



UNAIDS/WHO Working Group  
on Global HIV/AIDS and STI Surveillance

# Strategies and laboratory methods for strengthening surveillance of sexually transmitted infections 2012



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Strategies and laboratory methods for strengthening  
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## Abbreviations

AIDS	acquired immunodeficiency syndrome
AMR	antimicrobial resistance
DFA-TP	direct fluorescent antibody test for <i>Treponema pallidum</i>
DHS	demographic and health survey
EIA	enzyme-linked immunoassay
EQAS	external quality assessment survey
GASP	Gonococcal Antimicrobial Surveillance Programme
HIV	human immunodeficiency virus
IBBS	integrated biological and behavioural survey
HSV-2	herpes simplex virus type 2
MIC	minimum inhibitory concentration
MSM	men who have sex with men
NAAT	nucleic acid amplification test
NGO	nongovernmental organization
PCR	polymerase chain reaction
PICT	Pacific Island countries and territories
QRNG	fluoroquinolone-resistant <i>Neisseria gonorrhoeae</i>
RDT	rapid diagnostic test
RHR	Department of Reproductive Health and Research (WHO)
RPR	rapid plasma reagin
STD	sexually transmitted disease
STI	sexually transmitted infection
TOC	test of cure
TPHA	<i>Treponema pallidum</i> haemagglutination assay
TPPA	<i>Treponema pallidum</i> particle assay
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
USA	United States of America
VDRL	venereal disease research laboratory
WHO	World Health Organization



# 1. Introduction

It is estimated that a million people acquire a sexually transmitted infection (STI) including human immunodeficiency virus (HIV) every day. Approximately 498.9<sup>1</sup> million estimated curable STIs, namely those due to *Treponema pallidum* (syphilis), *Neisseria gonorrhoeae*, *Chlamydia trachomatis* and *Trichomonas vaginalis*, occur each year throughout the world, with the largest proportion in sub-Saharan Africa and Latin America and the Caribbean, followed by the Western Pacific Region. In addition, millions of viral STI infections also occur annually, attributed mainly to HIV, herpes simplex viruses (HSVs), human papillomaviruses and hepatitis B virus.

Although HIV surveillance has largely been institutionalized in almost all countries and data are more widely available, surveillance systems for STIs are generally weak, except for a few countries in western Europe and North America. The limited data available, however, suggest a huge burden of infection affecting people with high-risk sexual behaviours, as well as other vulnerable populations and the general population. The data that are available from developing countries relate mainly to bacterial STIs and there is a dearth of data on viral STIs, such as herpes simplex virus infections. Syphilis and chancroid are the common bacterial genital ulcer diseases but data on the prevalence and incidence of syphilis and chancroid are limited or unavailable. Similarly, surveillance data on gonococcal and chlamydial infections are also very limited in low- and middle-income countries. Much of the information on STIs from these countries is from either research studies or demographic health surveys.

This document is intended to provide a framework for ministries of health and public health decision-makers at national and subnational level for implementation of STI surveillance systems that generate consistent and reliable data to facilitate disease-control efforts. The publication emphasizes the timely collection, analysis and use of data. Although data obtained through routine public health surveillance activities need to be interpreted carefully in view of their biases and limitations, they provide valuable information on disease burden and aspects of programme services. The strengthening of STI surveillance systems should be viewed as a central component of the effort to strengthen STI/HIV-prevention programmes globally.

<sup>1</sup> WHO 2008 STI estimates *Global incidence and prevalence of selected curable sexually transmitted infections – 2008*

## 2. Background

### 2.1 Why this document is needed

One of the essential elements of the WHO *Global strategy for the prevention and control of sexually transmitted infections* is STI surveillance. The control of genital ulcerative diseases, including control of syphilis and elimination of congenital syphilis, is among the strategy's top 10 interventions that require solid data to guide the response.

The last STI surveillance recommendations were published in 1999 (2). The 1999 edition of the guidelines was developed by a group of experts from around the world and its recommendations were based on experiences from surveillance systems in different countries, with a focus on the components for data collection and the objectives of each of those components: brief guidance on analysis and interpretation of data; short sections on dissemination, communication and use of data; and evaluation of STI surveillance systems.

Some countries have undertaken surveillance activities based on the 1999 document (2). However, as new technologies have become available and the epidemiology of STI has changed, there is a need to review and update the STI surveillance guidelines to support countries, particularly within the context of second-generation HIV surveillance. The second-generation surveillance approaches have been strengthened over the past 10 years and there are opportunities to build upon these systems to improve STI surveillance.

Thus, the changing epidemiological situation and policy environment, as well as some surveillance practices, in combination with the need for new knowledge, technologies and strategies for STI control and prevention, creates justification to update the World Health Organization (WHO) recommendations on the strategic approaches to STI surveillance.

### 2.2 Guiding principles

The main framework for the development of this document is built on the WHO action plan for implementation of the *Global strategy for the prevention and control of sexually transmitted infections*.

The action plan has a specific expected outcome of enhanced STI surveillance. The development of recom-

mendations for surveillance is one activity that is needed to achieve this outcome. The action plan recommends that the document be developed or revised so that it:

- is based on the 1999 STI surveillance guidelines;
- is comprehensive, to include both general and high-risk populations;
- provides guidance on specific legal and human rights issues;
- provides laboratory guidelines, including the role of the laboratory at different levels of health-service delivery.

These points have been used as the main guiding principles for development of this document.

### 2.3 Methodology and process

The WHO Department of Reproductive Health and Research, RHR, as the lead institution for the development of guidelines for the prevention and control of STIs, convened a technical consultation of experts in 2008, in order to review and update the 1999 STI surveillance guidelines (2).

The technical consultation of experts included regional and country STI surveillance specialists (national programme managers who are responsible for and experienced in STI surveillance), internationally recognized experts in specific domains related to STI control and prevention (experts from the field of STI laboratory, epidemiology and surveillance), representative from the Joint United Nations Programme on HIV/AIDS (UNAIDS), WHO STI regional officers and WHO headquarters staff, including staff from the Departments of HIV and RHR (see Acknowledgments).

#### 2.3.1 Summary of declarations of interest

All non-WHO participants signed and submitted a declaration of conflict and interest form. One potential conflict was declared: Dr Graham Neilsen, Family Health International, Asia Pacific Regional Office, declared being in possession of shares of two Pharmaceuticals Companies, CSL and Stargamma, at the time of the technical consultation, but this was assessed by the WHO Secretariat, presented to the meeting participants, and deemed insignificant to preclude Dr Neilsen's participation in the consultation and in the process of formulation of recommendations. For the other participants, it was agreed that there was no conflict of interest.

### 2.3.2 Goal of the consultation

Twenty-five participants attended the 3-day workshop. The goal of the consultation was to clarify an essential package to guide and strengthen surveillance of STIs at the national level. The specific objectives were to:

- define essential components and sexually transmitted pathogens for STI surveillance at the national level;
- define laboratory needs to support national surveillance of STIs;
- outline areas of action needed to accelerate collection of data about STIs during 2008–2009.

### 2.3.3 Consultation process

The first day of the meeting was dedicated to plenary discussion, where formal presentations summarizing the most up-to-date information, mainly experience and lessons learnt in the field of STI surveillance, were shared and discussed among the meeting participants. This aimed to form a common understanding of progress made, as well as existing challenges in improving surveillance of STIs.

The next two days were used to discuss specific issues within small working groups. The participants were divided into two small groups to discuss specific items and formulate group recommendations, which were then presented and discussed in the plenary sessions with the whole group. Only the recommendations on which consensus was reached were included in the technical consultation report, i.e. the recommendations that were accepted by the majority of the respective small group first and then endorsed by the majority, or all, of the participants of the meeting during the plenary sessions.

In summary the specific objectives per respective small group were as follows:

- *group 1* – main STIs, their sequelae and STI syndromes to be recommended for STI surveillance at different levels of the health-care system as well as the diagnostic methods for STI surveillance purpose;
- *group 2* – main STI surveillance approaches to be recommended for STI surveillance (i.e. population based and antenatal screening, special studies, sentinel approach) and core and optional elements of the STI surveillance

system, as well as ethical, legal and rights issues within the context of STI surveillance (the detailed terms of reference as well as the distribution of the participants according to group can be found in Annex 6).

The endorsed recommendations were included in the technical report of the meeting, which was developed by the responsible officer of the STI team. After the meeting, the draft report was circulated for comments and revision among all participants of the technical consultation. The WHO Secretariat coordinated the revision and development of the final report. Full participant consensus on the expected outcomes of the 2008 technical consultation was reached during the consultation itself, as well as at the stage of developing of the technical report. This led to a set of concrete conclusions and recommendations to update the 1999 WHO STI surveillance guidelines (the meeting report is available upon request).

The WHO STI team, as the secretariat, embarked on the revision and updating of the 1999 WHO STI surveillance guidelines, based on the conclusions and recommendations of the meeting. This process also included regular online communication (via e-mail and teleconferences) with the experts involved in the technical consultation, in order to incorporate its recommendations fully into the updated version of the document as best as possible.

### 2.3.4 Resource materials

Other documents specific to STI surveillance that were used for updating the 1999 edition of the STI surveillance document include a report from a consultation in 2002 to guide the global estimation of STIs: *Estimation of the incidence and prevalence of STI. Report of a WHO consultation, Treviso, Italy, 27 February–1 March 2002* (3). This document focuses on considerations for measuring and estimating the prevalence and incidence of STIs, the use of STI measures as an indicator of recent changes in sexual behaviours, and recommendations for STI surveillance. Another document was *The laboratory diagnosis of sexually transmitted infections* (4), which provides standard procedures for clinical microbiologists and medical technologists for detection and diagnosis of STIs. WHO Regional Offices have also produced several guidelines to support STI surveillance, including guidance on methodologies for prevalence assessment, while others have incorporated STI surveillance

into second-generation HIV surveillance or integrated disease surveillance guidance – these were also used as background materials for this work.

It is important to highlight that the WHO HIV/AIDS (Acquired Immunodeficiency Syndrome) Department and UNAIDS have developed a number of guidelines that incorporate an STI surveillance component into HIV surveillance, particularly over the last 5 years. The *Guidelines for second generation HIV surveillance* (the 2000 edition) (5) and the *Guidelines for Second Generation HIV Surveillance: an update: know your epidemic* (6) include aspects of STIs for the purpose of HIV biological surveillance from sentinel sites such as STI clinics, and the use of STI burden to indicate risky sexual behaviours. Other HIV documents from the WHO HIV/AIDS Department and UNAIDS that were drawn upon include: *Pre-surveillance assessment: guidelines for planning serosurveillance of HIV, prevalence of STI and behavioural components of second*

*generation surveillance of HIV* (7); *Guidelines for using HIV testing technologies in surveillance: selection, evaluation and implementation* (8); *Guidelines on estimating the size of populations most at risk to HIV* (9); *HIV triangulation resource guide: synthesis of results from multiple data sources for evaluation and decision-making* (10); *Ethical issues to be considered and effective use of data from HIV Surveillance Systems* (11); and *Guidelines on surveillance among populations most at risk for HIV* (12). The WHO *Protocol for the assessment of national communicable disease surveillance and response systems: guidelines for assessment teams* from the Department of Communicable Disease Surveillance and Response 2001 (13) was also consulted, since it offers guidance that serves as a foundation for the assessment of STI surveillance systems and its strengthening, as an integral part of HIV surveillance as well as an essential component of a national integrated health system.

## 3. The prevalence of specific sexually transmitted infections

### 3.1 Herpes simplex virus infection

Herpes simplex virus type 2 (HSV-2) infection is the leading cause of genital ulcer disease worldwide. A global review of age-specific prevalence of HSV-2 infection in 2002 showed that HSV-2 seroprevalence was highest in areas of Africa, with 30% to 80% of women and 10% to 50% of men being infected. HSV-2 seropositivity increases progressively with age in all geographical areas, particularly among young women (15–24 years).

A national sero-behavioural survey in Uganda in 2004 found a HSV-2 seroprevalence of 44% among respondents aged 15–49 years, with women more likely to be infected (49%) than men (38%). According to the Ugandan survey results, HSV-2 seroprevalence ranged from 20% among those aged 15–19 years to over 60% in those aged over 40 years. HSV-2 seroprevalence was also higher among women than men for every age group.

Very few countries in the WHO European Region routinely collect data on HSV-2. Incidences of 20–70 per 100 000 population have been reported by the WHO Regional Office for Europe from countries such as Kyrgyzstan, the Republic of Moldova, Estonia, Armenia, the United Kingdom of Great Britain and Northern Ireland, Belarus and the Russian Federation during the period 2000 to 2005. Genital herpes is the most commonly diagnosed ulcerative STI in the United Kingdom, and an 18% increase in the diagnoses of genital herpes (first episode) was reported from the genitourinary medicine clinics in the United Kingdom between 1996 and 2005. The rate and number of genital herpes diagnoses have been higher among women than men in all age groups under 45 years since the mid-1990s. The highest rates of genital herpes were in the age group 16–24 years among women and 20–34 years in men.

In Asia, data on genital herpes are very limited, as facilities for diagnosis and reporting are not routinely available and very few population-based studies have been carried out. In Vellore, India, HSV-2 seroprevalence ranged from 8% among antenatal clinic attendees and 10% in male blood donors to 14.6% among female blood donors. In Colombo, Sri Lanka, sero-epidemiological data on HSV infection showed it was

8% among antenatal clinic attendees, 14% and 21% among male and female blood donors respectively, 33% among male STI clinic attendees and 49% in female STI clinic attendees. Genital herpes is also the most common (25%) genital ulcer disease diagnosed among patients attending STI clinics in Sri Lanka. In Melbourne, Australia, the epidemiology of genital herpes has changed from 1980 to 2003. Although HSV-2 was still the most common cause of genital ulceration, the proportion of genital ulcers due to HSV-1 has increased to one third of genital infections. More than 70% of people under the age of 20 years reporting genital herpes infections were infected with HSV-1. In the Republic of Vanuatu in the South Pacific region, a study carried out among pregnant women attending the major antenatal clinic, reported HSV-2 seroprevalence rates of 30%.

In the Middle East, data on the seroprevalence of genital herpes are scant. In the Kingdom of Saudi Arabia, a study among pregnant women indicated a HSV-2 seroprevalence rate of 27%.

In the United States of America (USA), consecutive national samples of adults showed that HSV-2 seroprevalence has increased from 16.4% to 21.7% between 1979 and 1991. However, the most recent data that span the 1999–2004 period suggest that overall prevalence has decreased to 17%, reflecting a lower rate of infection among teenagers and young adults. The cumulative lifetime incidence of HSV-2 was nearly 25% in Caucasian women and 20% in Caucasian men, compared to 80% in African American women and 60% in African American men. In Latin America, ad hoc studies carried out among women in Peru showed HSV-2 infection rates of 20%, while in Brazil, seroprevalence ranged from 43% in female blood donors to over 60% among male STI clinic attendees.

### 3.2 Syphilis (*Treponema pallidum*)

Syphilis, once the most common cause of genital ulcers globally, has now been superseded by genital herpes. However, with an estimated 10.6 million new cases occurring per year, it still remains a major cause of public health concern because of the adverse effects on pregnancy leading to stillbirth, spontaneous abortion, perinatal death, serious perinatal infection or low birth weight. Since the consequences of syphilis in pregnancy are severe, screening pregnant women for syphilis should be national policy in every country. Syphilis also increases HIV transmission.

