

STIs: LARGE BURDEN AND SERIOUS CONSEQUENCES

KEY POINTS FOR ACTION

- Scale-up of effective STI-prevention services

- ▶ STI case management and counselling
- ▶ Syphilis testing and treatment of all pregnant women
- ▶ Delivery of HPV vaccination

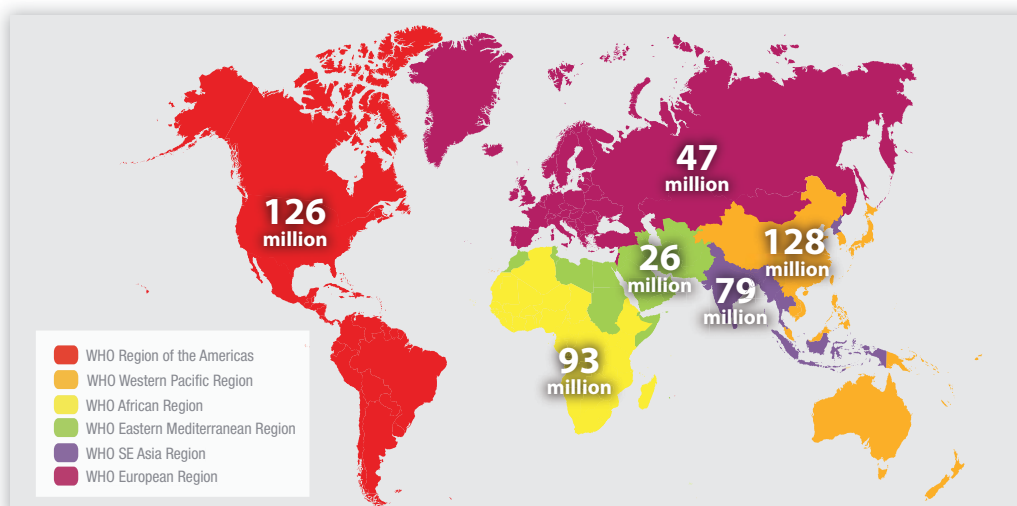
- Promotion of strategies to enhance STI-prevention impact

- ▶ Integration of STI services into existing health systems
- ▶ Advocacy to fight the stigma of STIs
- ▶ Measurement of STI burden

- Support for new technology development for STI prevention

- ▶ STI rapid diagnostic tests
- ▶ Additional drugs for gonorrhoea
- ▶ STI vaccines and other biomedical interventions

- More than a million people acquire a sexually transmitted infection (STI) every day:
 - ▶ an estimated **499 million new cases of curable STIs** (gonorrhoea, chlamydia, syphilis and trichomoniasis) occur every year
 - ▶ in addition, **536 million people** are estimated to be living with incurable herpes simplex virus type 2 (HSV-2) infection
 - ▶ approximately **291 million women** have a human papillomavirus (HPV) infection at any given point in time
 - ▶ the burden of STIs is greatest in low-income countries.



Estimated new cases of curable STIs (gonorrhoea, chlamydia, syphilis and trichomoniasis) by WHO region, 2008

Source: WHO, <http://www.who.int/reproductivehealth/publications/rts/stisestimates/en/index.html>

- The consequences of STIs have a profound impact on sexual and reproductive health:
 - ▶ **fetal and neonatal deaths:** syphilis in pregnancy leads to **305 000 fetal and neonatal deaths**, and leaves 215 000 infants at increased risk of dying from prematurity, low birth weight or congenital disease each year.
 - ▶ **cervical cancer:** HPV infection causes an estimated **530 000 cases of cervical cancer** and 275 000 cervical cancer deaths each year
 - ▶ **infertility:** STIs such as gonorrhoea and chlamydia are an important cause of infertility; in sub-Saharan Africa, untreated genital infection may be the cause of **up to 85% of infertility** among women seeking infertility care
 - ▶ **HIV risk:** having an STI such as syphilis or HSV-2 infection increases the chances of acquiring **HIV infection by three-fold** or more.
- In addition, the direct physical, psychological and social consequences of STIs have a major impact on quality of life and are a prime indicator of the quality of global sexual and reproductive health care.

