

9.1 Epidemiology of sexually transmitted infection

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ESSENTIALS Although accurate incidence figures are not available in most countries, sexually transmitted infections are a large cause of morbidity worldwide. The burden falls especially heavily on women and infants, with up to half a million perinatal deaths attributable to syphilis annually. Mobile populations, those with many sexual partners, and those whose partners have many partners are at increased risk, and the prevalence of treatable sexually transmitted infections is many times higher in poor populations, who often lack access to effective treatment. Other sexually transmitted infections, especially those that cause genital ulceration, increase the risk of human immunodeficiency virus transmission. Incidence In Western countries, the reported incidence of many sexually transmitted infections fell during the 1980s and 1990s, probably as a result of changes in sexual behaviour resulting from the human immunodeficiency virus epidemic, but has increased subsequently. The reported incidence of *Chlamydia trachomatis* infection has increased in the general population, especially in teenagers and young adults, and the incidence of syphilis and gonorrhoea has increased in high-risk groups, particularly men who have sex with men. Although accurate data are not available from most low- and middle-income countries, there is no doubt that sexually transmitted infections are more prevalent in the developing world. Strategies to control sexually transmitted infections These include health education and the promotion of condoms; the provision of accessible, acceptable, and affordable clinical services to provide effective treatment and hence prevent complications and further transmission; and partner notification to reach infected people who may not present to a health facility. Since many sexually transmitted infections are asymptomatic, screening programmes may also play an important role. Screening of pregnant women for syphilis is recommended policy in most countries, and has been shown to be cost-effective even where the prevalence is low. Screening programmes for *C. trachomatis* infection have recently been implemented in some Western countries, and there is some evidence that they have reduced the incidence of complications such as pelvic inflammatory disease. Introduction Few countries outside Western Europe and North America have accurate reporting systems for sexually transmitted infections (STIs). As a result, in most of the world's population, the incidence of these infections is unknown. Knowledge of their epidemiology is based on the results of improvised prevalence surveys undertaken in convenient

populations (e.g. antenatal clinic attenders), but these might not be representative of the population as a whole. In an attempt to calculate the worldwide incidence of the four most common curable STIs—syphilis, gonorrhoea, trichomoniasis, and chlamydial infection—the World Health Organization (WHO) estimated the prevalence of each infection by region, on the basis of published surveys, and divided this figure by the estimated duration of the infection. They concluded that, each year, an estimated 357 million cases of curable STIs (excluding chancroid) occur worldwide (Fig. 9.1.1). The most common (curable) is trichomoniasis (143 million cases), followed by chlamydial infection (131 million), gonorrhoea (78 million), and syphilis (5.6 million). In view of the uncertainty surrounding the prevalence estimates, the duration of untreated STIs, and the mean duration before effective treatment is received, these figures cannot be considered definitive.

Transmission of STIs The rate at which an STI spreads in a population depends on the average quantity of new cases of infection generated by an infected individual, that is, the basic reproductive number (R_0). This in turn depends on the mean rate of sexual partner change (c), the average duration of the infection (D), and its infectiousness (i.e. the likelihood of it being transmitted per sexual act, β). This relationship has been described by the simple formula $R_0 = \beta c D$. When R_0 falls below 1 in a given population, the infection will eventually disappear. However, even when R_0 is less than 1 in the general population, infections can be maintained in core groups with a high rate of change of sexual partners, and might continue to occur in the general population as a result of sexual contact with members of high-risk groups.

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Section 9 Sexually transmitted diseases 1590 The duration of a curable infection depends on the time that elapses before effective treatment is given, which is largely determined by the healthcare-seeking behaviour of the population and their access to healthcare. A disease such as chancroid, which almost always causes painful symptoms, is likely to be treated rapidly in populations with access to effective treatment. For this reason, it has almost disappeared in most industrialized countries, but remains endemic in core groups in some developing countries. In contrast, chlamydial infection, which is often asymptomatic in both sexes, is likely to be of longer duration and thus to persist even in affluent populations.