There has been a resurgence of syphilis in Europe, North America and China in recent years. Among countries in Europe, outbreaks of syphilis in populations with high-risk sexual behaviours have been reported, in particular among men who have sex with men (MSM), sex workers and drug users. In the United Kingdom during the period 1996–2005, the diagnoses of infectious (primary, secondary and early latent) syphilis at genitourinary medicine clinics increased markedly, from less than 200 in 1996 to over 1400 in 2005. This increase has been punctuated by a series of outbreaks across the United Kingdom. The largest outbreak started in London in 2001 and since then, a steep rise in infection rates has been reported, particularly among young men. Between 2001 and 2005, diagnoses among MSM increased by almost two-thirds.

In North America, in 2000, the number of infectious cases of syphilis reported dropped to its lowest rate since national reporting began in 1941. However, in 2001, the situation changed rapidly and the number of cases began to increase and has increased every year since then. In the current epidemic, case rates continue to rise, with an increase of almost 14% from 2005 to 2006. Cases are predominantly among men, with a male to female ratio of 5.2:1, and increase in MSM from 4% of total cases in 2000 to 62% in 2006.

The national sexually transmitted disease (STD) surveillance system of the Ministry of Health, The People's Republic of China, monitors STIs through a mandatory case-reporting from government facilities. In 1987, China established 16 sentinel sites and by 1993, 26 sentinel sites were reporting on syphilis. The reported rate of syphilis was just below 0.2 cases per 100 000 population from 1989 to 1993, whereas in 2005, primary and secondary syphilis alone accounted for 5.7 cases per 100 000 population. Over 70% of reported cases of syphilis from 1995 to 2005 were in people aged 20–49 years. The rate of congenital syphilis has also increased from 0.01 cases per 100 000 live births in 1991 to 19.68 cases per 100 000 live births in 2005.

In Africa, syphilis is still very prevalent, with rates reported in population-based studies in the late 1990s among men and women ranging from 2% (Benin) to 14% (Zambia). Serological testing for syphilis in a subsample from a demographic and health survey conducted in Madagascar in 2004–2005, found that 3.8% of the population in the 15–49 years age

group was seropositive, with equal prevalence among men and women. In Zambia, sentinel data on HIV and syphilis have been collected from antenatal clinics in 22 sites since 1993. The overall prevalence of syphilis among pregnant women in the 2004 survey was 6.9%. Among women who had been pregnant at least once prior to the present pregnancy, the prevalence of seropositivity was highest among those who reported having had no previous live births (14.04%) and lowest among women who reported five or more live births (6.77%).

In Asian countries, increasing rates of syphilis among MSM have been demonstrated recently. A study of reproductive tract infections and STIs carried out among high-risk population groups in Karachi and Lahore in Pakistan showed syphilis is still very prevalent. The prevalence of syphilis was 60% among the Hijras, while it was 36% in male sex workers and 18% in injecting drug users in Karachi. Compared to Karachi, the prevalence of syphilis was markedly less in Lahore, with 12% in Hijras, 6% in male sex workers and 4% in injecting drug users. Studies carried out in Indonesia and Nepal among MSM populations showed syphilis seropositivity rates of 1% and 7.3% respectively. According to surveillance data in Australia, after more than a decade of very low rates of infection, syphilis has re-established itself among homosexually active men in Sydney, where a 10-fold increase in the number of infectious syphilis notifications in inner Sydney between 1999 and 2003 has been recorded.

### 3.3 *Chlamydia trachomatis* infections

*Chlamydia trachomatis* infection is reported as the most prevalent sexually transmitted bacterial infection worldwide, with an annual estimate of 105.7 million new cases worldwide. Chlamydial infection is common among sexually active young men and women. If left untreated, it can lead to complications, including endometritis, salpingitis, pelvic inflammatory disease, chronic pelvic pain and ectopic pregnancy in women, reduced fertility in both men and women, and neonatal infections such as ophthalmia neonatorum and pneumonia.

In high-income countries, data on *Chlamydia trachomatis* infection are generally more available, as it is a notifiable infection in many of these countries, and chlamydia screening and treatment programmes are routinely conducted. In the USA, according to 2009 national surveillance data, 1 244 180 cases were reported, up by 2.8% from the reported cases for 2008. In countries in Europe, the rate of *Chlamydia trachomatis*

diagnoses ranged from 7 cases per 100 000 population in Slovenia to 585 cases per 100 000 population in Iceland. However, these differences are highly affected by the screening and diagnostic tests used, as well as the completeness of case-reporting and epidemiologic surveillance. The number of reported genital chlamydial infections in England, United Kingdom was 189 612 in 2010. In Australia, more than 61 000 cases of *Chlamydia trachomatis* infection were reported in 2009.

Although *Chlamydia* screening is not routinely conducted in low-income countries, some information based on special studies is available. Studies conducted among low-risk women in African countries indicated a prevalence of *Chlamydia trachomatis* infection ranging from 0.6% among prenatal women in Tunisia to 5.5% among women in the general population in Gambia and 19.7% in women attending antenatal clinics in Nigeria (global STI estimates data). In a study conducted among men in the general population in four sub-Saharan African cities, *Chlamydia trachomatis* prevalence rates ranged from 5.9% in Yaoundé to between 2.1% and 2.6% in Ndola, Cotonou and Kisumu.

In Brazil, *Chlamydia trachomatis* infection among women attending a STI clinic was found to be 20.7%. Results from a population-based survey conducted among the general female population in Colombia and Argentina reported *Chlamydia trachomatis* prevalence of 5%, while a study carried out in Peru showed a prevalence of 6.8% among low-risk women.

A survey carried out in 2004–2005 in six sentinel Pacific Island Countries and Territories (PICTs) – Fiji, Kiribati, Samoa, Solomon Islands, Tonga and Vanuatu – among pregnant women attending for their first antenatal visit, showed an 18% prevalence of *Chlamydia trachomatis* infection. A prevalence survey conducted among sex workers and women attending antenatal clinics in Malaysia showed that *Chlamydia trachomatis* infection was the most prevalent STI, with prevalence rates of 6.3% and 1.6% respectively. In Indonesia, studies carried out among female sex workers have indicated *Chlamydia trachomatis* prevalence rates ranging from 12% to 39%, while in Bangladesh, among brothel-based sex workers, the prevalence rate was 15.5%. High rates of rectal chlamydial infection have also been reported among MSM in the Philippines (9.2%) and in Nepal (20.5%). A survey carried out in Pakistan reported *Chlamydia*

*trachomatis* prevalence rates of 11% in female sex workers and 1.5% in male sex workers in Lahore, while reported rates were 5% among female sex workers and 1.2% among male sex workers in Karachi.

### 3.4 Gonococcal infections

Gonococcal infections are still prevalent throughout the world and remain a serious public health problem, with an estimated 106.1 million new infections per year.

In South Africa, microbiological surveillance of STIs carried out in Johannesburg in 2007 among men presenting with urethral discharge showed *Neisseria gonorrhoeae* to be the most common cause of urethritis (62.3%) compared to *Chlamydia trachomatis* (19.3%) and *Trichomonas vaginalis* (3%).

In Cairo, Egypt, studies have shown a prevalence rate of 8.8% for gonorrhoea among MSM, 7.7% among female sex workers, 2.7% among injecting drug users and 2% among antenatal clinic attendees. A population-based survey carried out in Nigeria reported a 2.6% prevalence of gonococcal infection among the general female population. The prevalence of gonococcal infection reported for men in four African cities ranged from 0% to 1.6% (Cotonou 1.1%, Yaoundé 1.6%, Kisumu 0% and Ndola 0.6%), while the prevalence was slightly higher among women (0.9% to 2.7%).

In Yemen, among male outpatient clinic attendees, the prevalence of gonococcal infection was found to be 10.3%, while in female outpatient clinic attendees it was 5%. A very low prevalence of gonococcal infection (0.7%) has been reported among patients attending obstetrics and gynaecology services in Jordan.

In South and South-East Asia, data on gonococcal infections are mainly available from studies carried out in sex workers. In Pakistan, female sex workers surveyed in two large cities showed a prevalence of gonococcal infection ranging between 10% and 12%, while in male sex workers the prevalence was lower (3% to 8%).

In Europe, the reported rate of gonorrhoea varied from 0.5 cases per 100 000 population in Portugal to 32.4 cases per 100 000 population in Latvia in 2006. During the same year, the proportion of gonorrhoea cases acquired homosexually ranged from 24% in the Czech Republic to 80% in Belgium.

In the United Kingdom in 2006, the overall rate of gonorrhoea among men and women was 46 and 18 per 100 000 respectively.

Although the reported rate of gonococcal infections in the USA showed a 74% decline from 1975 to 1997, the rate increased during 2005 and 2006. In 2006, the gonorrhoea rate was 120.9 cases per 100 000 population, an increase of 5.5% since 2005, and the Healthy People 2010 objective for gonorrhoea is 19.0 cases per 100 000 population.

### 3.5 *Trichomonas vaginalis* infections

Information regarding the prevalence of *Trichomonas vaginalis* is scarce, due to limited diagnostic techniques, an absence of screening programmes and lack of disease reporting, even in high-income countries.

*Trichomonas vaginalis* infection (trichomoniasis) is the most common non-viral STI, with an estimated 276.4 million cases annually worldwide. It has been associated with a range of adverse reproductive health outcomes, including preterm birth, atypical pelvic inflammatory disease and post-hysterectomy infection. Recent evidence indicates that *Trichomonas vaginalis* is epidemiologically associated with HIV infection.

A study carried out in women in four cities in sub-Saharan Africa found that *Trichomonas vaginalis* infection was significantly higher in two cities with high HIV prevalence (29.3% in Kisumu, Kenya, and 34.3% in Ndola, Zambia) than in two cities with relatively low levels of HIV infection (3.2% in Cotonou, Benin, and 17.6% in Yaoundé, Cameroon). Among rural women from the highlands, jungle and coastal regions of Peru, *Trichomonas vaginalis* was detected in 16.5%. The prevalence of *Trichomonas vaginalis* was lower than the prevalence of bacterial vaginosis (43.7%) among these women.

In countries of the Middle East, ad hoc studies have indicated a prevalence ranging from 29.9% among women attending female outpatient clinics in Yemen, and 12% in obstetrics and gynecology patients in Jordan to 19.9% among female sex workers in Egypt.

In Lisbon, Portugal, a study among imprisoned women found a high prevalence of trichomoniasis (31.2%), and more than 75% of women with trichomoniasis also had other STIs.

Community-based data on trichomoniasis are almost non-existent in Asia. In Sri Lanka, routine reporting from STI clinics over the last decade since 1995 show a reduced number of trichomoniasis cases, from 262 reported cases in 1995 to 155 in 2005.

Men with *Trichomonas vaginalis* infection are predominantly asymptomatic. A study carried out in seven west African countries (Benin, Burkina Faso, Cote d'Ivoire, Ghana, Guinea, Mali and Senegal) among men who presented to primary health-care institutions with a complaint of urethral discharge found *Trichomonas vaginalis* in 15% of men with non-gonococcal, non-chlamydial urethritis. The prevalence of *Trichomonas vaginalis* varied 10-fold between countries: from 2.5% in Cote d'Ivoire to 24.5% in Senegal. This intercountry variation was observed whether *Trichomonas vaginalis* infection occurred alone, or with *Neisseria gonorrhoeae* and/or *Chlamydia trachomatis*. In a more recent study from Johannesburg, South Africa, *Trichomonas vaginalis* was isolated in 4.1% of males presenting with symptomatic urethritis, while among those with genital ulcer syndrome, it was the most frequently isolated (19.7%) urinary pathogen.

### 3.6 Antimicrobial resistance monitoring for *Neisseria gonorrhoeae*

The emergence of multi/drug resistant gonococcal infection is one of the most important public health problems today.<sup>1</sup> Gonococcal infections have critical implications to reproductive, maternal and newborn health including: (a) increase in HIV transmission; (b) infertility in women and men; (c) ectopic pregnancy and maternal morbidities; (d) first trimester abortions; and (e) severe neonatal eye infections that may lead to blindness.

Effective antimicrobial therapy forms an essential component in the management of gonococcal infections. Over recent years, the gonococcus has rapidly acquired resistance to commonly used antibiotics and very few treatment options remain; hence, regular monitoring of antimicrobial resistance is very important. However, many low- and middle-income countries lack the laboratory facilities required to conduct antimicrobial resistance monitoring, resulting in very limited, or a complete lack of, ongoing surveillance.

<sup>1</sup> WHO *Global action plan to control the spread and impact of antimicrobial resistance in Neisseria gonorrhoeae*

## 4. STI surveillance systems

Surveillance is the systematic collection, collation and analysis of data, with prompt dissemination to those who need to know, for relevant action to be taken. A well-functioning disease surveillance system provides information for planning, implementation, monitoring and evaluation of public health intervention programmes. STI surveillance is usually conducted through existing health-care services, as well as through periodic surveys of assessments of the prevalence and etiologies of syndromes.

### 4.1 Rationale for STI surveillance

STI surveillance has been weak over the years, for reasons such as:

- lack of clear national guidelines;
- lack of political and financial commitment;
- lack of capacity to analyse and use data;
- the asymptomatic nature of some STIs, particularly in women;
- stigma and discrimination within the context of key populations at higher risk of STI;
- limited reporting from the private and informal health sectors where most STIs are treated.

Reliable and consistent information on the burden of STIs guides effective prevention and control efforts. Countries that have implemented STI surveillance successfully have been able to target their resources where needed. For example, Thailand has long been recognized as a country in South-East Asia with a consistent STI/HIV surveillance system. In the early 1980s, the main mode of transmission of STIs was between female sex workers and male clients. Approximately 60 000 to 100 000 STI cases were reported among male clients during 1982 to 1988. This information was used to design and implement an integrated STI control programme by the Ministry of Public Health, including 100% condom use in brothels in the late 1980s. The success of the intervention was demonstrated by a substantial reduction in the number of reported STI cases and a fivefold reduction in the number of males treated at the STI clinics between 1990 and 1995. This trend was found to be uniform across the country.

Routine case-reporting relies primarily on symptomatic cases. However, due to the largely asymptomatic nature of a number of STIs, screening is required to identify these infections. Information from screening programmes for STIs has been used to supplement data from routine surveillance. Such strategies have been effective in identifying resurgence of syphilis and used to implement interventions that are effective, feasible and cost effective for the prevention of long-term sequelae and adverse outcomes of pregnancy. However, screening for other STIs such as *Chlamydia trachomatis* is expensive and not feasible in many settings and its cost effectiveness has not been clearly demonstrated.

This document aims to address important issues related to STI surveillance and to give guidance to countries to establish and implement STI surveillance systems and to use the data generated from surveillance to improve STI care services.

### 4.2 The objectives of STI surveillance

Information from STI surveillance helps to:

- describe and monitor the magnitude of infections that are sexually transmitted, their distribution in diverse populations and trends of STIs over time;
- provide information for advocacy, programme planning and management, by:
  - providing data to monitor and evaluate the impact of interventions
  - helping to define needed resources for the prevention and care of STIs;
- determine etiologies and antimicrobial susceptibilities of STIs, to improve patient care.