LITTLE PROGRESS IN REDUCING THE GLOBAL BURDEN OF STIs

Despite the availability of several simple, cheap and cost-effective interventions to combat STIs, little progress has been made. An estimated 499 million new cases of curable STIs occurred in 2008, suggesting no improvement over the 2005 estimate of 448 million cases. STIs other than HIV have been overshadowed in recent years by the heightened public-health focus on HIV treatment, despite the strong association between STIs and HIV acquisition. In addition, stigmatization of sexual health issues has led to lack of political will and neglect of STI services in many countries. Many high-income countries have developed quality services for diagnosis and treatment of STIs. Low- and middle-income countries lag far behind. Yet, with renewed energy and commitment, opportunities are available to jump-start STI-control efforts in low- and middle-income countries and integrate STI care into existing primary health-care, reproductive-health and HIV services. This document provides public health programme managers, health policy-makers, and public health organizations with evidence-based information about STI burden, strategic areas of focus and potential new tools for STI prevention and control.

PROGRESS CAN BE MADE: TOOLS FOR PREVENTION OF STIs

Most STI-prevention tools and interventions have been available for years, but the extent of their use in resource-limited settings varies and is dependent on a number of facilitators and barriers.

STI case management

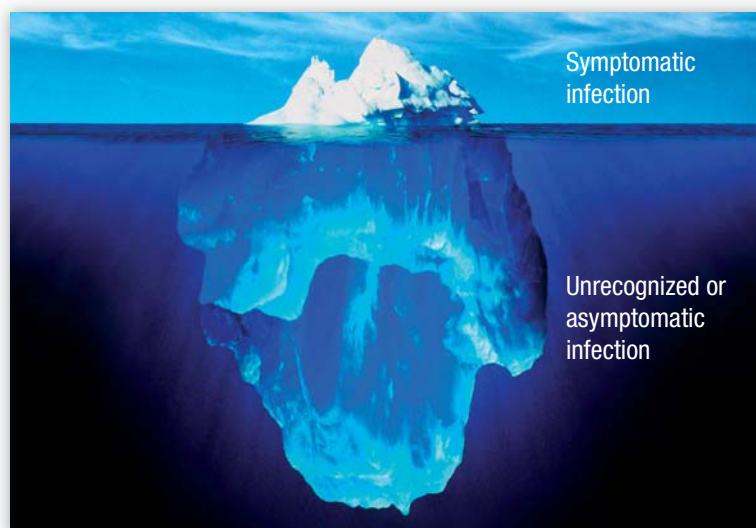
STI control in low- and middle-income countries has been shaped by clinical case management guidelines promoting syndromic management. This approach uses algorithms based on groups of genital symptoms to guide STI treatment for people seeking care, without the use of laboratory tests.

Syndromic management is simple, assures rapid, same-day treatment, and avoids the expensive diagnostic tests that are often unavailable in resource-limited settings. Syndromic management is accurate and cost-effective for the syndrome of urethral discharge.

However, it may perform less well for other syndromes. The approach to vaginal discharge, in particular, is very poor for predicting STIs. This can lead to overtreatment and a false STI diagnosis, with its attendant social implications.

Most important, syndromic management misses asymptomatic infections, which are by far the greatest burden of disease. The vast majority of chlamydia and gonorrhoea infections have few or no symptoms, yet these infections can still lead to serious complications, including pelvic inflammatory disease, ectopic pregnancy and infertility.

An important component of STI case management is notifying and treating sexual partners of infected patients. This is an efficient way to find STI cases and can prevent patient reinfection and STI transmission to new partners. In many countries, partner-notification strategies have not been widely implemented to date.



Symptomatic sexually transmitted infections are just the “tip of the iceberg”

Counselling and behavioural interventions

Counselling and behavioural interventions offer primary prevention against STIs including HIV, as well as unintended pregnancies. These interventions can be incorporated into many different settings and include comprehensive sex education, safer sex/risk-reduction counselling, condom promotion and provision, and targeted interventions for high-risk and vulnerable populations, such as adolescents, sex workers, and men who have sex with men. In addition, counselling can aim to improve STI symptom recognition and care-seeking. These interventions are available, but lack of awareness and training, discomfort with discussing sexual health issues, and stigma related to STIs remain barriers to their use.

Diagnostic tests

Multiple accurate diagnostic tests for STIs exist and are widely used in high-income countries, for both diagnosis and screening for asymptomatic infection. However, in low- and middle-income countries, there is inadequate infrastructure to allow standard laboratory testing in most settings. Even when testing is available, it is often expensive, may not be accessible to many people, and the time delay in receiving results may be too long, leading to loss to follow-up.

Accurate rapid, point-of-care diagnostic tests for syphilis are now available. They are cheap, provide results in 15–20 minutes, and are easy to use with minimal training. These rapid syphilis diagnostic tests are used in some resource-limited settings, but not enough. Barriers include lack of awareness and training, and lack of a reliable source of funding for procurement. Rapid diagnostic tests for STIs other than syphilis are not currently available.