Risk factors for STIs By definition, STIs are usually transmitted by sexual intercourse, although mother-to-child transmission is also of great public health importance in the case of syphilis and gonorrhoea. Those at highest risk are therefore those with many sexual partners, frequent change of partner, or those whose partners have many partners; in other words, those who belong to high-risk sexual networks. These include sex workers and their clients, and mobile populations such as migrant labourers, truck drivers, fishermen, and soldiers. The youngest sexually active age groups are at particularly high risk, with 15- to 24-year-olds accounting for nearly half of all newly diagnosed STIs in the United Kingdom, despite representing only 25% of the sexually active population (Fig. 9.1.2). In Western countries, the incidence of lymphogranuloma venereum (LGV) and syphilis is high among men who have sex with men (MSM), many of whom are also HIV positive. STIs are more common in poor populations. The incidence of gonorrhoea in black communities in the United States is 12 times that of white communities, and similar to that in many developing countries. Poor people are at increased risk of STIs for several reasons. They might have to travel long distances away from their families in search of work. Many poor rural villagers have migrated into cities in low- and middle-income countries (LMICs) in the last few decades, and many more have been displaced by wars and famines. Poverty and lack of education drive many women into sex work. Health education messages warning of the dangers of HIV/AIDS might be lost on those whose most pressing need is

the cost of their next meal. But perhaps most importantly, poor people often lack access to effective treatment for curable STIs. However, the control of STIs in resource-limited 18 million 31 million 63 million 64 million WHO Region of the Americas WHO Eastern Mediterranean Region WHO European Region WHO South-East Asia Region WHO Western pacific Region WHO African Region The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement. 39 million 142 million Fig. 9.1.1 The global distribution of four curable STIs (syphilis, gonorrhoea, chlamydial infection, and trichomoniasis), 2015 data. Reprinted from WHO Factsheet: Sexually transmitted infections (STIs). © World Health Organization 2015. <http://www.who.int/mediacentre/factsheets/fs110/en/>

9.1 Epidemiology of STIs 1591 settings is achievable, with countries including Thailand and Cuba reporting sustained reductions comparable to the countries of North America and Europe. In China, paradoxically, rapid economic development has co- incided with a dramatic increase in the incidence of reported STIs. Rates of syphilis, which were bordering on elimination in the 1960s following a massive public health campaign including compulsory screening and treatment for those at risk, increased by more than 20-fold between 1990 and 2005. This reflected the loss of free healthcare, which made screening and treatment in- accessible, particularly to the many migrant workers from rural areas seeking work in the cities. Since 2008, however, the Chinese government has invested heavily in surveillance and early treat- ment of STIs, and introduced point-of-care syphilis screening for pregnant women. Between 2008 and 2012, the number of re- ported cases of syphilis fell by 17%, and primary and secondary syphilis by 46%. STIs in developed countries In the United Kingdom, a free and confidential service for people with STIs was established in 1916. Details of patients seen at genito- urinary medicine (GUM) clinics are reported to the public health agency for that country and, since few patients are treated for STIs outside these clinics, the data are believed to be fairly complete and comprehensive. Since the epidemiology of STIs is similar in most countries in Western Europe, the figures for the United Kingdom will be cited as an example. Gonorrhoea The number of reported cases of both gonorrhoea and syphilis de- clined steadily from a peak in the early 1980s to the late 1990s, pre- sumably as a result of changes in sexual behaviour following the HIV epidemic (Fig. 9.1.3). Following this, the number of cases of 6000 4000 2000 0 2000 4000 6000 15–19 20–24 25–29 30–34 35–39 40–44 45–49 50–54 55–59 Rate per 100 000 Age group (years) Women Men Fig. 9.1.2 Rates of newa STI diagnoses in England 2016 by age and gender. a New STIs include chlamydia, anogenital warts (first episode), nonspecific genital infection, anogenital herpes (first episode), gonorrhoea, syphilis (primary, secondary, and early latent), new HIV diagnoses (acute infection and AIDS-defining illness), as well as chancroid/LGV/donovanosis, molluscum contagiosum, pelvic inflammatory disease (PID) and epididymitis, scabies/pediculosis pubis, and trichomoniasis). © Crown copyright. Reproduced with permission of Public Health England. 1925 – 10 000 20 000 30 000 40 000 50 000 60 000 Male Female Total

- Scotland & Northern Ireland data are excluded as they are incomplete from 1925–2003
Data source: KC60 statutory returns Number of diagnoses of gonorrhoea by sex, GUM clinics, England and Wales*: 1925–2005 1930 1935 1940 1945 1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 Sexually Transmitted Infections, HPA Centre

for Infections Fig. 9.1.3 The annual number of reported gonorrhoea diagnoses in England and Wales, 1925–2005. Health Protection Agency.

Section 9 Sexually transmitted diseases 1592 gonorrhoea increased in the late 1990s, and has increased further since 2008, particularly in males (Fig. 9.1.4). In England, reported cases increased by 15% between 2012–2014, and by 26% in MSM. The incidence in London was more than twice the national average and, as in the United States of America, was highest in ethnic minorities of African and Caribbean origin. Efforts to reverse the resurgence of gonorrhoea are hindered by increasing antimicrobial resistance. Resistance to third-generation cephalosporins, the last class of antibiotics to which *Neisseria gonorrhoeae* is susceptible, is becoming more prevalent. In the last 15 years, more than 10 countries have confirmed isolates with full resistance to extended spectrum cephalosporins, and a further 42 have noted strains with reduced susceptibility.