### 4.3 Principles of STI surveillance

The principles discussed next apply within the above objectives.

#### 4.3.1 Feasibility

The STI surveillance has to be adapted to a health system's structure and capacity. It is better to have a simple system that works than a complex one that does not work.

In order for all sites and areas in the system to report consistently, surveillance should be an integral part of routine case-management procedures. This will be made easier if

reporting forms and procedures are made simple, easy to understand and user-friendly and only information that will be used is collected.

An increase in the volume of data collected leads to increased complexity of reporting forms; as a result, reporting and analysis is likely to be incomplete because it is considered too cumbersome and complex. If more detailed information is needed, specific studies in selected sites are recommended.

#### 4.3.2 Continuity and sustainability

In order to be coherent and comprehensive, STI surveillance requires long-term investment to ensure continuity.

If data are not regularly available, interpretation and decision-making will be difficult, resulting in ineffective use of resources, so sustainable human and financial resources should be assured.

#### 4.3.3 Standardization and consistency

In order to interpret data meaningfully and compare across time and place, it is important that data are collected using standardized procedures, and changes in data-collection methods should be kept to a minimum.

Uniform case definitions and reporting forms, as well as consistent reporting procedures should be implemented by all reporting sites in the systems. All sites should, at a minimum, report the same data elements for each case. It is important when undertaking trend analysis, to only include data collected at the same sites.

Should new technologies necessitate change, this should be done systematically and with careful planning, taking into account the resources, the structure of the health system and training needs. For example, new technology may allow the reporting of syphilis seroprevalence data based on the results of rapid testing. However, careful interpretation of data will be needed during the transition period. The new testing approach and the data obtained have to be validated by using the testing algorithm that was used before the new test became available.

#### 4.3.4 Confidentiality of STI surveillance data

All STI surveillance programmes should observe the principle of medical confidentiality that prevents unauthorized disclosure of personal identifying information on patients and ensures the protection of human rights. Reporting of surveillance data should be anonymous. STI control programmes should develop a written policy on confidentiality and anonymity for STI surveillance data, which include the following:

- all personal identifying information should be removed at the health-care facility before data are reported to the next level. Such reporting can usually be based on aggregated data. Staff responsible for recording, storage and reporting of STI surveillance data should be educated about the importance of privacy and confidentiality;
- all raw data should be stored in a secure place with access limited to authorized personnel only.

For more details use the UNAIDS interim guidelines: *Guidelines on protecting the confidentiality and security of HIV information* (14).

#### 4.3.5 Regular feedback

It is important that timely feedback (through meetings, newsletters, etc.) is provided to all personnel that are involved in the surveillance system.

### 4.4 Core components of STI surveillance

The core components of STI surveillance for effective STI control programmes consist of:

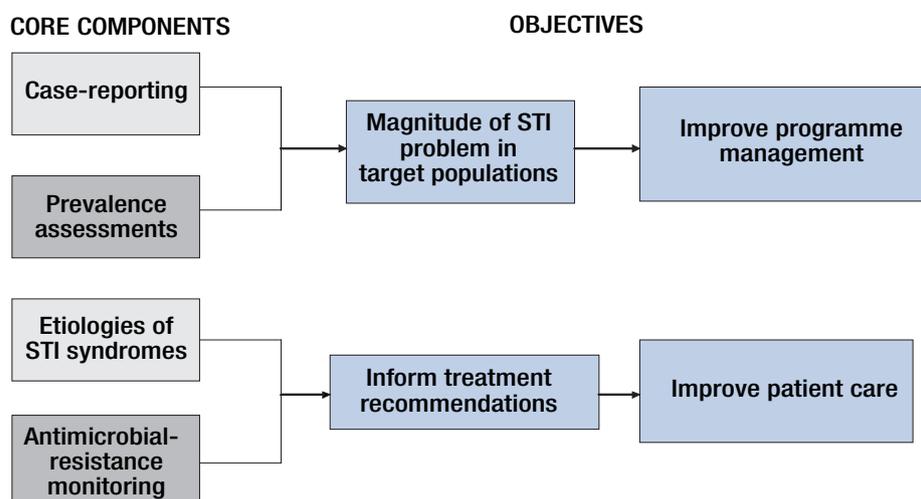
- *STI case-reporting using syndromic and etiologic approaches*: information obtained from case-reporting is used to define the magnitude of the STI problem in the populations presenting for STI care;
- *assessment of the etiologies of syndromes*: the etiologies of STI syndromes need to be assessed periodically, to inform correct treatment recommendations and to estimate the disease burden when combined with syndromic case-reports;
- *antimicrobial resistance monitoring*: periodic assessment of antimicrobial resistance patterns, particularly for *Neisseria gonorrhoeae*, are needed to inform correct treatment recommendations;

- *prevalence assessment and monitoring*: prevalence studies are used to determine the magnitude of STIs among persons in defined populations. Prevalence assessment and monitoring identifies subgroups at risk and, when conducted consistently over different points in time, serves to monitor trends of infection in defined populations.

In addition to prevalence studies, behavioural studies may yield important information for interpreting infection surveillance data (health-care seeking) and for planning and monitoring of primary prevention strategies (risk determinants). These studies are usually complex and strongly dependent on the respective society settings. They will not be discussed in detail in this document. However, more information on behavioural studies in the context of second-generation HIV surveillance can be found in Section 4.6.

These core components complement each other and provide a framework for surveillance that can be adapted for use in most countries. The methods by which they are implemented will depend on the existing STI surveillance infrastructure, particularly the extent to which laboratory testing is available for routine clinical care, and on the structure of the health information systems that are already in place for reporting as part of integrated disease surveillance. When the information obtained from components of STI surveillance (see Figure 1) is used together, it provides a comprehensive picture of the burden of STIs in a country.

**Figure 1**  
**Objectives and core components of STI surveillance**



#### 4.5 Making use of surveillance data

Data generated from surveillance should be up to date, complete, consistent and used to improve STI services. STI surveillance data have to be analysed and converted to information. This information will assist STI control programmes to target interventions where needed and revise treatment guidelines that will help improve patient care. STI surveillance data must be used at local, regional and national levels for prevention activities and advocacy at each level. Regional and national information on STI burden also informs the development of global STI estimates. Data from STI surveillance can also contribute to HIV surveillance.

#### 4.6 STI surveillance as a component of second-generation HIV surveillance

First-generation HIV surveillance relied solely on data from acquired AIDS case-reporting. In the year 2000, second-generation HIV surveillance was promoted, to tailor surveillance systems to the epidemic state of a country. Specifically, it was proposed that second-generation surveillance should:

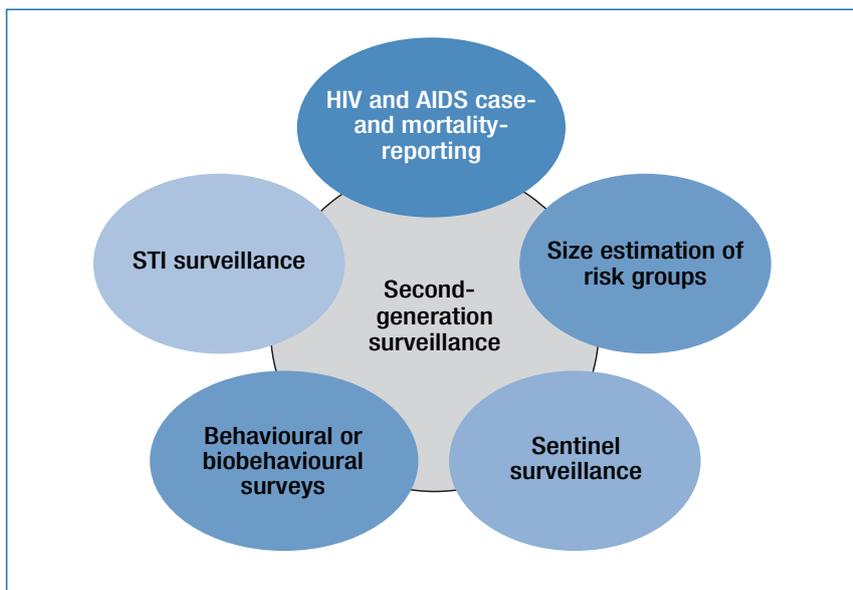
- be dynamic and change with the epidemic;
- use data-collection resources to generate the most useful information;
- combine biological and behavioural data for maximum explanatory power;
- integrate information from other sources;
- use results to increase and improve the response.

A more recent update in 2012 has retained STI as an important element of second-generation surveillance (6).

STI surveillance has a special role in second-generation HIV surveillance by being an essential component of this surveillance approach (see Figure 2). STI surveillance is not only its own core component, but can also be a part of other components such as behavioural or biobehavioural surveys

and sentinel surveillance. Furthermore, data obtained through second-generation HIV surveillance, such as size estimation of risk groups and behavioural surveys, for example, can be informative for STI surveillance purposes.

**Figure 2**  
**Components of second-generation HIV surveillance**



Adapted from *Guidelines for second generation HIV surveillance: an update: know your epidemic*. Geneva, World Health Organization, 2011 (6).

As STIs are markers of unprotected sexual intercourse, surveillance for incident STI (for example, urethral discharge, primary and secondary syphilis, and gonorrhoea) within second-generation HIV surveillance can serve as:

- early warning of the epidemic potential of HIV from sexual transmission in a particular population, particularly where HIV infection has not yet been established;
- an indication of ongoing high-risk sexual activity that may need more aggressive programme interventions to reduce risk;
- strengthening of the surveillance of STIs is, therefore, an important component of second-generation HIV surveillance.

## 4.7 Criteria for selecting STIs for surveillance

Criteria to select and prioritize diseases for surveillance include: the burden of disease or impact on health, the epidemic potential of the infection, changing patterns of disease, the preventability through public health activities and the social and economic impact. Determination of which STIs to prioritize for surveillance can be done by ranking each infection against these criteria. Using this exercise, key conditions and STIs to be included in STI surveillance are as follows (see Box 1 for details):

- *etiologic*: syphilis, gonorrhoea
- *syndromic*: urethral discharge and genital ulcer disease

### Box 1

#### Key conditions for STI surveillance

##### Etiologic conditions

###### *Syphilis*

Syphilis caused by *Treponema pallidum* is a key infection for STI surveillance. Some reasons identified to support this recommendation are:

- it is a preventable and treatable infection;
- it is considered a public health problem because untreated early syphilis in pregnancy causes stillbirths and neonatal deaths, even in low-prevalence settings;
- maternal screening and control of syphilis is a cost-effective intervention;
- as a genital ulcer disease, it facilitates HIV transmission and acquisition;
- there are global efforts to control genital ulcer diseases and congenital syphilis;
- it can serve to monitor trends, if the appropriate diagnostic tools are used.

###### *Gonorrhoea*

Gonorrhoea caused by *Neisseria gonorrhoeae* should be considered a key infection for STI surveillance for the following reasons:

- it is a preventable and treatable infection;
- untreated, it leads to severe complications and sequelae;
- it has a high morbidity rate in both men and women;
- the infection has a high epidemic potential;
- high levels of resistance to traditional antimicrobials and increasing resistance to currently recommended treatment options may render this infection untreatable;
- it can serve to monitor trends, if the appropriate diagnostic tools are used.

###### *Chlamydia*

*Chlamydia trachomatis* infection:

- is preventable and treatable;
- may have similar epidemic potential as gonorrhoea;
- has a high burden of disease, especially among adolescents;
- causes adverse health outcomes such as pelvic inflammatory disease, infertility, ectopic pregnancy and neonatal infections.

Screening for *Chlamydia trachomatis* infections is not feasible in many settings and, therefore, cannot be recommended for inclusion in routine surveillance programmes in all countries. However, infection may be monitored as part of discharge syndromes and be included in prevalence assessments, see Sections 6 and 7.

### **Chancroid**

Chancroid caused by *Haemophilus ducreyi* is more susceptible to control measures than other common STIs and is feasible for eradication. It is a cofactor for the spread of HIV infection. Because of difficulty in diagnosis, it cannot be recommended for routine etiological surveillance in every setting. However, it should be monitored as part of genital ulcer disease syndrome, see Section 6.

### **Trichomoniasis**

Trichomoniasis caused by *Trichomonas vaginalis*:

- is a preventable and treatable infection;
- is the most prevalent non-viral STI;
- if untreated, leads to adverse outcomes in pregnancy and may potentiate HIV transmission.

However, diagnostic facilities for trichomoniasis are still limited, and in terms of cost and performance it cannot be recommended for routine surveillance in all countries. However, it may be monitored as part of discharge syndromes and be included in prevalence assessments, see Sections 6 and 7.

## **Syndromic conditions**

### **Urethral discharge syndrome**

Urethral discharge syndrome is considered a key syndrome for STI surveillance for the following reasons:

- it is a preventable and treatable syndrome;
- the burden of urethral discharge syndrome is high;
- the most common causative agents (*Neisseria gonorrhoeae* and *Chlamydia trachomatis*) are prevalent and lead to adverse health outcomes;
- the syndrome itself is generally indicative of a STI.

### **Genital ulcer disease syndrome**

Genital ulcer disease syndrome is also considered a key syndrome for STI surveillance because:

- the burden is high;
- classical causes are syphilis and chancroid, which are preventable and treatable;
- it facilitates HIV transmission;
- the increasing role of HSV as the most prevalent cause of genital ulcer disease requires close monitoring and appropriate management.

### **Vaginal discharge syndrome**

Bacterial vaginosis is the commonest cause of vaginal discharge syndrome and is not sexually transmitted. Thus, inclusion of vaginal discharge syndrome for STI surveillance should be interpreted with caution.

- Cases of vaginal discharge should not be recorded and included in the tally for STIs.
- However, the syndrome indicates the burden of infections other than STIs in women and enables estimation of drug requirements.
- Periodic assessment of the etiologies of vaginal discharge will allow an estimation of STIs in women with vaginal discharge in that setting.

### **Lower abdominal pain syndrome in women**

As with vaginal discharge, lower abdominal pain syndrome in women can be useful by providing information on the number of cases seen, and assists with the allocation of resources and pharmaceuticals. However, this syndrome is not reliable for assessment of STI incidence or prevalence or to measure the impact of a STI programme, since it can be caused by other pathogens as well as STIs.

#### 4.7.1 Populations for STI surveillance

Universal case-reporting generally captures only symptomatic patients seeking care at health-care facilities. However, a significant proportion of symptomatic people with STIs do not seek care and need to be captured for purposes of more comprehensive surveillance. This proportion includes most-at-risk and vulnerable populations, who often have limited access to health-care service, including sex workers, users of injected drugs, MSM, long-distance truck drivers,

migrants and adolescents. Special targeted approaches may be needed to identify these populations and determine the burden of infection among them. Such population groups need to be determined locally according to country situations and assessments. The optimum and representative sites for collecting data from such populations will also need to be determined by each national programme.

Table 1 presents the WHO-recommended components of STI surveillance, as well as approaches and methods within the context of different populations.