Vaccines and other biomedical interventions

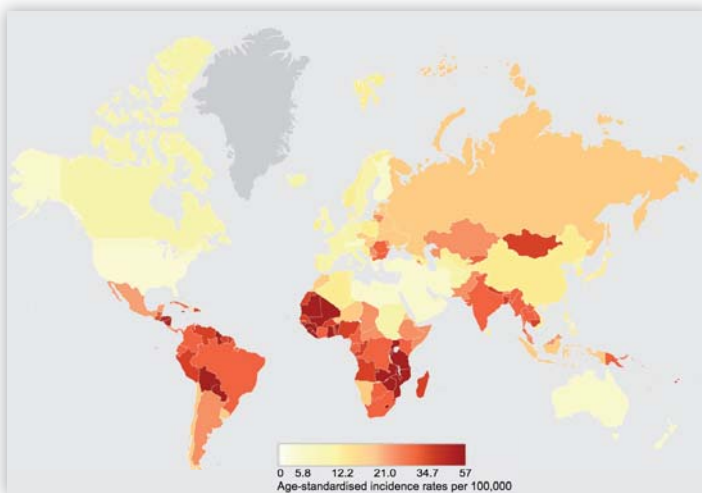
Two relatively new HPV vaccines are safe and very efficacious against HPV types causing 70% of cervical cancers; one vaccine also prevents genital warts. HPV vaccination has been successfully implemented in several high-income countries, and benefits in reducing HPV-related disease have already been demonstrated in areas with high vaccine coverage. However, HPV vaccination has not yet been implemented in most low- and middle-income countries, which are the countries with the highest cervical cancer rates. HPV vaccines are given during early adolescence and vaccination programmes for HPV may be harder to implement than those for immunization of infants. Additional barriers may include the three-dose regimen, high start-up costs, and public discomfort related to a vaccine against STIs that is given to adolescents.

Antimicrobial treatment

Effective treatment is currently available for several STIs; however, the emergence of drug-resistant organisms, especially gonorrhoea, may undermine STI control in some settings. Antimicrobial resistance to cephalosporins, the last available class of first-line drugs that are effective against gonorrhoea, is being increasingly reported.

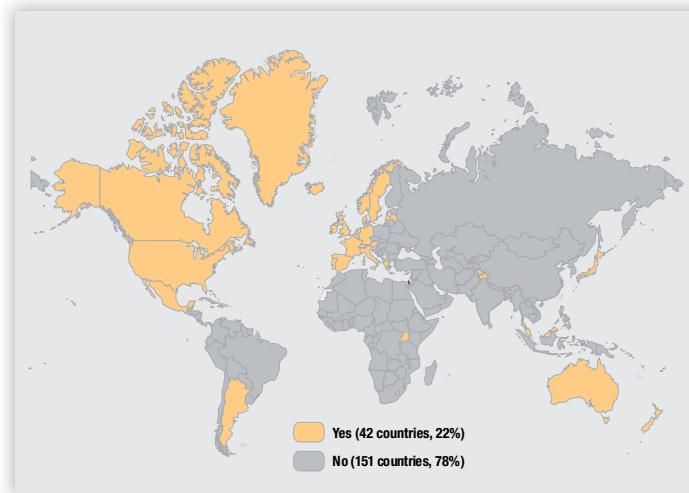
Barriers to treatment include cost, lack of patient compliance with multidose regimens, and difficulties with administering injectable medications.

Many facilities in low-income countries also face challenges in procuring and managing drugs to treat STIs, and STI treatment is often accessed outside of traditional clinical settings.



Estimated cervical cancer incidence worldwide, 2008

Source: GLOBOCAN 2008, International Agency for Research on Cancer, http://globocan.iarc.fr/cervix_uteri_fact_sheet



Countries using HPV vaccine in national immunization schedule, 2011

Source: WHO, *New and Under-utilized Vaccines Implementation (NUVI)*, http://www.who.int/nuvi/hpv/decision_implementation/en/index.html

Hepatitis B vaccine is safe and effective and has been universally recommended by the World Health Organization (WHO) since 1992. Over 90% of countries have now introduced hepatitis B vaccination into their national infant immunization programmes, and the majority of these countries have already achieved over 90% vaccine coverage. No other STI vaccines are currently available aside from HPV and hepatitis B vaccines.