Syphilis In England, the number of reported cases of primary and secondary syphilis increased by 35% between 2005 and 2014 (Fig. 9.1.5). This increase is largely due to cases among MSM in whom HIV was a common coinfection. In Eastern Europe, an epidemic of syphilis in the newly independent states of the former Soviet Union was reported in the 1990s. This was linked to changes in health infrastructure, sexual behaviour, and the emergence of the HIV/AIDS pandemic. In 1999, the annual incidence of reported syphilis in these countries ranged from 55 to 180 per 100 000, with increases particularly evident in older adolescents. There was a 20-fold increase in the reported incidence of syphilis in Russia between 1992 and 1996. Incidence peaked in 2007 before falling by fourfold to 59.9 per 100 000 population; however, accurate current data for these areas are not easily obtained.

Chlamydial infection In Western countries, reported case numbers have increased dramatically since 2005. It is not clear to what extent this increase is due to an increase in the number of people tested, with some countries having started national screening programmes, or to the use of the more sensitive nucleic acid amplification tests, which became widely used in the late 1990s. Data from the latest national survey of sexual attitudes and lifestyles study (NATSAL) suggests that the increased reported incidence is largely due to increased testing, as most that tested positive for chlamydia had not been previously tested or attended a sexual health clinic in the last year, and the reported incidence increased considerably after the screening programme was introduced. Encouragingly, the reported incidence of complications of chlamydial infection, such as pelvic inflammatory disease (PID), epididymitis, and ectopic pregnancy, declined over the same period, presumably due to earlier identification and treatment of infections (Fig. 9.1.6). Reported incidence rates vary across the United Kingdom, ranging from 93/100 000 (total male and female Northern Ireland) to 384/100 000 (total England). As part of the NATSAL, there was a population-based prevalence survey for *C. trachomatis* infection in men and women aged 16–44 in the United Kingdom.

Year	WSW	Heterosexual men	MSM	Heterosexual women
2010	20 000	18 000	16 000	14 000
2011	16 000	14 000	12 000	10 000
2012	12 000	10 000	8 000	6 000
2013	10 000	8 000	6 000	4 000
2014	8 000	6 000	4 000	2 000

Number of diagnoses reported Number of diagnoses of gonorrhoea reported by gender and sexual risk, England, 2010–2014

9.1 Epidemiology of STIs 1593 4000 3500 3000 2500 2000 1500 1000 500 0 Number of diagnoses reported Number of diagnoses of syphilis reported by gender and sexual risk, England, 2010–2014

Year	WSW	Heterosexual men	MSM	Heterosexual women
2010	20 000	18 000	16 000	14 000
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2013	10 000	8 000	6 000	4 000
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Number of reported cases of syphilis by sex and sexual risk. Data from Public Health England. ©

Crown copyright. Reproduced with permission of Public Health England. 500 25 20 15 10 5 0 450
 400 350 300 250 Diagnosis of chlamydia per 100 000 population Diagnosis of chlamydia per 100
 000 population 200 150 100 50 0 2005 2006 2007 2008 2009 Year 2010 2005 2012 2013 2014
 Diagnosis rate of chlamydia and chlamydial PID/epididymitis in the United Kingdom Chlamydia -
 male Chlamydia - total Chlamydial PID/Epipdidimytis - total Chlamydial epipdidimytis Chlamydial
 PID Chlamydia-female Fig. 9.1.6 Incidence of Chlamydia trachomatis infection, PID, and
 epididymitis in the United Kingdom.

Section 9 Sexually transmitted diseases 1594 Infection was found in 1.1% of men, and 1.5% of women, with the highest prevalence in men aged 20–24 (3.4%) and women aged 18–19 years (4.7%). Lymphogranuloma venereum (LGV), caused by the more invasive L1, L2, and L3 strains of *C. trachomatis*, had been a rare disease in industrialized countries since the 1960s, and was generally considered a ‘tropical’ STI until 2003, when there was an outbreak of LGV proctitis due to the L2 serovar among homosexual men in the Netherlands. The disease has subsequently spread in the MSM community across Western Europe, the United States, and Australasia, resulting in recommended screening in some countries including the United Kingdom and United States. The majority in whom the diagnosis is made are HIV positive. Rates of LGV rose steeply since 2003, peaking in 2010, and it is now considered to be endemic in the United Kingdom.