**Table 1 WHO-recommended populations, components and approaches for surveillance**

Population category	Population	Component of surveillance	Possible sites	Surveillance approaches and methods
General population	Sexually active men and women	Routine case-reporting (universal or sentinel)	Primary health-care clinics (at which STI consultations take place) Specialized referral STI clinics Family planning clinics Gynaecology clinics Urology clinics	Syndromic surveillance Laboratory-based surveillance (where feasible)
	Pregnant women	Routine case-reporting (universal or sentinel)	Antenatal clinics Primary health-care clinics	Laboratory-based (syphilis serology) and syndromic surveillance
	Adolescents	Routine case-reporting (universal or sentinel) Prevalence assessment	Community-based adolescent-friendly health services Youth centres School-based clinics Primary health-care clinics (STI clinics where STI clinics are part of primary health care)	Syndromic surveillance Laboratory-based surveillance
Bridging	Clients of sex workers Bisexual men Patients seeking treatment for STIs Country-specific population, e.g. military; seafarers; transport workers	Routine case-reporting (universal or sentinel) Prevalence assessment	Primary health-care clinics STI clinics  Military clinics Occupational health clinics Clinics for seafarers	Laboratory-based surveillance (syndromic surveillance where laboratory facilities are not available)
Most-at-risk population	Sex workers People who use drugs MSM Clients of sex workers	Routine case-reporting (universal or sentinel) Prevalence assessment	Primary health-care clinics “Hot spots” <sup>a</sup> STI clinics	Laboratory-based surveillance. (syndromic surveillance where laboratory facilities are not available)

<sup>a</sup>“Hot spots” or catchment areas that countries have utilized for surveillance include seaports, mines (e.g. South Africa and China), long-distance truck stops (e.g. India and East Africa), brothels and entertainment parlours (e.g. Thailand, Cambodia), and gay-bars, clubs and saunas (Europe, north and Latin America).

## 4.8 Measurement issues in surveillance

There are over 30 different pathogens that are sexually transmissible. Some of them produce symptoms, while others are asymptomatic. Infections and syndromes that have an acute onset, are symptomatic and are specific for recent infection with an STI pathogen(s) are the best indicators of STI incidence. STIs with largely acute and symptomatic presentations include:

- primary and secondary syphilis
- gonorrhoea in men (urethral discharge)
- chancroid.

### 4.8.1 Incidence

The incidence of a health problem is defined as the number of new cases occurring in a population during a defined period of time. The incidence is the number of new cases of a health problem that occur in a population at risk within a specified period of time. The numerator is the number of new cases occurring in a population during a defined time period. The denominator is the population at risk during the same period:

$$\text{Incidence } (I) = \frac{\text{number of new cases of a specific infection during a defined period}}{\text{population at risk in the same time period}}$$

### 4.8.2 Prevalence

The prevalence of a health problem is defined as the total number of cases in the population at a given time. The prevalence is the total number of cases in the population, divided by the number of individuals in the population during a defined period. The numerator is the total number of infections or diseases during a defined period and the denominator is the total population during the same period. Expressed mathematically, if “A” is the number of individuals in the population with the infection or disease at a given time, and “B” is the number of individuals in the population without the infection or disease at the same given time, then:

$$\text{Prevalence } (P) = \frac{\text{number of persons with a specific infection or disease at a given time } (A)}{\text{total population at the same time } (A + B)}$$

The prevalence of infection measures how common a condition is within a population during a defined period. However, because of the variable health-seeking behaviour patterns of people, the asymptomatic nature of STIs, the limited availability of laboratory tests and the poor sensitivity of affordable diagnostic tests, the determination of both incidence and prevalence of STIs is difficult. Therefore, to better define the burden of STIs, prevalence-assessment surveys are carried out among specific population groups such as sex workers, women attending family planning clinics, pregnant women, migrants, adolescents, etc.

## 5. Core components of STI surveillance

### 5.1 STI case-reporting

STI cases can be identified through symptomatic individuals seeking care for STIs and through other additional strategies as follows.

#### 5.1.1 Case-finding

This involves opportunistic testing of persons attending health-care facilities for reasons other than for STI care, e.g. youth, women in general, sex workers, family planning clinic attendees, among others:

- examination of women attending clinics for maternal and child health and family planning;
- contact tracing – tracing and treating contacts of persons presenting with STI;
- examining and investigating persons attending health-care facilities who may be at greater risk for infection, such as sex workers.

#### 5.1.2 Screening

Screening involves examining and investigating asymptomatic persons not attending health-care facilities. This may be targeted at groups considered to be at higher risk for infection in the community, such as sex workers, long-distance truckers, uniformed services, youth, travellers, intravenous drug users and users of volatile substances.

*All STI cases identified through either case-finding or screening, or a combination of both approaches, should be captured by the surveillance system and reported.*

Case-reporting is the process of reporting cases of diseases from health-care facilities or laboratories to public health authorities. STI surveillance has traditionally relied on cases reported from health-care facilities as a core surveillance activity, to help assess the burden of disease and to monitor trends over time.

Case-reporting of STIs can be conducted on a *universal* or *sentinel* basis, depending on the national reporting system as well as on how services for the prevention and control of STIs are organized and delivered. Universal case-reporting is the process where all health-care facilities tally and

report every case seen. Sentinel-site case-reporting is the collection of data from a select number of sites to capture health problems among “sentinel” populations thought to be representative of a population group of interest.

In most settings, on-site laboratory support is not available and *syndromic* case-reporting is the only option. *Etiologic* STI case-reporting, used in many high-income countries, is feasible if STI diagnostic tests are routinely available at every health-care facility.

*Depending on the availability of resources, reporting of diagnosis can be based on syndromic or etiologic approaches.*

STIs considered essential for etiologic STI case-reporting are:

- *Treponema pallidum* (syphilis);
- *Neisseria gonorrhoeae*.

As recommended in the UNAIDS/WHO *Guidelines for sexually transmitted infections surveillance*, the only syndromes that are useful for monitoring trends in STI incidence are *urethral discharge in men* and *genital ulcer disease* (non-vesicular) in both men and women (see also Section 4.7).

#### 5.1.3 Case definitions for surveillance of STIs

A case definition is a set of criteria using clinical and/or laboratory parameters to denote whether or not a person has a particular infection or disease. In order for a particular infection, such as syphilis, or disease, such as genital ulcer disease, to be consistently considered a case, it is essential to define and standardize the methods of measuring the chosen criteria, and as far as possible to be precise and unambiguous. Using the same case definitions throughout a country's public health system assures comparability over time and across regions.

Case definitions for the purposes of STI surveillance may be based on syndromic or etiologic diagnosis.

Syndromic case definitions do not require laboratory diagnostic tests. A syndrome is a collection of signs and symptoms that tend to occur together and are clinically indicative of a particular disease.

Syndromic case definitions that can be used for surveillance purposes are listed in Box 2.

## Box 2

### WHO-recommended clinical criteria for syndromic case definition for surveillance purposes: key STI syndromes

#### Genital ulcer disease

An ulcer (a visible break in the skin) on the penis, scrotum or rectum in men, and in women on the labia, vagina, cervix and rectum. Genital ulcer disease syndrome can be caused by *Treponema pallidum* (syphilis), *Haemophilus ducreyi* (chancroid), *Chlamydia trachomatis* (strains L1–L3 (*Lymphogranuloma venereum*), *Klebsiella granulomatis* (granuloma inguinale) or HSV-1 or HSV-2 (genital herpes).

#### Urethral discharge

A discharge in men (with or without dysuria) seen at the urethral meatus with or without milking/expressing the urethra. Urethral discharge syndrome is commonly caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.<sup>a</sup>

<sup>a</sup>Other infectious agents associated with urethral discharge syndrome include *Mycoplasma genitalium*, *Ureaplasma urealyticum* and *Trichomonas vaginalis*.

Reporting based on etiologic case definitions is only possible where well-developed systems of laboratory diagnosis are incorporated into routine STI clinical care. For certain STIs (e.g. syphilis), the stage of the disease is defined by clinical findings and history, while the definitive etiology is identified by laboratory tests.

In cases where etiologic case definitions are used, further case classification can be made into probable case or confirmed case, depending on the ability of the laboratory test to definitively identify the organism (see Annex 1).

*All probable and confirmed cases should be reported.*

Etiologic case definitions that can be used for surveillance purpose are listed in Boxes 3 and 4.

## Box 3

### WHO-recommended clinical and laboratory criteria for etiologic case definition for surveillance purposes: gonorrhoea

- *Probable*: microscopic demonstration of Gram-negative intracellular diplococci in a sample from the endocervix or urethra or rectum.
- *Confirmed*: isolation by culture of oxidase-positive, Gram-negative intracellular diplococci confirmed with sugar utilization (or other specific species-confirmatory method) or demonstration of *Neisseria gonorrhoeae*-specific DNA in a clinical specimen (from the endocervix, urethra, rectum or pharynx) by a properly evaluated nucleic acid detection test.

Active or untreated syphilis can be differentiated from previously treated syphilis by using a combination of treponemal (such as *Treponema pallidum* haemagglutination assay (TPHA) or a rapid treponemal test) and non-treponemal (such as venereal disease research laboratory (VDRL) and rapid plasma regain (RPR) tests).

#### Box 4

#### WHO-recommended clinical and laboratory criteria for etiologic case definition for surveillance purposes: syphilis

##### Primary and secondary

- *Probable*: an illness with ulcers (primary) or mucocutaneous lesions (secondary) and a reactive serologic test (non-treponemal or treponemal).
- *Confirmed*: demonstration of *Treponema pallidum* in clinical specimens by dark-field microscopy, direct fluorescent antibody test for *Treponema pallidum* (DFA-TP), nucleic acid test or equivalent methods.

##### Latent<sup>a</sup>

- *Probable*: no clinical signs or symptoms of syphilis. Laboratory criteria for latent syphilis for surveillance purpose:
- *in a patient with no prior syphilis diagnosis*: syphilis-treponemal-positive serology (rapid treponemal test or TPHA) confirmed by a non-treponemal test (VDRL or RPR) without titration;
- *in a patient with a prior syphilis diagnosis*: syphilis-treponemal-positive serology (rapid treponemal test or TPHA) confirmed by a non-treponemal test (RPR) with titration demonstrating fourfold or greater increase from the last non-treponemal test titre.

<sup>a</sup> Latent syphilis may be further characterized as *early latent*, if there is evidence that the infection was acquired within the previous 24 months, and *late latent*, if there is evidence that the infection has been present for more than 2 years.

#### 5.1.4 Data elements

To better describe the distribution of STIs in the population, details about each individual, referred to as data elements, are essential. The potential data elements for STI surveillance include demographic information such as age and sex, education, residence and employment; clinical details such as diagnosis, treatment, previous infections; and sexual behaviours such as condom use, sexual partners and sexual orientation. The selection of data elements will depend on the specific purposes for which the data will be used and the type of surveillance in a particular country.

For better quality and utility of data and to enhance the participation of a wider variety of facilities, a limited number of core data elements should be collected. These are age, sex and diagnosis.

Information and data collected should be from various population groups, including adolescents. Therefore, details about age should be recorded so that STIs can be monitored by age groups. In most cases, STI data will be reported for the youngest sexually active age groups (15–24 years) as well as across the reproductively active age range of 15–49 years. Desirable age categories, especially for the younger age groups, should be by 5-year intervals of 10–14 years, 15–19 years, 20–24 years, 25–29 years and over 30 years.

At minimum, the age categories of 15–24 years and above 25 years should be used for reporting on STI.

Women, particularly of adolescent age, are more vulnerable and at greater risk for STIs, due to a variety of factors including sex inequalities and biological and sociocultural factors, as well as lack of information on STIs and means to prevent infection. It is important that information is collected and disaggregated by sex, in order to monitor the distribution of STIs and implement appropriate interventions for prevention and care.

#### 5.1.5 Universal case-reporting

Universal case-reporting is a commonly implemented form of STI surveillance in many countries and is used to obtain data on the facility-based burden of STIs. Universal case-reporting from health-care facilities does not provide data on the burden of STIs in the population of a country. This is in part due to the limited use of health-care facilities that routinely report STI cases, and to geographical, financial and sociocultural barriers. However, when consistent, STI data generated from universal reporting can be used to identify trends. To obtain data on the burden of STI in the population, other methods are necessary. These may include data from prevalence assessments, screening interventions and special studies.

In countries where a national reporting system for infectious diseases or integrated disease surveillance exists, STI case-reporting should be an integral part of the national health information system. The responsibility of ensuring the quality of STI data rests with the STI control programme or the person or unit responsible for STI control.

In primary health-care clinics, as a part of universal integrated disease surveillance, a reporting form is used to monitor the number of new STI cases by clinic site and date; this form should provide the data elements for reporting by sex, age and diagnosis. Where feasible, additional data elements on patients can be collected; information such as marital status, occupation, residence and education can be

included. Universal case-reporting will be more meaningful if standard protocols and case definitions are used.

Universal case-reporting has limitations, for the reasons stated above. However, it has the advantage of being simple and readily able to be integrated into other disease surveillance systems. Universal case-reporting also provides information that is important for planning health services at the health-facility level and when data are aggregated at upper level according to the health system structure, i.e. district, subnational and national level.

Strengths and limitations of universal STI case-reporting are summarized in Table 2.

**Table 2**  
**Universal STI case-reporting: strengths and limitations**

Description	Minimum set of data elements collected on all STI cases from all health care facilities
Approaches	Syndromic or etiologic case-reporting.
Information obtained	Facility-based burden and STI trends.
Advantages	Surveillance of entire facility-based population. Able to track trends of STIs within the setting. Provides information useful for planning STI services.
Limitations	Difficult to interpret trends because of underreporting, underdetection and fluctuations in health-care-seeking behaviours.

### 5.1.6 Sentinel-site case-reporting

Within the context of the above-mentioned STI surveillance objectives, reliable estimates of the magnitude of STIs and, particularly, trends over time are needed. However, in order to obtain this information, it is not necessary to collect data about all cases. Sufficient reliable results can be obtained, assuming that the STI or syndrome or other information of interest, as well as representative facilities or populations, can be defined and respective data collected and reported at sentinel sites.

In sentinel-site case-reporting, a sample of health-care facilities known as sentinel sites report all cases of STIs and/or other related conditions of interest. Countries may also decide to add more data elements to collect about each case. The additional data elements may include patients'

demographic, behavioural and sociocultural profiles, as well as information about partner notification and treatment. Data from sentinel surveillance sites can be used in conjunction with data obtained from universal case-reporting to help describe the national burden of STIs.

The objectives of STI sentinel surveillance will depend on the existing STI surveillance system.

In countries where a national universal reporting system exists, the objectives of sentinel surveillance are to improve the quality of STI surveillance data in terms of completeness and consistency; to capture cases of STI in specific populations of interest; and possibly to provide a wider range of information about each case.

Active surveillance through sentinel sites should ensure higher-quality data and the collection of additional data such as demographic, behavioural and partner notification information. These data complement information collected from universal case-reporting. A combination of information from universal and sentinel sites provides a better understanding of the populations infected with respect to the distribution of STIs in the community and the behaviours putting them at risk.

Therefore, data obtained through universal case-reporting can be calibrated and complemented by sentinel surveillance.

In countries where no universal reporting system exists, a case-reporting system may be instituted at specially designated sentinel sites. In this case, the objectives of STI surveillance are to assess the proportion of clinic attendees with STIs or STI syndromes; determine the epidemiology of STIs that are seen at the clinics; determine the characteristics of STI patients who attend the sentinel sites; and assess trends in the numbers of cases at sentinel sites as a possible indication of trends in infection prevalence in the community (although many factors, in addition to morbidity, may affect case numbers).

