infection could have a dramatic impact on HIV spread [96], in addition to preventing neonatal herpes and alleviating suffering associated with genital herpes symptoms, and is a critical need for global public health [97].

5.2. Chlamydia

The global burden of chlamydia-related PID, infertility, ectopic pregnancy, and pregnancy complications has yet to be quantified accurately but is likely very high. In low-income countries without laboratory infrastructure, most chlamydia infections are missed with current control strategies. New rapid diagnostic tests that can be used in remote settings may soon be available, but decisions about whether to screen for asymptomatic infection, among whom, and at what costs will not be completely straightforward [98].

Chlamydia screening programs have been difficult to bring to scale in high-income countries. Even in countries with longstanding chlamydia screening recommendations, the proportion of women screened regularly remains low [89,99]. Although these programs have likely contributed to reductions in PID incidence, their impact on chlamydia incidence is unclear, and they do not appear to have dramatically reduced chlamydia prevalence [88,99]. In addition, while it is clear that screening can reduce clinical PID, the effect of screening on infertility prevention has not been directly assessed, and it is unknown the degree to which some tubal damage has already occurred at the time of screening.

One of the main reasons for ongoing chlamydia transmission is the frequency of repeat infections [85,86]. It has been hypothesized that screening programs might make repeat infections more likely, through reductions in population-wide protective immunity [100]. This is a major concern because animal models show greater tissue destruction during repeat chlamydial infection compared with initial infection, although it is not clear whether repeat infections after screening are inherently more harmful in humans [101].

Improving partner treatment strategies to reduce repeat infections, continued broadening of chlamydia screening coverage where available, and validation of new chlamydia rapid tests are absolutely essential. However, the difficulties in program implementation and reduction of chlamydia prevalence in existing screening programs highlight the complexities of current chlamydia control efforts and the need for continued work toward an effective chlamydia vaccine [102].

5.3. Gonorrhea

Gonorrhea is an STI for which effectively implemented public health control strategies can reduce the burden of infection [69,70]. However, gonorrhea prevention is being threatened by the increasing prevalence of organisms with resistance to cephalosporins, the only class of first-line drugs recommended to treat gonorrhea [77,79]. Given that 106 million cases of gonorrhea occur each year [9], millions could be left at risk of developing gonorrhea-associated PID, infertility, ectopic pregnancy, pregnancy-related complications, and enhancement of HIV transmission.

Rapid development and evaluation of new antibiotics for the treatment of gonorrhea are critical, and two clinical trials of new regimens are ongoing [78]. However, *N. gonorrhoeae* has successively acquired resistance to four different classes of antibiotics since it was first treatable in the 1940s [78], and the rate of development of resistance appears to be increasing. While efforts are made to find new effective drug regimens for gonorrhea, to improve diagnostic capacity for gonorrhea in low-income settings, and to scale-up existing case management strategies, progress toward a gonorrhea vaccine is also urgently needed [103].

5.4. Trichomoniasis

More cases of trichomoniasis are estimated to occur each year than gonorrhea, chlamydia, and syphilis cases combined [9]. Genital symptoms, especially vaginal discharge and irritation, may have important adverse effects on quality of life. Trichomoniasis is also associated with more serious consequences, including preterm delivery among pregnant women and enhancement of HIV transmission. A lack of available diagnostic tests hampers control efforts globally, but especially in low-income countries. Although not yet at the same level of urgency as for gonorrhea, reports of low-level trichomonal antimicrobial resistance are worrisome, as just one drug class treats trichomoniasis [65]. Additional drug regimens and diagnostic tests for trichomoniasis should be pursued, while continued work is done toward developing trichomoniasis vaccines [104].

5.5. Syphilis

Among the curable STIs, syphilis has the lowest global incidence but accounts for the greatest number of DALYs lost [58], primarily related to the devastating consequences of mother-to-child transmission [28]. More than half a million adverse outcomes of syphilis in pregnancy are estimated to occur each year [28]. Congenital syphilis has been virtually eliminated as a public health problem in most high-income countries [69,70]. However, only about 30% of infected pregnant women in sub-Saharan Africa receive syphilis testing and treatment [28,87]. New point-of-care diagnostic tests, cheap curative treatment with one dose of penicillin, and an ante-natal platform to access infected pregnant women may now make it feasible to prevent a substantial proportion of congenital syphilis outcomes [64,105], and WHO has launched an initiative to eliminate congenital syphilis as a global public health problem [64]. However, if implementation remains challenging and prevention efforts do little to reduce community-wide prevalence, a syphilis vaccine will be an important pursuit [106].