Genital herpes The incidence of reported genital herpes in women in England was 73/100 000 and 45/100 000 in men in 2014, both these figures increasing by at least two-thirds since 2005. The worldwide prevalence of genital herpes simplex virus (HSV) infection is over 500 million. Classically, genital herpes is due to herpes simplex virus type 2 (HSV2), while herpes simplex type 1 (HSV1) causes oral lesions and is a common childhood infection. Once acquired, these infections persist for life, causing recurrent vesicular and ulcerative lesions. In the United Kingdom, the proportion of genital ulcers due to HSV1 is increasing, presumably because of changing sexual practices. Human papillomavirus (HPV) HPV affects more than 290 million women worldwide, making it one of the most common STIs. Certain types of HPV (predominantly 6 and 11) cause genital warts, while others (predominantly 16 and 18) cause cervical carcinoma, the second most common cancer worldwide in women. Genital warts are the most frequently reported viral STI in GUM clinics in the United Kingdom, most commonly affecting those aged 18–28. In England there were more than 70 000 reported cases in 2014, increasing slightly from 2005 but showing a downward trend from 2008. To reduce and ultimately prevent HPV-associated cervical cancer, programmes administering HPV vaccines to young adolescent girls are being implemented in many countries. In the United Kingdom, HPV vaccination of girls was introduced in 2008, but adolescent boys are not vaccinated as they are in the United States and Australia. In 2014 vaccination coverage in the United Kingdom was approximately 80% of the targeted population, and NATSAL 3 reported lower rates of HPV types 16 and 18 in 18- to 20-year-olds than NATSAL 2. In the future, using HPV tests for cervical screening rather than cytology could greatly improve the identification of women at risk of cervical cancer.

STIs in developing countries Few reliable data are available on the incidence of STIs in developing countries, although the latest global burden of disease study confirmed that the impact in terms of healthy life years lost was greatest in sub-Saharan Africa. Based on numbers of cases seen at health facilities, it has been suggested that the incidence of gonorrhoea is at least 50 times higher in sub-Saharan Africa than in the United Kingdom. Several large population-based surveys have confirmed that the prevalence of STIs is high in sub-Saharan Africa, even in rural populations. For example, 5–10% of adults have been found to be infected with syphilis, 20–30% of women, and 10% of men with *Trichomonas vaginalis*, and up to 50% of women

were found to have bacterial vaginosis. Between 2.5% and 17% of pregnant women in Africa are infected with syphilis. A population-based serological study in rural Tanzania found that 50% of women and 25% of men were infected with HSV2 by the age of 20 years. Seropositivity was rare before the age of 16 in both sexes, confirming that HSV2 is mainly transmitted sexually in this population. The proportion of genital ulcers caused by HSV2 has increased in Africa as a result of the HIV epidemic, as recurrences become more frequent and prolonged in the immunocompromised. At the same time, chancroid has apparently become less common in high-risk populations in Africa, perhaps as a result of behavioural change resulting from the HIV epidemic. HPV causes 266 000 cervical cancer deaths per year, 88% of which occur in low-income countries, and it is easily the most common malignancy in women in much of the developing world. This is secondary to the high incidence of sexually transmitted HPV infection. Despite this, few LMICs include HPV vaccination into their national immunization programmes. If 70% coverage can be achieved in these countries, then more than four million female deaths could be prevented. Interactions between HIV and other STIs Diseases such as chancroid, syphilis, and herpes, which cause genital ulceration, facilitate sexual transmission of HIV by increasing infectivity and susceptibility. A prospective study of STI clinic attenders in Nairobi, Kenya showed that the likelihood of a man who had acquired a genital ulcer from an HIV-positive sex worker also acquiring HIV was about 1 in 6 after a single sexual exposure. This suggests that the presence of a genital ulcer increases the risk of transmission 50–100-fold. STIs such as gonorrhoea that cause genital discharge increase shedding of HIV in both seminal and cervicovaginal secretions. A community-randomized trial in Mwanza, Tanzania, found that improved STI services in rural health centres and dispensaries, using the syndromic approach, reduced the incidence of HIV infection by 40% over a two-year period. In Uganda, a community-randomized study found that periodic mass treatment for STIs had no impact on the incidence of HIV. In this trial, the HIV epidemic was more advanced, and a high proportion of genital ulcers were caused by HSV2, which was not treated. HIV and HSV2 appear to facilitate transmission of one another, leading to a vicious circle (Fig. 9.1.7). Control of HSV2, perhaps by vaccination, could greatly reduce transmission of HIV in the developing world, although clinical trials of suppressive treatment for herpes failed to show an impact on HIV incidence. Control of STIs Strategies for the control of STIs aim to reduce β (transmissibility), c (rate of partner change), or D , the duration of infection.