Another option is to perform universal case-reporting in sentinel districts; that is, to select specific geographic areas where reporting from all facilities will be standardized. This may enable generation of a minimum population-based rate of disease for those areas under surveillance.

A major advantage of STI sentinel-site case-reporting is that it is more manageable to use fewer sites, which are more easily supervised and can participate in a more systematic and consistent manner to collect higher-quality data.

A disadvantage is that sentinel sites may not be entirely representative of the populations of interest, as the acceptability and accessibility may be limited by factors such as location, health-care provider attitude, business hours, etc.

For STI sentinel surveillance data to be most useful, it is important that:

- reporting is consistent, complete and regular;
- trained staff and adequate financial resources are available;

- laboratory capacity and quality, if instituted, are sustained;
- regular supervision and feedback are available;
- sites are representative of the populations of interest;
- standard protocols, reporting forms and case definitions are available.

## 5.2 Factors to consider when selecting and implementing surveillance in sentinel sites

Sentinel-site case-reporting should not be confused with other STI surveillance activities that can be performed at “sentinel sites” – specialized clinics – or among “sentinel populations”, including assessment of STI prevalence and syndrome etiologies, antimicrobial resistance monitoring, and special studies, as discussed next. The term “sentinel surveillance” has frequently been used to refer to any or all of these activities, without clarifying the objectives and methods for each.

*The selection of sentinel sites depends on the objectives of STI sentinel surveillance.*

All antenatal clinics should screen all pregnant women for syphilis and regularly record and analyse test results. Where feasible, some antenatal clinics may be selected as sentinel sites, to assess the prevalence of active syphilis by conducting confirmatory testing among women with positive treponemal serology and additional STIs such as gonorrhoea and *Chlamydia trachomatis*. If combined with postnatal care, these sites could also collect data on cases of ophthalmia neonatorum and congenital syphilis. Congenital syphilis may be used as an indicator of the quality of the maternal and child health-care system.

Many countries have specialized STI service facilities. They are generally well equipped and often participate in some surveillance activities. These facilities can be used as sentinel sites to collect the information needed for defining diagnostic and treatment schemes, including the distribution of pathogens (etiologic diagnosis) and, where feasible, antimicrobial susceptibility testing. However, these facilities usually cover only a small number of all STI patients. The population covered by these facilities, and thus the denominators, are unknown. Therefore, data collected in these facilities should not be used to estimate the magnitude of the problem or trends over time. A combination of information from universal case-reporting and sentinel sites can be triangulated and

provides a better understanding of the populations infected and the extent of the burden of infection.

In order to improve the quality of data and to capture the populations of interest, selection of sentinel sites should take into consideration the structure of the health-care-delivery system and the involvement of other disciplines in the provision of STI prevention and care.

Key factors to consider for the selection of sentinel sites include the following:

- geographical representativeness, to ensure inclusion of both rural and urban populations;
- inclusion of public and private sectors and nongovernmental organizations (NGOs) that provide health services;
- inclusion of sites that provide services to populations of interest and hard-to-reach populations;
- inclusion of populations that are proxy for the general population, e.g. antenatal and family planning clinic attendees;
- inclusion of specialized clinics (e.g. STI clinics), where additional studies such as antimicrobial resistance testing and determination of etiologies of syndromes may be conducted;
- inclusion of other relevant specialties such as dermatology, gynaecology, paediatrics and urology;
- adequate financing and provision of commodities;
- human resource in terms of numbers and trained of staff.

Facilities that may be important to capture the distribution of STIs in the population of interest include primary health-care clinics; reproductive health services such as antenatal and family planning clinics; adolescent and school-health services; occupational health clinics for factory workers, military personnel, seafarers and migrant workers; as well as “hot spots” for populations at higher risk of infection, including vulnerable young people; and other relevant outlets such a pharmacies. Other sectors to be considered include not-for-profit health services provided by NGOs or faith-based organizations (see Box 5).

<b>Box 5</b> <b>Sentinel site STI case-reporting: strengths and limitations</b>	
Description	Fewer sites collect and report higher-quality data.
Approaches	Syndromic or etiologic case-reporting.
Information obtained	Prevalence of STIs among population of interest, STI trends and other information of interest.
Advantages	More feasible to obtain higher-quality data. More manageable in terms of supervision, training and logistics Specific studies, such as resistance patterns, can be more easily added. Can be initiated in a limited number of sites where training, manpower and resources are available (“control of STIs”).
Limitations	Acceptability and accessibility of sites may be limited Possible bias if sentinel sites are non-representative of populations of interest.

The extent to which the private sector should participate in STI surveillance will depend on the degree to it provides STI care. If a significant proportion of STI care is provided by the private sector, it will be important for STI programmes to actively involve them in case-detection and case-reporting. The feasibility of collecting STI data from the private sector should be tested in a few sites before scaling-up throughout the entire country.

One of the difficult tasks for a government is to involve the private sector. To encourage participation of the private sector, the following methods may be used:

- involving private practitioners in national training programmes that offer continuing education units;

- instituting certification and accreditation schemes, peer reviews and self-regulatory mechanisms involving health professional associations;
- involving private practitioners in defining and implementing a research agenda.

The STI control programme needs to link with any such schemes taking place at the national level, to ensure that STI surveillance becomes a component of public–private partnership.

*In some countries, the same health-care providers often work in both private and public sectors and can, thus, be included in the site selection, as they may already be sensitized to the importance of STI surveillance.*

The STI control programme should put in place a mechanism to ensure sustained implementation of sentinel surveillance. It will need to define operational issues such as how often sentinel sites will report – quarterly, half-yearly or annually – and how often to conduct supervision. A training cycle will need to be put in place to ensure that all sites have adequately trained staff, taking into account staff turnover and expansion of capacity and the number of sentinel sites.

## 5.3 Data-collection and management

### 5.3.1 Data-collection

Collection of STI data is an integral part of STI case management. Data may be collected for both case management and surveillance. When data are collected for surveillance purposes, all health-care providers should have a clear understanding of their role in data-collection and recording, by being fully acquainted with the prevailing policy and instruments for recording and reporting.

### 5.3.2 Recording and reporting formats

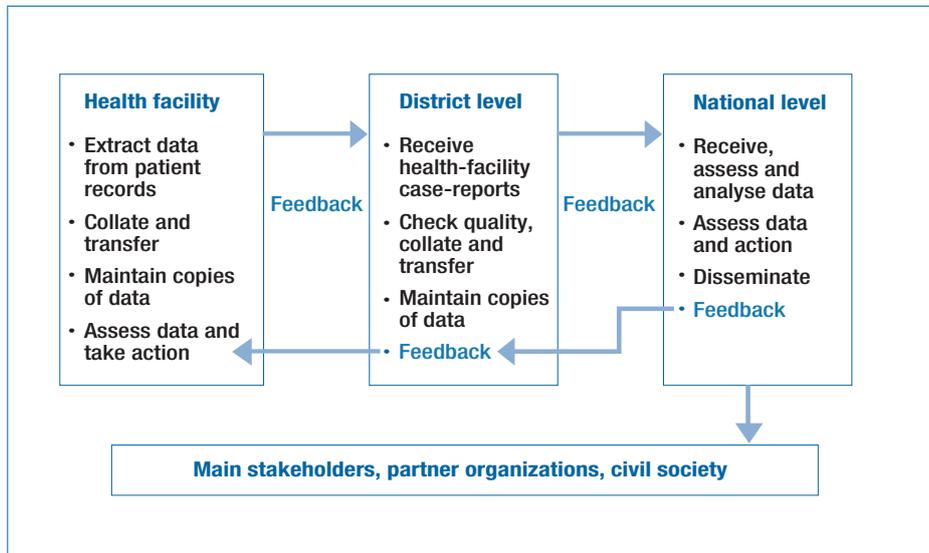
The process of data-collection requires different surveillance forms for specific purposes, which include recording and reporting. Recording forms usually include patient records

that contain personal identifiers, such as name and address. These details are confidential and should therefore be kept secure. Reporting forms, normally used to transfer data from one location to another, should be anonymous and not have any personal identifiers. When information from individual patient records is transferred to reporting forms, personal identifiers must be removed before the data are transferred. Reporting forms should be designed to facilitate data-collection. Simple, user-friendly forms with explanatory notes as needed should be used, so that demand on staff time and interference with patient care is as minimal as possible.

Countries have a variety of ways of capturing data for surveillance purposes, but it is recommended that within any particularly country or administrative setting, the same standardized forms are used at all sites. In Annex 3, samples of tally sheets are included that allow health-care providers to collect data with minimal additional human and technical resources. In this type of data-collection instrument, a check mark is made for each individual in the respective field for each case diagnosed. If an individual is diagnosed with two or more conditions (STI and/or syndrome), a check mark should be made for each diagnosis. This will give a more accurate estimate of the prevalence, incidence and trends of the different cases diagnosed. Data entry may include only new cases (first visit for the current complaint) or new and reattendances for the same complaint. Interpretation of the data needs to take this into account. Only new cases may indicate the incidence of infection. Keeping a record of both new cases and reattendances helps with estimation of the workload and requirements for drugs and commodities. Therefore, operational procedures need to be clear about whether only new cases or new and re-attendances are to be recorded and reported. The form should be structured in a way that clearly indicates whether it is the number of *persons* or *cases* or *both* that will be entered (see Annex 3).

The operational procedure should describe the flow of data and the frequency of reporting of data from the various levels (see Figure 3). At each level of reporting, there should be a designated person or a supervisor to check the completeness and correctness of data. Any missing or incomplete data should be followed up and corrected as much as possible.

**Figure 3**  
**Data collection and flow**



### 5.3.3 Data management

Before processing for analysis, data should be checked for:

- the completeness of data elements such as age, sex and diagnosis;
- the proportion of facilities from which data have been received;
- validity, in terms of the correctness of parameters entered for each case;
- the timeliness of reports received from all locations and facilities.

### 5.3.4 Data analysis

STI data should be analysed monthly, quarterly and annually, depending on the country situation. It is important that data are analysed at each level, as the results can be used to assess the STI situation at that level and take appropriate action. The overall analysis of data usually takes place at the national level.

At the national level, there may be an epidemiology unit for analysis of surveillance data on infectious diseases. Collaboration between this unit and the STI control programme is essential.

STI data are analysed by the following categories, to identify sites that are not reporting consistently:

- *geographic area:*
  - urban
  - rural
- *reporting site:*
  - primary health-care clinics
  - family planning clinics
  - gynaecology clinics
  - urology clinics
  - antenatal clinics
  - community-based adolescent-friendly health services
  - youth centres
  - school-based clinics
  - STI clinics
  - military clinics
  - occupational health clinics
  - “hot spots”
  - other
- *sex*
- *age group*

**Table 3 Types of data analysis**

Type of analysis	Description
By person	Analysis of specific STIs or syndromes stratified by age group and sex.
By place	Analysis to provide information about where clustering of disease might be occurring.  Stratified analysis by geographical area or reporting site to show if there are significant differences between places.
By time	Analysis to detect if there are any trends in case-reports over time (for example incidence increasing or decreasing).  Data for a specific quarter should be compared with the same quarter in the previous year.

STI data should generally focus on three parameters: person, place and time. Table 3 explains these parameters.

Data should also be analysed separately for each syndrome (if syndromic case-reporting is conducted), or for each infection (if etiologic case-reporting is conducted).

#### **Analysis by person**

Analysis by person is recommended for describing the population at risk of the disease under surveillance. A simple count of persons does not provide all the information needed to understand the impact of a disease on the community, health-care facility or district. It is useful to calculate a simple percentage of the number of cases reported from a site during a given period, in order to determine:

- the proportion of attendees of health-care facilities diagnosed with STI or STI syndromes;
- the distribution of various STI or syndromes among attendees of health-care facilities.

This percentage is also useful for comparing data collected at health-care facility, district or regional level.

The first step in analysing person data is to identify the numerator and denominator for calculating a percentage.

The numerator is the actual number of cases reported from a site during a given period (e.g. the number of urethral discharge syndromes reported during a year at a health-care facility).

The denominator is the total number of persons who attended the site for services during the given period (e.g. the total number of men who attended the health-care facility during the same year).

A simple percentage can be calculated to compare data from populations of different sizes. For example:

*The number of cases of urethral discharge syndrome diagnosed and reported in a year at a health-care facility:*

- health-care facility A: 24 200
- health-care facility B: 23 283

*Total number of men attending the health-care facility during the year:*

- health-care facility A: 672 222
- health-care facility B: 895 500

*The percentage of urethral discharge syndrome in health-care facility A:*

$$= 24\,200/672\,222 \times 100 = 3.6\%$$

*The percentage of urethral discharge syndrome in health-care facility B:*

$$= 23\,283/895\,500 \times 100 = 2.6\%$$

#### **Analysis by place**

Analysing data according to place gives information about where a disease is occurring.

As part of routine surveillance, it is advisable to create a map where places of relevance can be marked and be used to determine the areas where diseases are occurring. See also Section 4.6.1.

### **Analysis by time**

Analysing data to detect changes in the numbers of cases over time is the purpose of “time” or trend analysis.

Observing disease trends over time helps to show when regular changes occur and can be predicted. By examining events that occur before a disease rate increases or decreases, it may be possible to identify causes and appropriate public health action for controlling or preventing further occurrence of the disease. Data about time are usually shown on a graph. The number of cases is placed on the vertical or *y* axis. The time period being evaluated is placed along the horizontal or *x* axis. Graphs can show how many cases have occurred in a given time. It is easier to see changes in the number of cases by using a graph, especially for large numbers of cases, or to show cases over a period of time.

Analysis of sentinel-site surveillance data and universal-reporting data is similar, with the following exceptions:

- when analysing by place, it is important to be cautious in interpreting clustering (a “cluster” of patients from different health-care facilities being selected as a sampling unit), since sentinel sites may not be representative of other sites;
- compared to universal reporting, it may be more difficult to calculate population-based rates of STI in a sentinel system. However, if the population from which the clinic population is drawn is known, it can serve as a denominator to calculate prevalence.

To improve monitoring of STI incidence trends in a universal case-reporting system, it may be possible to selectively analyse data from reporting sites that provide consistent and high-quality data on time. These data may also be compared with case-reports of non-STI conditions from the same sites, to provide an estimate of the proportion of morbidity caused by STIs, in relation to other causes of morbidity over time.

The magnitude of STIs by category and trends should help in drawing preliminary conclusions about the burden of STIs.

At all levels of analysis, the data should be clearly summarized in tables, graphs or charts, so they are easily understood. Patterns and trends can be identified by doing so.

### **5.3.5 Interpretation of data**

*Interpretation of STI trends has to be undertaken carefully and should not be made outside the context of STI control programmes or the health-care system.*

The analysed data should be reviewed and the trends observed to assess if the reported cases for a given disease/syndrome are stable, decreasing or increasing. Increases and decreases may be due to factors other than a true increase or decrease in the number of cases being observed. The objective of the STI control programme should be to decrease the number of STI cases over time.