5.6. Implementation of STI vaccines

HPV vaccination has not yet been implemented in low- and middle-income countries with the highest cervical cancer rates. Mathematical models estimate that if 70% vaccination coverage is achieved in low- and middle-income countries, HPV vaccines could prevent the deaths of more than 4 million women vaccinated over the next decade [107]. The GAVI Alliance has approved initial funding for HPV vaccination in eligible low-income countries, which is a major step toward ensuring universal access to HPV vaccine. However, the barriers related to providing a vaccine in early adolescence are even greater than those of including HBV vaccine in the infant immunization schedule. Barriers include difficulties accessing 11–14-year-olds in areas where health-care seeking and school attendance may be low, and parental or societal hesitation related to a vaccine against STIs for adolescents.

A great deal will be learned from current implementation of HPV vaccine to inform delivery of future STI vaccines. Most STI vaccines are being developed for early adolescents, to provide maximal protection before and during the time of highest risk. For some vaccines, there may be compelling reasons for infant vaccination in addition to implementation issues, for example, an HSV vaccine that would also protect against HSV-1 infection. Nonetheless, new adolescent platforms for health intervention delivery are needed to respond to a global agenda to improve adolescent health, especially sexual and reproductive health [108]. HPV vaccine implementation is an opportunity to develop these adolescent platforms, which can be used not only for currently recommended prevention services, but also for future STI vaccines. Given common risk factors, high rates of co-infection, and epidemiologic overlap in STI-related complications, combination STI vaccines for adolescents would be an important future goal. HPV vaccine implementation will also provide insight on monitoring vaccine impact, which will need to be considered for other STI vaccines well in advance of vaccine availability.

6. Conclusion

In the face of almost half a billion curable STIs occurring annually[9], more than half a billion people with a viral STI at any point in time [11,14], and the resulting burden of STI-related complications affecting sexual, reproductive, and maternal-child health, new prevention paradigms are needed. Existing STI prevention interventions can be optimally scaled up within a broad framework of health promotion and wellness, with normalization and integration of STI services into primary and reproductive healthcare settings. This includes strengthening sexual health education and condom promotion, optimizing STI diagnosis and screening where available, implementing effective partner treatment strategies, ensuring syphilis testing for all pregnant women, and broadening delivery of HPV vaccine. At the same time, given the unique obstacles to achieving global STI control for most existing interventions, innovative biomedical solutions are also critical. Validating new rapid diagnostic tests for curable STIs, evaluating new drug regimens for gonorrhea, and testing new microbicides against STIs will be extremely valuable, but these interventions may not fully solve long-term barriers to STI control. Thus, continued advancement of STI vaccines is crucial for sustainable global STI prevention and control.

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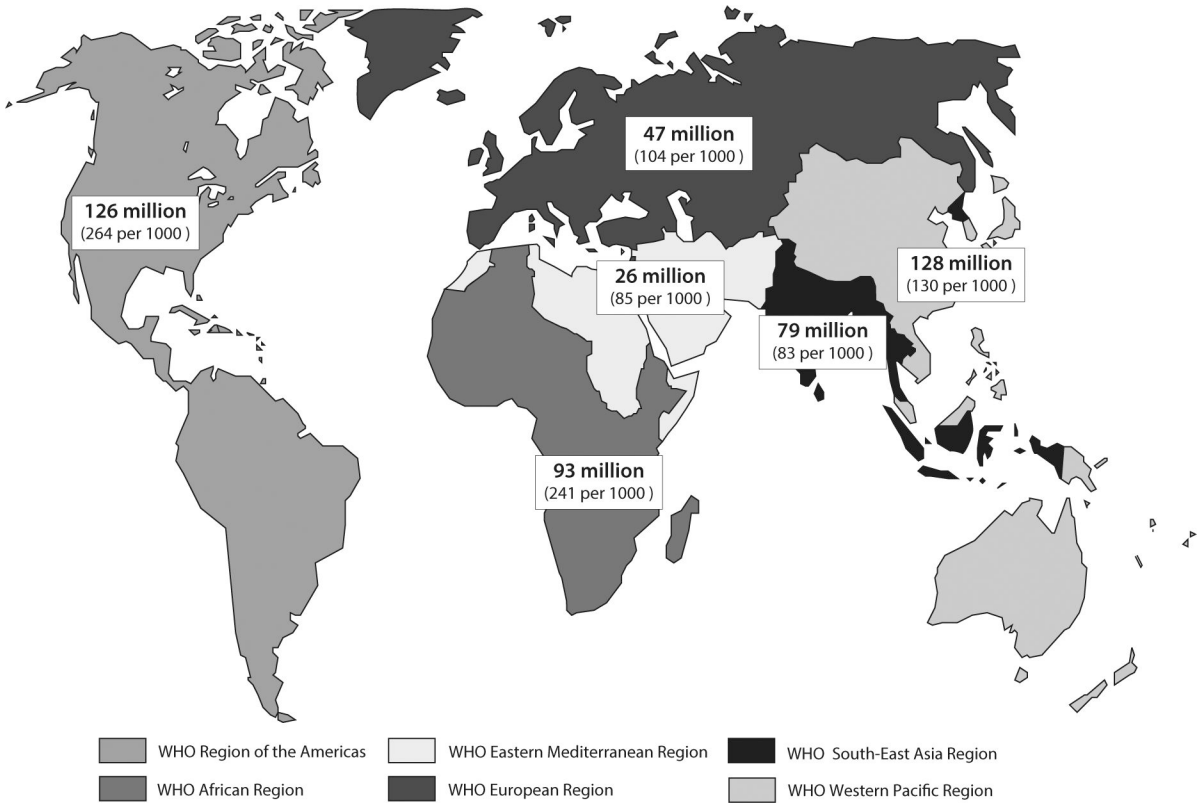