9.1 Epidemiology of STIs 1595 Primary prevention Transmissibility can be reduced by the use of condoms. Health promotion and health education aim to encourage the use of condoms, and to persuade people to have fewer sexual partners. This is sometimes referred to as primary prevention, since these measures can prevent people from ever becoming infected. There have been few formal trials of health education in the primary prevention of STIs; but the example of health education in schools suggests that, although education often improves knowledge, it seldom influences behaviour. Education programmes were most effective when given by health workers, over a prolonged time, and with community involvement rather than just in school. It was also more effective when comprehensive rather than promoting abstinence only. In Thailand, legislation to close down brothels where condom use was not mandatory was successful in reducing the incidence and prevalence of HIV infection in the general population. Transmissibility can also be reduced by biomedical means, such as HPV vaccination, microbicidal gels, and male circumcision, which has been shown to reduce the risk of heterosexual transmission of HIV by 60% as well as offering some protection against other STIs. Secondary prevention: case management The duration of treatable STIs can be reduced by the provision of accessible, acceptable, and

affordable clinical services, combined with partner notification. Prompt treatment of STIs should be seen as a 'public good', equivalent to the treatment of pulmonary tuberculosis, since it prevents transmission to others, as well as benefiting the person treated. The aims of patient care are:

- to detect or rule out infection
- to give treatment if necessary
- to educate and counsel on treatment compliance, STI/HIV prevention, and condom use
- to ensure that sexual partner(s) are evaluated and managed (contact tracing)
- to test for other STIs, including HIV

In most developing countries, case management of STIs must be syndromic, because laboratory diagnosis is not available outside a few specialist centres. Syndromic management of genital ulcers and genital discharge in men is straightforward and cost-effective, but syndromic management of vaginal discharge in women is not, because symptoms are poor predictors of the presence of an STI. A cheap, simple, point-of-care (POC) test for gonorrhoea and chlamydial infection in women would be valuable in the control of these infections. To provide an adequate clinical service, the following components are needed:

- Training should be given to health workers, for instance in the use of flowcharts to simplify the management of sexually transmitted infection (STI) patients, or to strengthen their health education and counselling skills.
- Laboratory services need to be expanded, depending on the level of healthcare provided. A reference laboratory should be developed in each country to provide quality control, monitor the antimicrobial susceptibility of *N. gonorrhoeae*, and support operational research, for example, on the aetiology of common syndromes.
- Information systems or surveillance are needed to gather epidemiological data, to assess trends, and to provide data for programme planning and monitoring. Various surveillance methods can be used—clinician notification, laboratory notification, sentinel site surveillance (either of syndromes or of aetiological diagnoses), or prevalence studies in specific population groups.

Screening programmes Many people with STIs have no symptoms, and so do not seek medical care. While effective programmes for partner notification may identify some of these, screening programmes have been advocated to identify and treat these people. Because of the severe adverse effects of syphilis on the fetus, screening of pregnant women for syphilis is recommended policy in most countries, and remains a highly cost-effective intervention even when the prevalence of syphilis in pregnant women is less than 0.01%, as in the United Kingdom. POC tests are now available which can be performed anywhere, since they do not require laboratory equipment or electricity, and a combined POC test for HIV and syphilis offers an important opportunity to increase the coverage of antenatal screening for the prevention of mother-to-child transmission of both infections. Screening of other groups is more controversial. In some countries where sex work is legal or tolerated, screening programmes for sex workers are routinely implemented. A study in the United States found that population-based screening for chlamydial infection reduced the incidence of pelvic inflammatory disease (PID).

Conclusion A successful STI control programme, by reducing both the incidence and prevalence of STIs, will reduce the morbidity, suffering, and economic cost associated with these infections. By eliminating STIs as a facilitating factor for HIV transmission, and by contributing to behavioural changes towards safer sex, it will play an

Altered frequency, natural history and response to Rx UNPROTECTED SEXUAL INTERCOURSE HIV Herpes Cofactor effect? IMPAIRED IMMUNITY Transmission, and progression to clinical disease? Fig. 9.1.7 Interactions between HIV infections and genital herpes.

Section 9 Sexually transmitted diseases 1596 important role in the prevention and control of HIV/AIDS. In the longer term, control of STIs will depend on targeting and modifying high-risk behaviour in key populations, and improved access to services for poor people, particularly women.

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