If decreases are not occurring, or marked decreases are seen in the absence of effective interventions, it is important to consider whether any of the following factors are affecting reporting:

- has there been a change in the number of health-care facilities reporting?
- has there been a change in the case definition being used to report diseases?
- is the increase or decrease a seasonal variation?
- has there been a change in screening or treatment programmes?
- are there any community outreach or health-education activities that would result in more people seeking care?
- has there been a recent immigration or emigration to the area, or change in refugee populations?
- have there been factors affecting health-seeking behaviour, such as opening of additional health-care facilities or a change in the opening hours?
- has there been any change in the quality of services being offered, such as availability or unavailability of medications or introduction of user fees, health-care staff being more helpful, drug availability?
- have there been any factors affecting reporting practices, such as changes in staffing or the training of staff handling case-reporting and data?

This information should normally be available as a part of monitoring and evaluation of the STI programme.

If there are any unexpected fluctuations (declines or increases in case-reports), officers at the national or regional level should investigate the cause(s) for the fluctuations by contacting and visiting the relevant sites.

Thus, variation in case-reporting should not be interpreted as weakness of the surveillance system, but as one way to obtain information on how the system of STI care and reporting is functioning.

To improve monitoring of STI incidence trends in a universal case-reporting system, it may be possible to selectively analyse data from reporting sentinel sites or special studies (see Sections 5.1.4; 5.2 and 7).

### 5.3.6 Use of data

It is important that the data generated from case-reporting is used at each level (health-care-facility level, district level and national level) to monitor the STI situation and take necessary action. Data should not be collected only for purposes of surveillance and reporting to a higher level. Surveillance is data-collection for action. Therefore, the information generated from surveillance data must be used to improve STI services.

#### ***At health-care-facility level***

1. Identify the physical features of the area:

- understand the population distribution and density of the area;
- show the distance between health-care facilities and villages;
- show significant occupation sites such as mines, construction sites, transport depots, etc.
- spot locations of disease cases and identify key populations at higher risk of STI;
- plan routes for supervisory visits (the list of questions to be addressed through a supervisory visit at each level can be found in Section 5.3.5).

2. Assess the incidence (new cases) of reported STI and compare data quarterly and annually for the health-care facility concerned. If using syndromic management, assess the incidence (new cases) of STI syndromes in the health-care-facility population.

3. Is there an increase or decrease in the number of cases reported?

- assess the proportion of attendees of health-care facilities diagnosed with STI or STI syndromes (from recorded new cases and follow-up treatment) in the health-care-facility population;

- get an approximate idea of the STI prevalence in the catchment population (if the clinic attendance pattern of the population is known).

4. Improve STI service delivery:

- estimate and order the STI medicines and condoms required for the health-care facility, depending on the STIs that are reported;
- provide in-service training in STI management to health-care providers;
- have quarterly/annual review meetings and disseminate surveillance data to the health administrators and to the health-care providers (including private providers) who manage patients, and discuss the findings.

5. Conduct prevention interventions for health-care-facility attendees and the key population at higher risk of STI in the catchment area; if known:

- provide the most up-to-date preventive message through STI counselling;
- make education and information material (posters, leaflets etc.) available and update them on regular basis;
- introduce a community-based outreach service for vulnerable and key populations at higher risk of STI.

#### ***At district level***

1. Identify the physical features of the area:

- understand the population distribution and density of the area;
- show the distance between health-care facilities and villages;
- show significant occupation sites such as mines, construction sites, transport depots, etc.
- spot the locations of disease cases and identify key populations at higher risk of STI;
- plan routes for supervisory visits.

2. Assess the trends in incidence (new cases) of reported STI (by syndrome or by etiology) and compare data quarterly and annually by health-care facility and district:

- is there an increase or decrease in the number of cases reported?
- is the difference in reported numbers uniform across the health-care facilities or only in some?

3. Assess the prevalence of STIs (from recorded new cases and follow-up treatment) for the district.

4. Communicate the finding with health-care facilities and conduct supervisory visits, if needed.

5. Improve STI service delivery:

- estimate and order the STI medicines and condoms required for the district, depending on the STIs that are reported;
- provide in-service training in STI management to health-care providers;
- have quarterly/annual review meetings and disseminate surveillance data to the district health administrators and to the health-care providers (including private providers) who manage patients, and discuss the findings.

6. Plan and monitor prevention interventions at health-facility and community (outreach) level.

#### ***At national level***

1. Assess the trends in incidence (new cases) of reported STI (by syndrome or by etiology) and compare data quarterly and annually by district and nationally:

- is there an abrupt increase or are the trends stable, or is there a gradual rise or fall of numbers?
- if trends are increasing or decreasing, is this observed across all districts or only in some districts?

2. Assess the prevalence of STIs (from recorded new cases and follow-up treatment) nationally and compare data with previous years.

3. Estimate the STI burden for the country.

4. Communicate with districts on the findings and quality of surveillance reports, and conduct supervisory visits, if needed.

5. Improve STI service delivery:

- develop or update national STI strategies, policies and regulations where this is needed, including on surveillance;
- develop a costed national STI workplan, including surveillance;
- mobilize funds to implement the national STI workplan;
- ensure continued in-service training in STI management to health-care providers and for laboratory and surveillance staff;
- conduct regular supervisory visits to districts;
- have quarterly/annual review meetings and disseminate surveillance data to the central-level health administrators and to the health-care providers (including private providers) who manage patients, and discuss the findings;
- use the data to advocate with local-level policy-makers and politicians for resources to control STI.

6. Plan and monitor prevention interventions at district level.

## 6. Assessing STI syndromic etiologies

Determining the microorganisms that cause urethral discharge, genital ulcer disease and vaginal discharge constitutes the second core component of STI surveillance. This activity is especially important in countries where syndromic management and case-reporting are usually performed. Knowing the organisms that cause the STI syndromes allows the STI control programmes to recommend effective treatment and to interpret syndromic case-reports.

The national STI control programme is responsible for organizing and conducting STI syndrome etiologic assessment. These surveys are conducted to assess the relative contribution of the major STI pathogens, such as:

- the syndrome of urethral discharge in men (gonorrhoea, *Chlamydia trachomatis* infection and trichomoniasis);
- the syndrome of genital ulcer disease in men and women (syphilis, HSV-2 and chancroid).

Syndrome etiologies should be reassessed every 2–3 years, or more frequently if the need arises. For example, during a new outbreak of genital ulcer disease, it may be necessary to reassess which microorganisms are causing the disease.

### 6.1 Objectives

The main purposes of assessing syndrome etiologies are to:

- provide data for guiding STI syndromic treatment;
- assist in the interpretation of syndromic case-reports and the assessment of disease burden due to specific pathogens;
- develop or modify guidelines for treating urethral discharge and genital ulcers.

### 6.2 Laboratory requirements

Laboratory staff who are experienced in STI diagnostic tests should develop laboratory protocols for determining which organisms are causing the symptoms. Laboratories should also have quality-assurance and quality-control protocols in place.

Ideally for surveillance purposes, the most sensitive and specific tests available should be used and, preferably, those tests that directly identify organisms rather than serological assays.<sup>1</sup>

There is a broad range of diagnostic tests that may be used. Many new tests are being developed. Selection of the test to use will depend on the local availability of resources. Table 4 summarizes the general types of laboratory tests that may be used for assessing syndrome etiologies:

**Table 4 Laboratory tests for specific STI syndromes<sup>a</sup>**

Syndrome	Corresponding laboratory tests
Urethral discharge in men	<p>Microscopy (Gram stain of urethral discharge to identify Gram-negative diplococci, primarily <i>Neisseria gonorrhoeae</i>)</p> <p>Testing for gonorrhoea, <i>Chlamydia trachomatis</i> and <i>Trichomonas vaginalis</i>:</p> <ul style="list-style-type: none"> <li>• culture for <i>Neisseria gonorrhoeae</i>.</li> <li>• direct fluorescent antigen and enzyme-linked immunoassay (EIA) for <i>Chlamydia trachomatis</i>.</li> <li>• polymerase chain reaction (PCR) and other nucleic acid-based tests for all three pathogens.</li> </ul> <p>Ideally, antimicrobial resistance testing for <i>Neisseria gonorrhoeae</i></p>
Genital ulcer diseases in men and women	<p>Syphilis serologic testing (non-treponemal and treponemal)</p> <p>Dark-field or direct fluorescent antibody test for syphilis</p> <p>Culture for <i>Haemophilus ducreyi</i></p> <p>HSV-2 culture or antigen detection tests</p> <p>PCR for <i>Treponema pallidum</i>, <i>Haemophilus ducreyi</i> and HSV-2 (multiplex PCR) – available in some settings</p>

<sup>a</sup> Adapted from *The laboratory diagnosis of sexually transmitted infections*, Geneva, WHO, 2011 (4).

<sup>1</sup> This recommendation is based on the expert opinion formulated at the 2008 Technical Consultation Meeting and on the approaches to laboratory diagnosis of STIs formulated in the WHO guidelines on *The laboratory diagnosis of sexually transmitted infections (4)* and the *Atlas of sexually transmitted diseases and AIDS (15)*.

### 6.3 Populations and settings

Selection of populations for assessing syndrome etiologies depends on the number of cases available for examination at a single site. Syndrome etiologies should ideally be assessed in:

- different types of populations (general population, population at higher risk of STIs, and vulnerable populations);
- populations with presumed high rates of STIs and low rates of STI;
- different geographical locations (urban, rural).

If a country has limited resources, it is advisable to begin with an assessment of urethral discharge and genital ulcer disease at a single specialized STI clinic. The clinic should:

- have well-trained personnel that can perform high-quality Gram-stain examinations and microscopy;
- be able to perform syphilis serological testing.

In many low- and middle-income countries, reliable dark-field microscopy is unavailable, due to a shortage of trained personnel.

Closer collaboration with a well-equipped laboratory may enable an assessment of the role of *Chlamydia trachomatis* in the syndrome of urethral discharge, and the level of antimicrobial resistance in *Neisseria gonorrhoeae*. The laboratory can also assess the contribution of *Haemophilus ducreyi* and herpes in genital ulcer diseases. It should also be remembered that syphilis serologic testing alone provides an incomplete assessment of genital ulcer etiology. This may be because patients with chancroid and/or HSV-2 ulcers have reactive syphilis serologic tests from previously treated infections, or because a negative test is due to the fact that it was performed too early for sero-reactivity to be detected.

### 6.4 Sample size

The sample size depends on the specific etiology and the expected prevalence of pathogens. A minimum sample size of 100 specimens from consecutive patients with the specified syndrome (or other type of systematic sample) will provide preliminary information for analysis.

### 6.5 Analysis

It is important to analyse STI data separately for each specific infection, rather than reporting findings together. For example, cases of gonorrhoea should be analysed separately from cases of syphilis. The frequency of various STIs and risk behaviours should then be calculated and analysed by:

- sex
- age group
- geographic area
- marital status
- other relevant characteristics.

These tests are usually performed at the same time as the patient is treated syndromically, based on symptoms and examination findings.

### 6.6 Dissemination of results

The national STI control programme is responsible for disseminating the results of etiologies of syndromes to all health-care workers (public and private) who provide STI care. They must also be disseminated to:

- ministry of health officials, as this information will have a bearing on the procurement of medicines for STIs;
- the national guidelines development committee;
- the national medical association.

#### **Donor organizations**

- donor organization United Nations (UN) agencies and programmes such as UNAIDS, the United Nations Population Fund (UNFPA) and WHO;
- other stakeholders such as academia and research centres.

## 7. STI prevalence assessment and monitoring

Prevalence surveys are cross-sectional surveys that establish the frequency of disease and other factors in a community. They are useful to estimate the number of people in a population who have disease, and can also identify differences in the frequency of diseases in different population groups.

Prevalence assessment is the fourth core component of STI surveillance. Prevalence surveys generate population-based STI data. Most countries have not conducted prevalence assessment and monitoring, for a variety of reasons. STI control programmes need prevalence data to monitor trends in STIs and to understand which population groups are at greater risk for infection. Prevalence assessments determine demographic information about populations at risk of STIs.

### 7.1 Definitions and terms

*Prevalence:* the proportion of people in a population who have the disease or infection at a given point in time.

*Prevalence monitoring:* following up of prevalence trends over time to see if they are increasing or decreasing.

*STI prevalence assessment and monitoring:* using surveys to determine what percentage or how many people have STIs when compared to the total population.

### 7.2 Objectives of STI prevalence assessment and monitoring

The objectives of STI prevalence assessment and monitoring are to:

- measure the overall prevalence of STIs in population of interest;
- identify population groups with a high prevalence of STI;
- monitor trends in STI prevalence among defined populations.

### 7.3 Uses of prevalence assessments

STI prevalence data are of great use in STI and HIV programme planning, management and evaluation.

They are used to:

- develop national estimates of STI prevalence, as well as the relative prevalence of symptomatic versus asymptomatic infections;
- identify population groups at high risk for STI/HIV infection (as evidenced by high rates of STIs) and plan for effective and appropriate interventions;
- guide funding and resource allocation for STI- and HIV-prevention programmes;
- monitor the effectiveness of STI- and HIV-prevention programmes at national and global level;
- strengthen surveillance capacity.

Potential opportunities for conducting prevalence assessments are as:

- part of a national seroprevalence survey;
- a stand-alone project;
- part of a combined STI/HIV biobehavioural survey.

### 7.4 Frequency of prevalence surveys

Prevalence assessment surveys should be carried out once every 3 to 5 years, depending on the availability of resources.

### 7.5 Populations for prevalence assessment

The essential population groups to include for STI prevalence surveys are key populations at higher risk of STI, such as sex workers, people who use drugs, MSM, and bridging populations such as clients of sex workers. Countries may decide to include other population groups such as long-distance truck drivers and adolescents. Such population groups need to be determined locally according to country situations and assessments. Population-based surveys may also be considered when resources are available. Factors to be considered when determining a study population are listed in Table 5.

**Table 5 Potential study populations for prevalence studies of STIs**

Proposed types of population subgroup	Definition of population subgroup	Characteristics of population subgroup
Sex workers (brothel; massage parlour/ bars; casual freelance) MSM People who inject drugs	Key population at higher risk of STIs – a subgroup of people experiencing high rates of STI exposure (unprotected sexual intercourse, sexual intercourse with multiple partners)	High rates of STIs compared to the general population; high rates of risk behaviour; poorer access to health-care facilities
Clients of sex workers STI clinic attendees (usually males) Other subgroups according to the local evidence: <ul style="list-style-type: none"> <li>• military</li> <li>• police</li> <li>• mobile populations (e.g. transport workers, fishermen)</li> </ul>	Bridging (medium-risk) or proxy for bridging population – a subgroup of people who are characterized by sexual contact with both the key population at higher risk of STI exposure and low-risk individuals (general population)	High rates of STIs compared to the general population; high rates of risk behaviour (sexual contact with key populations; for some subgroups, poorer access to health-care facilities (e.g. mobile population)
Women attending antenatal clinics	Proxy for the general population – a subgroup of people who are similar by sociodemographic and behavioural characteristics to the general population (relatively lower rates of sexual partners and concurrent relationships, smaller numbers of sexual networks and relatively limited contact with other population subgroups)	Low-risk sexually active population. Equivalent to the general sexually active population – rates of infection give a proxy indication of the burden of infection

Among the most common seroprevalence surveys are those based on syphilis screening programmes. The two most common settings for general population serological surveys for syphilis are antenatal clinics and blood donation sites. They are especially useful in countries where few other data on STI prevalence are available.