With respect to other biomedical interventions, adult male circumcision not only substantially reduces the risk of heterosexual HIV acquisition, but also provides some protection against other STIs, such as HSV-2 and HPV. No additional biomedical interventions, including microbicides, are currently available for STI prevention.

OPPORTUNITIES FOR ENHANCED GLOBAL PREVENTION AND CONTROL OF STIs

Many opportunities are now available for:

- scale-up of existing simple, effective and cost-effective STI-prevention services
- strategies to enhance the impact of STI-prevention efforts.

Scale-up of existing STI services

Case management and counselling: syndromic management, partner notification and treatment, education and condom promotion

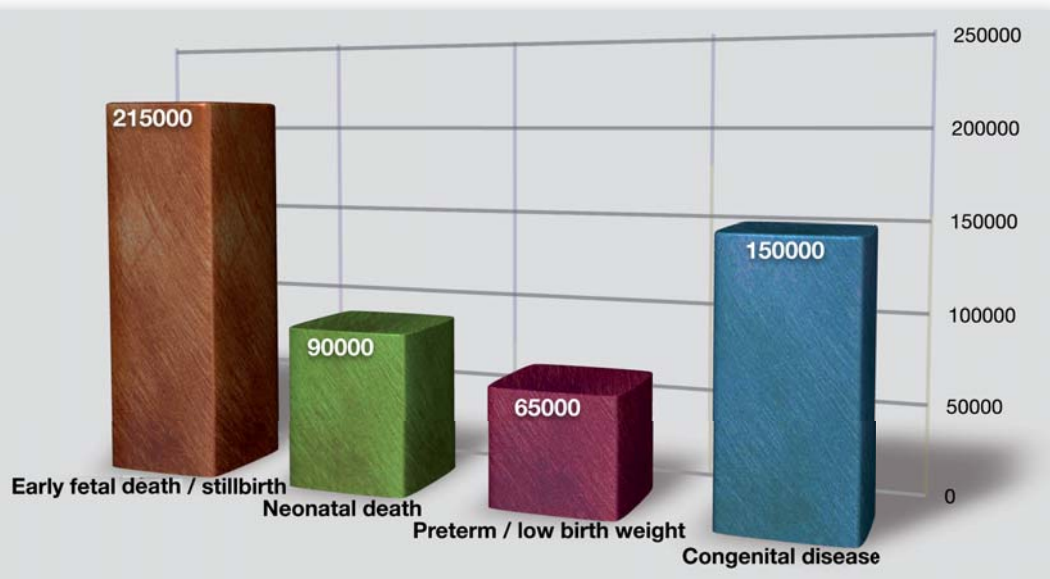
Opportunities exist to scale up integration of available STI clinical services into primary health-care, reproductive-health and HIV-care settings. Improved management of STIs, along with condom promotion, will not only help alleviate the physical and psychosocial suffering associated with STI symptoms and complications, but may also be a cost-effective HIV-prevention measure. This will involve updating and disseminating STI clinical management guidelines and training health-care personnel about syndromic management, which, in the absence of diagnostic tests, is the best available approach to combating STI transmission.

Resources are needed to ensure that partner notification and treatment is implemented as an integral part of STI case management. Further, new work is needed to determine the most efficient and effective ways of ensuring treatment of sexual partners and reducing barriers such as partner violence. Modelling work is increasingly showing that strategies for partner notification and treatment are critical for STI control in a population.

Continued scale-up of health education and counselling about STI risk reduction, condom promotion and provision, and STI symptom recognition are also essential components of STI care and prevention, especially for adolescents and other vulnerable or high-risk populations. WHO has estimated unsafe sexual intercourse to be the second most important global risk factor to health.

Syphilis testing and treatment of pregnant women

Renewed efforts are needed to ensure scale-up of syphilis testing and treatment for all pregnant women in high-burden countries.



Global estimates of adverse outcomes of syphilis in pregnancy, 2008

Source: Newman L, Kamb M, Hawkes S, et al. PLoS Med 2013;10(2):e1001396.

“Congenital syphilis is a neglected public health problem, despite the fact that it is easily preventable and treatable.”

Congenital syphilis is a neglected public health problem, despite the fact that it is easily preventable and treatable. Rapid, point-of-care testing for syphilis can be easily performed in primary care and antenatal care settings, and a single cheap, curative dose of penicillin can prevent congenital syphilis. WHO is coordinating a global initiative to eliminate congenital syphilis, and most countries have antenatal syphilis screening policies in place. However, implementation remains poor; only about 30% of pregnant women with syphilis in sub-Saharan Africa receive testing and treatment.