Fig. 1.

Estimated numbers of new cases and incidence rates per 1000 population of curable sexually transmitted infections (gonorrhea, chlamydia, syphilis, and trichomoniasis) among 15–49 year-olds by WHO region, 2008 [9].

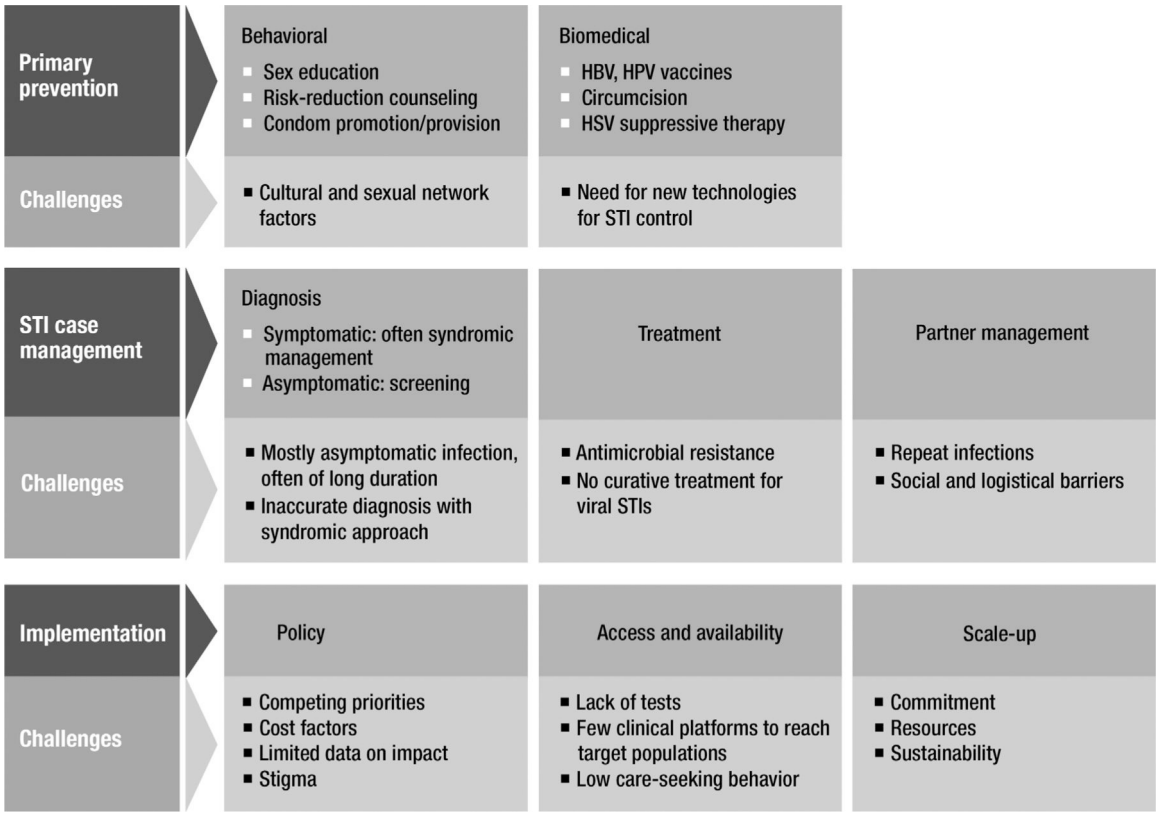

Fig. 2.

Key interventions and challenges for sexually transmitted infection prevention and control.