Screening pregnant women for syphilis is national policy in almost all countries. *However, data on positive syphilis tests among pregnant women are often not captured in the STI surveillance system.*

National blood transfusion programmes also screen all donated blood for syphilis and these data may provide an indication of syphilis in a low-risk population group, but can be biased by the self-deferral of persons who donate blood. These data (number positive and the number screened) should be forwarded, without personal identifying information, to the STI control programmes for assessment.

Other populations among whom screening for syphilis has been conducted include:

- new clients attending family planning clinics;
- candidates undergoing pre-employment medical examinations;

- prisoners at entry into detention facilities;
- military recruits;
- sex workers undergoing routine examinations.

Although there tends to be less selection bias when the people being tested are from such facilities than when people are seeking care because they have STI symptoms, the sexual behaviours of people attending these facilities need to be carefully assessed for interpretation of the data.

## 7.6 Syphilis screening at sentinel sites

Syphilis screening can also be carried out at sentinel sites that are participating in the sentinel case-reporting system. Data can be collected from all patients screened at the sentinel site or for specific demographic or populations at risk, such as:

- pregnant women under 24 years of age screened at an antenatal clinic (for interpretation of data obtained from this population subgroup see Section 5.3.5);
- commercial sex workers screened at an STI clinic.

As with sentinel case-reporting, sites should be representative of facilities that provide STI care. They can be STI clinics, hospital-based clinics, primary health-care centres and/or private clinics. Participating sites should be located at different geographical regions of the country and should include both urban and rural sites. The sites should be able to collect a sufficient number of samples to represent the target population, in order to usefully interpret the information and to monitor trends.

## 7.7 Recommended STIs for inclusion in prevalence surveys

Prevalence surveys can be conducted for many different STIs but *T. pallidum* (syphilis), *Neisseria gonorrhoeae* (gonorrhoea), *Chlamydia trachomatis* (chlamydial infection) and *Trichomonas vaginalis* (trichomoniasis) are recommended for inclusion in STI prevalence surveys (Table 6). These STIs are curable, cause considerable adult and infant morbidity and mortality, are spread primarily by sexual transmission and are often asymptomatic, particularly in women. HIV testing should also be included in these surveys, where possible.

**Table 6**  
Classification of pathogens responsible for STIs for inclusion in prevalence surveys

Pathogen	Priority/sex
<i>Treponema pallidum</i>	High/male and female
<i>Neisseria gonorrhoeae</i>	High/male and female
<i>Chlamydia trachomatis</i>	High/male and female
<i>Trichomonas vaginalis</i>	High/female and male <sup>a</sup>

<sup>a</sup> Relatively recent publications have shown a high prevalence of infection with *Trichomonas vaginalis* in a male population (16). However, microscopy and culture that have been mainly used for detecting *T. vaginalis* have a low sensitivity compared to new molecular diagnostic tests. Where possible, new-generation diagnostic tests (e.g. PCR) that are more sensitive and specific should be used in order to determine more accurately the prevalence of *T. vaginalis* infection in both symptomatic and asymptomatic men and women.

## 7.8 Laboratory methods

Assessment of STI prevalence is primarily based on the diagnosis of infections that are frequently asymptomatic. The aim of a prevalence survey is to obtain the most accurate and valid laboratory-based diagnoses of the specified STIs from the samples collected.

*Laboratory methods must be selected consistently to ensure the comparability of prevalence data, especially for monitoring and evaluation purposes.*

The degree of precision required in the survey should be determined before decisions are made about the types of samples to be used and which tests the laboratory will use.

There are three main categories of samples:

- blood
- urethral, vaginal and cervical secretions
- urine

When choosing the sample and laboratory test, it is important to consider the following:

- local technical laboratory capacity (a wide range of laboratory methods can be used for institution-based studies, such as in an antenatal clinic: microscopy, culture and antigen detection);

- the sensitivity and specificity of the test in the proposed survey population (generally, the most sensitive and specific laboratory methods a country can afford should be used);
- the degree of ease and non-invasiveness in sample collection and the size of sample required;
- the robustness and logistics of sample transportation and storage;
- the cost of tests.

A laboratory protocol containing options for sample collection, transport and laboratory testing of syphilis, chlamydial infections, trichomoniasis and gonorrhoea, including antimicrobial resistance testing, should be developed.

Serological methods are needed for assessment of syphilis seroprevalence but both treponemal and non-treponemal tests are required to define a confirmed active infection. In addition, clear guidance is needed on the interpretation of various syphilis test results for the purposes of consistency.

There are several serologic tests for syphilis that can help differentiate between probable primary, secondary and latent syphilis from previously treated syphilis (see also Box 4).

Once the treponemal tests (such as the TPHA or *Treponema pallidum* particle assay (TPPA) are reactive, they remain so for the patient's lifetime and cannot, on their own, distinguish adequately between treated syphilis and active infection. Non-treponemal syphilis serologic tests (such as VDRL and RPR) are better indicators of active infection, especially if the samples are titrated and tested at various dilutions. Treponemal point-of-care tests, or rapid diagnostic tests (see also Section 8.2) alone are not recommended for surveillance purposes, since, in common with other treponemal tests, they measure lifetime exposure to the infection and significant decreases in seroprevalence rates following successful interventions would take many years to emerge.

Tests that do not require gynaecological or genital examinations can facilitate prevalence assessment outside of clinic settings. Urine tests for gonorrhoea and chlamydial infection based on nucleic acid amplification methods can be used for this purpose, although their cost may limit their utilization. It should be noted that, currently, urine samples for these

molecular-based tests cannot be used for antimicrobial susceptibility testing.

## 7.9 Data elements

Data elements for prevalence assessment and monitoring are the same as those used for case-reports. The minimum information needed for the prevalence survey is:

- study identification number
- study site
- date of specimen collection
- sex
- date of birth or age

Additional data elements can be collected at some sites, which will provide more detail of patient demographics, risk characteristics and diagnoses.

## 7.10 Study design

The most appropriate design for STI prevalence surveys is a cross-sectional study. Cross-sectional studies are observational studies in which a sample of subjects in a population (e.g. pregnant women attending an antenatal clinic) is investigated for specific characteristics, in this instance laboratory-confirmed STI. Prevalence studies do not establish causality.

## 7.11 Sampling considerations

The elements to consider in deciding which sampling procedures to follow are:

- a sampling frame that is representative of key epidemiological and socioeconomic factors;
- study sites that have sufficient numbers of clients;
- medical and laboratory expertise and capacity;
- clients that are likely to consent to participation;
- government support for the prevalence study.

In a prevalence survey, it is not feasible to examine every individual of a population. Instead a sample is taken. If the sample is representative of the population, one can generalize the findings from the sample to the population they represent. The advantages of using a sample are saving time, study personnel and costs. The disadvantage of a sample is that precision is lost by not observing the whole population. Therefore, the sample estimate will have some margin of error.

There are two types of sampling errors:

- sampling errors that occur because only a part of the population is included (generally the larger the sample size the smaller the sampling error);
- selection bias, which occurs if the sampling procedure is flawed and the sample is not representative of the whole population (e.g. freelance sex workers are not included in a study of female sex workers because sampling for the study is only from brothels). Selection bias is independent of the sample size.

### 7.12 The sample frame

A convenience sample with consecutive sampling should be used in STI prevalence surveys. Enrolment should continue until the required number of study participants has been reached.

A convenience sample is where the study population is already accessible for a reason not related to the study, such as pregnant women attending a hospital for antenatal care. Convenience sampling is used because it is convenient, practical and usually cheaper than recruiting specific study participants. It uses an existing infrastructure such as clinic facilities and staff. The disadvantage is that the sample population may not be representative of the study population in an economic, cultural or geographical sense.

Within a convenience sample framework, sampling can either be:

- *random*, where everyone has the same probability of being selected, making the sample more representative of the population of interest (for example, in a clinic, for random sampling, a full count of all clinic attendees for the study period is needed)<sup>a</sup>;
- *non-random* (e.g. consecutive), where all eligible subjects are recruited into the study until the sample size is reached.

<sup>a</sup> Ideally the duration of the survey should not be longer than 2 to 3 months

Random sampling complicates recruitment, specimen collection and potentially clinical management of asymptomatic infections. Consecutive sampling is simpler, reduces the study period and is less expensive, but it may increase selection bias.

The proposed sample frame should include persons aged 15–49 years. Ideally there should be oversampling of persons aged less than 25 years, so that half the sample is aged 15–25 years. The aim of oversampling young persons is to determine the prevalence of disease in those who have most recently become sexually active. This also provides a baseline for monitoring the impact of the STI and HIV in that population.

### 7.13 Criteria for selection of the study site

The study site depends on the local characteristics and conditions. Characteristics to consider in the selection of a site are listed in Table 7.

For female sex workers, the study site will depend on local conditions. The female sex worker may visit private or public clinics, outreach services, nongovernmental services or other venues such as pharmacies. If the site identified is a public-sector STI clinic, it should be selected, provided the clinic sees a sufficient number of new STI patients each month.

For pregnant women, the antenatal clinic may be identified as a site, provided the clinic sees the required number of new pregnant women each month to support the sample size needed for the study. For military recruits, the selected site might be a military clinic; for transport workers or fishermen, a mobile clinic may have to be set up during the study period.

**Table 7 Characteristics to consider when selecting a study site**

Characteristics to consider	Criteria for selection of study setting
Acceptability	The study is acceptable to the government, local authorities and the proposed study population
Location	Urban (big city, town), rural/farming/coastal or remote
Disease prevalence	Areas are likely to have high or low STI prevalence
Sample size	A site that has a sufficient number of subjects/clients available for recruitment to the study
Sector	Government (health or military) or local or foreign nongovernmental or semi-governmental organizations (aid agencies, universities, trade unions, private clinics, outreach programmes)
Local capacity	Technical and organizational skills to follow the study protocol
Suitability of the setting	Physical layout, availability for the whole study period
Commitment	Available and interested supervisor in the study setting
Confidentiality and privacy	Capacity to follow the study protocol requirements on confidentiality and privacy issues and record-keeping
Laboratory	Technical and organizational skills to follow the study protocol requirements; adequate quality-control and quality-assurance programmes in place

### 7.14 Sample size

The prevalence survey is designed to obtain an estimate of the magnitude of STIs in a population at a given point in time. The minimum acceptable sample size for assessing the prevalence depends on:

- the expected prevalence of the disease in the population, based on prior estimates or similar situations in neighbouring cities and countries;
- the degree of precision/certainty wanted in that prevalence estimate;
- whether the sample will be used to monitor trends in prevalence over time.

Generally, the more precise the estimate desired, the larger the sample size required. The sample size required is also much larger if the intention is to monitor trends over time. This means that it needs to be large enough to be able to detect the difference between two point prevalence estimates. Statistically, this is referred to as the margin of error.

The statistical approach for determining the sample requires:

- an estimate of STI prevalence in the population to be surveyed;

- the margin of error considered acceptable (for example  $\pm 3\%$ ); this is called the interval width;
- the level of confidence desired (a 95% confidence interval means that, if the survey were done 100 times, the prevalence in 95 surveys out of the 100 would fall within the 95% confidence interval).

#### 7.14.1 Practical considerations

In practice, sample sizes are balanced against the technical and financial resources available for each collection of the survey. Very large sample sizes in a sentinel site can provide useful information on the local epidemic. However, there may not be enough resources to carry out surveys with very large sample sizes.

#### 7.14.2 Formula to determine sample size

An exact formula to determine the sample size ( $N$ ) to achieve a certain prespecified interval (for example  $\pm 3\%$ , which is the same as a width of 6%) with a specified level of confidence (for example 95%) is:

$$N = 4z^2P(1 - P) \div W^2$$

where  $z$  is the factor that corresponds to the desired confidence interval (for a 95% confidence interval,  $z = 1.96$ );  $P$  is the expected proportion of patients with the outcome (such

as syphilis prevalence); and  $W$  is the width of the interval, for example the width for a margin of error of  $\pm 3\%$  is 0.06.

A feature in the Epi Info statistical software StatCalc provides a simple, user-friendly sample-size calculator and therefore be used in order to calculate a specific sample size. See also Annex 2, which provides an approach to determination of sample size according to estimated differences in seroprevalence between two proportions.

## 7.15 Logistics support

Logistics support is an important aspect that should be taken into consideration when conducting prevalence assessment surveys. Very often, this aspect is neglected, and once the study has started the investigators are faced with many problems that would not have arisen had logistics support been thought of and incorporated into the study proposal. Some of areas where logistics support is required are:

- supplies and equipment for the survey;
- staff capacity;
- storage of specimens;
- transportation (e.g. transporting specimens to the laboratory);
- coordination of collection of specimens and times of delivery to the laboratory;
- communication facilities.

## 7.16 Ethical considerations

Effective public health activities, including public health surveillance, depend on a trusting relationship between the public health workers and the public they are trying to assist. Some of the obligations the public health worker has to fulfil are presented next.

### 7.16.1 Protect the confidentiality and privacy of the community

*Privacy* is the right of patients to choose what information they will release about themselves and to whom.

*Confidentiality* is the obligation of the public health workers to keep information about individuals restricted only to those persons who absolutely need it for the health of the community. Patients have a right to know why they are providing information, to refuse to provide information, and to expect that information will be handled as confidential.

Information, even when it does not include names, can still be used to identify persons and lead to discrimination against or other consequences for individuals. Therefore, such information must be protected. In many countries and districts, even a few pieces of information that may seem to be unimportant can be used unintentionally to identify a patient. Additionally, consideration should be given to how to protect patients from identification, while still allowing the public health system to trace contacts when required. A good information system should be based on careful decisions about what information is essential for public health action.

### 7.16.2 Maintaining professionalism and public trust

To perform public health functions, including surveillance, it is essential that there is public support. Trust is an expression of confidence that public health workers will be fair, reliable, ethical and competent.

### 7.16.3 Consent

It is important that STI control programmes use patient information for the purposes for which it was intended. There may be national or international policies and regulations that specify what the uses should be and when additional consent is required from the patient. The public health workers must respect these regulations.

#### *Consent form*

STI prevalence surveys should use a voluntary confidential testing methodology. Voluntary confidential testing is where individuals may themselves ask for STI tests or may consent to a test on recruitment into a study/survey. Therefore, a form to obtain consent should be prepared that indicates that the survey participant has decided to take part in the study of their own free will.

The consent form has two parts:

- a statement describing the survey and the nature of the subject's involvement in it;
- a certificate attesting to the subject's consent.

Both parts should be written in sufficiently large letters and in simple language so that the subject can easily read and understand the contents. As far as possible, medical terminology should be avoided in writing up the consent form.

#### 7.16.4 Ethical clearance

Since STI prevalence surveys involve taking biological specimens from people, it is essential that the proposed survey(s) is/are carried out in accordance with existing ethical guidelines in the country. Ethical approval should be obtained from the relevant authorities prior to conducting the survey. The consent form should be included in the survey protocol when submitting it for ethical approval.

#### 7.17 Confidentiality and data security

The issues of confidentiality and security of data discussed in Section 5.1 also apply to prevalence assessment surveys. In this situation, data should be restricted to the principal investigator responsible for the survey, and other persons nominated by him/her.