Syphilis testing and treatment efforts will involve increasing awareness about congenital syphilis among health-care providers and pregnant women, integrating rapid syphilis testing into the basic antenatal care package, and strengthening health systems to ensure adequate resources for screening and treatment. Given its minimal incremental prevention cost, rapid syphilis testing can and should be easily integrated into programmes to prevent the mother-to-child transmission of HIV infection.

Delivery of human papillomavirus vaccine

HPV vaccines could prevent the deaths of more than 4 million women vaccinated over the next decade in low- and middle-income countries if 70% vaccination coverage can be achieved. WHO recommends HPV vaccination as part of a comprehensive strategy to prevent HPV-related disease, and the GAVI Alliance has committed to funding initial HPV vaccination efforts in GAVI-eligible countries. HPV vaccine is especially important for women in countries where there is little or no access to cervical cancer screening and treatment methods; 88% of cervical cancer deaths occur in these countries. This inequity can be eliminated with effective implementation of HPV vaccination.

HPV vaccine implementation will require strong and consistent commitment to overcome potential barriers, such as difficulties in providing a vaccine to 11–14-year-old girls in areas where health-care seeking and school attendance may be low. Integrating HPV vaccine delivery with other recommended prevention services for early adolescents, such as comprehensive sex education, is an important strategy to evaluate.

Strategies to enhance the impact of STI-prevention efforts

Integration with existing services

Basic, quality, confidential STI services need to be integrated into existing primary health-care, reproductive-health and HIV-care settings. In low-income countries, STIs and their complications are one of the top five reasons that adults seek health care. Integration will not only maximally benefit patients seeking quality care for STI-related symptoms, but will also provide the most efficient and cost-effective avenue for scaling up STI-prevention efforts.

Innovative strategies to link health services can optimize STI-prevention efforts for a small incremental cost. For example, rapid syphilis testing and treatment can easily be scaled up within existing antenatal care packages, especially those already providing point-of-care testing for HIV. STI prevention can be incorporated into family planning services to maximize dual protection messaging and interventions. Procurement of medications and tests, training, and quality-assurance mechanisms can also be integrated for greater cost efficiency.

Advocacy to fight the stigma of STIs

Advocacy is needed to fight the stigma associated with STIs and their symptoms, to normalize conversations about sexual intercourse and sexual health, and to frame STI services as what they are: essential components of routine primary health care. Advocacy efforts can foster the political will and commitment required to scale up existing prevention services and develop new prevention tools. Strategies to fight STI stigma include education and awareness campaigns providing clear, neutral, and nonjudgmental information about STIs and how common they are. These efforts could also improve STI

care-seeking behavior and reduce partner violence related to STI diagnoses. Advocacy efforts will need to be multidimensional, involving both public and private sectors, professional and civil society organizations, and academic and other institutions. Special attention will need to be paid to reducing stigma among adolescents and other vulnerable populations, such as men who have sex with men. The ability to simply and cost-effectively prevent hundreds of thousands of STI complications like neonatal deaths and cervical cancer should not be held back because of lack of awareness and lack of political will related to stigmatization.

Measurement of the burden of STIs

Strengthening laboratory infrastructure to allow collection of basic STI data is essential to target valuable resources to areas with the greatest need, determine the optimum treatment packages for syndromic management, and monitor the effect of STI interventions. In low-income countries, systematic STI surveillance is not usually conducted. Improving systems to monitor antimicrobial resistance to gonorrhoea is especially important. Global estimates of STI burden have depended on a small number of prevalence studies conducted in varied settings, which have a number of limitations. Thus, better country-level data would also facilitate improved estimation of the global burden of STIs.

NEW TECHNOLOGIES TO FACILITATE PREVENTION OF STIs

Rapid diagnostic tests for STIs

One of the most urgent needs for STI prevention and control in low- and middle-income countries is rapid, point-of-care diagnostic tests, such as those available for syphilis testing, for other STIs. Current syndromic management algorithms are simply not accurate for some syndromes and do not address the much larger burden of asymptomatic STIs. With sustained commitment, new simple, rapid-testing technologies for STIs like chlamydia and gonorrhoea are on the immediate horizon. Development and trials of these tests are ongoing, and several may soon be available. A mathematical model estimates that a test for chlamydia and gonorrhoea requiring no laboratory infrastructure, used just among sex workers in sub-Saharan Africa, China, and southeast Asia, could save more than 4 million disability-adjusted life years and prevent more than 16.5 million new gonorrhoea and chlamydia infections and more than 212 000 HIV infections over four years.

These rapid STI tests would not only allow better targeting of treatment, screening for asymptomatic infection, and interruption of onward STI transmission, but would also make integration of STI services into primary health-care, antenatal, and HIV-care settings far simpler and more feasible. In fact, several bundled rapid diagnostics are being developed and tested – for example, a single point-of-care test to detect syphilis, HIV and malaria for pregnant women. Resources are urgently needed to ensure continued development, validation and implementation of new rapid diagnostic tests for STIs.

New single-dose, affordable drugs for STIs

Given increasing reports of gonorrhoea resistance, investment in the development and validation of new drugs for the treatment of gonorrhoea is critical. Without attention to the problem of drug-resistant gonorrhoea, there may soon be no effective first-line treatment options for this common infection. For maximal impact, new gonorrhoea drugs would ideally be single dose and able to be taken orally. Development of cheap, single-dose, oral medications to improve accessibility and compliance is a goal for treatment of all STIs.

New vaccines and other biomedical interventions for STIs

New effective vaccines and other biomedical interventions against STIs, such as those available for HPV and hepatitis B virus, would be a major advance. For HSV-2, these interventions could have a dramatic impact on HIV spread, in addition to alleviating the suffering associated with genital



herpes symptoms. People who have been infected with this incurable, lifelong STI have a three-fold increased risk of acquiring HIV infection. In populations with 80% HSV-2 prevalence, which are not uncommon in sub-Saharan Africa, almost 50% of HIV infections are thought to be attributable to HSV-2 infection. Although antiviral medications can treat HSV-2 symptoms, current medication regimens do not prevent HIV acquisition. Thus, the only way to reduce the excess risk of HIV infection related to HSV-2 is through primary prevention of HSV-2 infection.

New HSV-2 vaccines are currently under development and evaluation. Vaccines against other STIs such as chlamydia are earlier in development, but several promising platforms exist. Implementation of HPV vaccination programmes should provide valuable experience to facilitate delivery of future STI vaccines for adolescents.

Other biomedical interventions for STI prevention may also become available. Recently, a microbicide gel containing tenofovir was found to halve the risk of HSV-2 infection in one clinical trial, and is currently being evaluated in other trials. Active research will continue to evaluate new microbicides, including those delivered by vaginal rings, to prevent HIV, HSV-2, and other STIs. Adult male circumcision, currently being scaled up for HIV prevention, may also have benefits for prevention of other STIs.

Resources are needed for continued advocacy, coordination and advancement of STI vaccines, microbicides, and other new biomedical interventions, especially for HSV-2, which are a major priority with respect to STI control for HIV prevention. New technologies that provide dual protection against STIs and unintended pregnancies would be highly desirable.

TIME FOR ACTION

Combating STIs is one of the core aspects of WHO's *Global Strategy on Reproductive Health* (WHA57.12), based on recognition that STIs are extremely common, cause genital symptoms affecting quality of life, lead to serious direct consequences, and indirectly affect health and economic growth through enhancement of HIV transmission. To respond to this call for improved sexual and reproductive health, in 2006 the World Health Assembly endorsed a specific *Global Strategy for the Prevention and Control of STIs* (WHA59.19). In 2010, both of these strategies were reinforced by the UN Secretary-General's *Global Strategy for Women's and Children's Health*, in which STI prevention is included in a comprehensive, integrated package of essential interventions and services.

These strategies have been clearly delineated; now it is time to implement them to contribute to attainment of Millennium Development Goals (MDGs) 4, 5 and 6:

- universal syphilis testing and treatment in pregnancy to prevent up to 305 000 fetal and neonatal deaths each year
- vaccination of at least 70% of girls against HPV in low- and middle-income countries over the next decade to prevent 4 million deaths from cervical cancer
- validation and use of new rapid diagnostic tests for curable STIs to prevent millions of new STI cases and associated outcomes such as infertility and increased HIV risk
- development of new effective drugs against gonorrhoea to ensure continued ability to treat 106 million new cases of gonorrhoea each year.

STI prevention is a fundamental component of global sexual and reproductive health. With commitment and support, existing simple, effective, and cost-effective STI-prevention services can be scaled up, while new technologies are developed and adapted to enhance STI prevention.

“Despite the availability of several simple, cheap and cost-effective interventions to combat STIs, little progress has been made.”

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Printed by the WHO Document Production Services, Geneva, Switzerland