#### 7.18 Analysis of prevalence data

The results of the prevalence survey should be analysed as follows for each study site:

- the number and proportion of persons with positive test results for each STI and HIV (if included in the protocol);
- the prevalence of each of the surveyed STI pathogens.

Results should be stratified by the population subgroup and by:

- age – which should be stratified into equal age ranges such as 5-year age groups depending on the sample size
- sex.

Where indicated, odds ratios should be calculated with 95% confidence intervals and/or chi-square tests to assess the association of variables with a particular STI.

#### 7.18.1 Calculating STI prevalence

To calculate STI prevalence, the number of patients who test positive for a specific infection (the numerator) is divided by the total number of patients tested (the denominator):

$$\text{Prevalence} = \frac{\text{total number of patients who test positive for a specific infection}}{\text{total number of patients tested}}$$

For example, the prevalence of syphilis among 15–24-year-old women can be calculated by dividing the number of women who are seropositive for syphilis by the total number of 15–24-year-old women tested for syphilis during assessment period.

#### 7.18.2 Calculating syndromic prevalence

When facilities for testing are not available for prevalence assessments, syndromic prevalence can be calculated based on whether symptoms are present in patients. In this situation, prevalence is calculated according to the following equation:

$$\text{Prevalence} = \frac{\text{total number of patients with sign and symptom for a specific syndrome}}{\text{total number of patients seen}}$$

Analysis of routinely collected prevalence data (for instance, data obtained from routine screening of women in antenatal care) is similar to the analysis of universal and sentinel case-reporting data. Quarterly and annual trends in prevalence should be analysed overall and stratified by basic categories, such as disease, sex, age group and geographical location.

## 7.19 Interpretation of data

Initial data analysis and interpretation should be conducted for each specific STI, rather than for combined STIs. For example, analysis of risk factors for patients with gonorrhoea should not be combined with that for patients with syphilis. At a minimum, the prevalence should be calculated by:

- sex
- age group
- geographical area
- marital status
- other relevant characteristics for each infection

Prevalence trends may be altered by changes in the population being screened, for several reasons:

- different types of clinics, for example, an STI clinic versus a clinic serving the general population may get different results;
- change in the population's health-seeking behaviour;
- changes in selection criteria for screening purposes;
- changes in diagnostic tests, especially for *Chlamydia trachomatis*, which often vary in sensitivity and specificity.

changes should be recorded and taken into account in the interpretation of trend data.

## 7.20 Dissemination of prevalence data

The results of the surveillance surveys described above should be distributed to national STI programme managers, national AIDS programme managers, district medical officers, health centres, clinicians, private health-care providers and laboratories that have participated.

The staff who participated in the study, as well as the population sampled should be informed of the outcomes of the study and preventive or other activities that arise from the study. This will help keep the interest of the study staff and the study population and assist in the implementation of any prevention programmes planned as a result of the study findings.

The national programme should prepare a report of the study design, study process, results and recommendations and distribute the report to the ministry of health, district and regional health authorities, laboratories that participated in

the study and other stakeholders. STI programme managers should take necessary action to improve services, depending on the results of the surveys.

## 7.21 Combined behavioural and prevalence surveys

Behavioural surveys can be combined with STI and HIV prevalence surveys (sometimes called integrated biological and behavioural surveys, or IBBSs). An example of this is the demographic and health survey with HIV testing (DHS+). Combined surveys can be conducted in known high-risk populations, proxy populations (such as antenatal care attendees) or the general population. Combined prevalence assessment and behavioural surveys collect data that allow comparison of high-risk and health-seeking behaviour with the presence of STIs and/or HIV.

The goal of combined prevalence assessment and behavioural surveys is to:

- assess the prevalence of STI and HIV in surveyed populations;
- identify population subgroups at higher risk of infection (for example, unmarried men aged between 20 and 29 years living in urban areas, who have given money or gifts for sex);
- assess health-seeking behaviour for STI and HIV services (for example, use of pharmacies for STI diagnosis);
- measure the effectiveness of STI/HIV-prevention programmes;
- determine the need for additional prevention and health services;
- guide funding and resource allocation for STI and HIV programmes.

*Combining STI/HIV prevalence assessment with behavioural surveillance surveys is more cost effective than conducting separate surveys.*

### 7.21.1 Data elements

The data elements for combined STI/HIV surveillance and behavioural surveillance are similar to those collected for STI case-reporting, but may also be more extensive to include more detailed demographic information and risk behaviours.

The types of behavioural data collected will vary depending on the populations surveyed. For example:

- in key population surveys, greater attention may be given to specific high-risk behaviours. For example, for long-distance truck drivers, questions may include whether an individual has sexual intercourse in exchange for money or gifts, and whether they use condoms for sexual intercourse with their primary partner and other partners;
- in general population surveys, questions about general risks along with demographic characteristics and health-seeking behaviours may be the priority. For example, questions may cover age, marital status, sex and occupation.

It is important to use consistent data elements to determine risk behaviour. For example:

- the number of sexual partners in the past 3 or 12 months;
- the number of new sexual partners in the past 3 months;
- condom use during the last sexual intercourse with someone other than a regular sexual partner;
- alcohol or drug use in the past 12 months;
- giving or receiving money or gifts for sexual intercourse in the past 12 months.

## 8. The role of the laboratory in STI surveillance

Accurate laboratory-based information is an essential component of disease surveillance. The strength of laboratory information is that it provides objective confirmation of the diagnosis. In a STI control programme, the laboratory is required to perform many functions, including diagnosis of specific STIs and assessment of microbiological susceptibility. Diagnostic testing is particularly critical for STIs, as many infected persons, particularly women, are asymptomatic. Sensitive diagnostic tests assist in early detection and treatment of STIs, prevent development of sequelae and interrupt transmission. Laboratory support is also required for medico-legal purposes and to assess treatment failures.

The roles of the laboratory in STI surveillance include:

- providing a definitive diagnosis in individual patients with symptoms. Although clinicians may sometimes make a confident diagnosis on the basis of symptoms and clinical signs, accurate diagnosis usually requires specific laboratory test(s);
- assessing the microbiological etiologies of STI syndromes, which:
  - provides data to guide STI syndromic management;
  - allows screening tests to be carried out for persons considered to be at risk of STIs;
  - enables asymptomatic or undiagnosed STIs to be detected by using screening tests;
  - provides microbiological data to assess the prevalence of STIs;
  - assists in obtaining population-based data on STIs
  - facilitates determination of antimicrobial susceptibilities of STI pathogens;
  - helps to select effective antimicrobial treatment for individual patients and inform treatment guidelines.

Syndromic management of STIs depends on providing treatment for the common pathogens that cause the symptoms. Hence, periodic assessment of the pathogens responsible for a particular syndrome is important to guide treatment protocols. Assessment of antimicrobial susceptibility is particularly important for STI pathogens such as *Neisseria gonorrhoeae*, which is known to acquire resistance rapidly to commonly used antimicrobials. For example, as of

2011, *Neisseria gonorrhoeae* has acquired resistance to penicillins, tetracyclines, macrolides and quinolones, to the extent that these can no longer be recommended for the treatment of gonococcal infections. More recently, there have been reports of decreasing susceptibility to extended-spectrum cephalosporins and treatment failures with the oral cephalosporin, cefixime. In conducting prevalence assessment surveys, the laboratory provides microbiological surveillance to assess the magnitude and distribution of STIs.

Ideally, for the purposes of surveillance, the most sensitive and specific laboratory tests available should be used and tests that directly identify pathogens rather than serological assays are preferred. Serology-based tests (such as for syphilis and HSV-2) are useful but their interpretation is often difficult. Nucleic-acid amplification tests are more sensitive than culture and non-amplified tests but are more expensive, and require a sophisticated laboratory and highly trained personnel to perform the tests. However, even if amplification tests are used, culture is still required to carry out antimicrobial susceptibility testing.

### 8.1 Rapid diagnostic tests for STIs

Many STI control programmes, especially in those regions where the burden of STIs is high, do not have ready access to diagnostic tests that are inexpensive, easily performed and of good quality. Most of the conventional and advanced diagnostic tests for STIs are costly and time consuming and require laboratory facilities with trained personnel. As a result, such facilities are not available at primary health-care settings and maybe even at higher-level facilities in many low- and middle-income countries. This hampers STI control, as patients are required to pay for expensive diagnostic tests that they may not be able to afford and they are required to come back another day for the results.

To overcome this problem, rapid diagnostic tests (RDTs) that are simple to perform have been developed for a number of STIs and a few are commercially available. Treponemal RDTs that can be used in settings where laboratory services are not available or are unreliable are now available. These RDTs have been shown to have reasonable performance characteristics, with sensitivities of 85–99% and specificities of 93–100% when compared with laboratory-based treponemal tests.

However, it must be noted that syphilis RDTs are *Treponema*-specific tests and cannot be used to differentiate between prior treated infection and probable active infection. Therefore, they may be less useful in high-prevalence settings where a high proportion of infected individuals have been treated previously.

RDTs for gonococcal, chlamydial and trichomonas infections are still relatively more costly, technically more difficult to perform and of lower sensitivity. Therefore, for the moment, they are not recommended for use in low- and middle-income country settings.

## 8.2 Selection of laboratory tests

The selection of laboratory tests for surveillance purposes should be based on the performance characteristics, such as accuracy, availability, accessibility, feasibility and assurance of quality of testing. The selection and use of diagnostic tests will depend on the local prevalence of disease and the cost of diagnostic testing. In addition, the selection will also depend on which tests have been approved for use by regulatory authorities in a particular country and which tests have been purchased for use in the health services.

Even if the above tests are available, many factors may influence the performance of laboratory tests and the accuracy of microbiological surveillance, including:

- training of clinical and laboratory staff
- the selection of cases
- the quality of the clinical specimens
- the viability of the clinical specimens
- quality assurance

## 8.3 Laboratory-based case-reporting

In addition to performing diagnostic testing, the laboratory also has a responsibility to report on STIs diagnosed. However, in many low- and middle-income countries, laboratory reporting often relies on paper reports delivered by mail. Hence, information obtained from the laboratories is necessarily less timely and often contains only scant clinical details. In high-income countries, electronic-based laboratory reporting is available and the information obtained in this way is more timely and complete.

In countries where laboratory services are readily available, clinicians may request laboratory tests to assist in the diagnosis and treatment of patients. They may also routinely screen asymptomatic patients using diagnostic tests. The quality and completeness of laboratory data will depend on consistent technical standards, together with consistent record-keeping and reporting that is timely, accurate and complete.

The STI control programme should actively encourage laboratories to report all STIs diagnosed, and have a regular system to collect laboratory data. It is also important to include the participating laboratories as recipients of surveillance reports and arrange for feedback on a regular basis.

Where laboratory-based reports are collected, it will be important to match them as closely as possible with other reported data, to avoid duplication of data.

## 8.4 Monitoring antimicrobial resistance

One of the core components of STI surveillance is antimicrobial resistance (AMR) monitoring. This component is dealt with in more detail in Appendices 1–4 of this document.

Resistance is the change within a pathogen that makes it non-responsive to a particular antimicrobial agent. Resistance monitoring entails laboratory examination of the effectiveness of various antimicrobial agents in inhibiting the growth of sexually transmitted pathogens. In resistance monitoring, various concentrations of a given antimicrobial agent are used to determine the minimum inhibitory concentration of that agent that is required to inhibit the growth of a particular organism. Depending on the concentration of the antimicrobial agent required to inhibit growth, the organism can be classified as sensitive, intermediate or resistant to a particular antimicrobial agent. Usually, the organism is checked for sensitivity against several different antimicrobial agents, often from different antimicrobial classes.

Sexually transmitted pathogens that particularly warrant antimicrobial monitoring include *Neisseria gonorrhoeae*, *Haemophilus ducreyi* and *Treponema pallidum* among bacteria and HSV-2 among viruses. However, since, a reliable laboratory test to culture *Haemophilus ducreyi* is currently not available in most countries, and facilities to culture HSV-2 are also lacking in many low- and middle-income countries, only

AMR monitoring for *Neisseria gonorrhoeae*, which causes gonorrhoea, is recommended for all countries. However, in countries where rates of chancroid are high, studies to assess AMR in *Haemophilus ducreyi* may also be performed if facilities are available.

The objectives of monitoring AMR are to obtain the data necessary for developing and revising national treatment guidelines and to detect newly emerging resistance.

## 8.5 Laboratory requirements

Surveillance surveys for AMR of pathogens causing STIs are usually organized and conducted by the national STI control programme. Sites are chosen that have health-care facilities with well-trained staff and laboratory expertise. Only selected sites will have the capacity to conduct these types of surveillance. A laboratory performing AMR testing for *Neisseria gonorrhoeae* should be able to accomplish culturing the organism, performing appropriate species-confirmatory tests and quality-assured AMR testing of antimicrobial agents.

If the national reference laboratory does not have this capacity, isolates may be sent to a regional laboratory in another country for analysis. An isolate is a culture of bacteria or other cells.

Regional networks supported by WHO collaborating centres have been established in several WHO regions to conduct antimicrobial susceptibility testing for *Neisseria gonorrhoeae*. *National reference laboratories are encouraged by WHO and UNAIDS to collaborate with these centres and participate in quality-assurance programmes.*

## 8.6 Sample size

The minimum acceptable sample size for assessing the proportion of resistant organisms depends on:

- the expected proportion of the disease in the population, based on prior estimates or similar situations in neighbouring cities or countries;
- whether the sample is intended to be used to monitor trends in the proportion of resistant organisms over time.

Sampling for resistance testing can be random, systematic or consecutive.

A *random sample* of gonococcal isolates is one in which each patient submitting a specimen from which the isolate is obtained would have an equal chance of selection. This type of sampling yields the most representative sample but is too difficult to conduct in most clinic settings.

A *systematic sample* (for instance, every tenth patient with discharge and a positive Gram stain during the sampling period), is an adequate sample and easier to obtain. Systematic sampling requires attention to procedural details and is subject to manipulation by clinic staff. An example of manipulation by clinic staff is a staff member excluding eligible patients that come in on busy days because of time constraints. For these reasons, systematic sampling is not feasible in some situations.

A *consecutive sample* entails selecting every patient that meets the inclusion criteria until the required sample size is achieved or the survey period is over. Consecutive sampling can be used if it is felt that systematic sampling will not work in a particular setting.

A sample of 100 isolates per sentinel site during a defined time interval, such as 3 months or a year, is usually large enough to identify local patterns of resistance during that interval. A finding of zero cases of resistant isolates among 100 isolates tested provides a probability of 95% that the true proportion of resistant isolates is below 5% (if a random sample of isolates is tested). If the resistance level is between 3% and 10%, enhanced AMR surveillance is recommended (for more details refer to Appendix 1).

## 8.7 Recommended collection

Sentinel sites for collection of gonococcal isolates should be representative of the major regions in the country. Urban STI clinics that have the capacity to perform cultures are usually used as sentinel sites. Isolates should be obtained from both men women if possible. Obtaining from men who have purulent urethral discharge is easiest, since a high proportion of these symptoms will be due to gonorrhoea. A sample of cervical discharge from women is necessary for isolation of the organism but it is more difficult to identify women with gonorrhoea. Using Gram stain to help in selecting specimens makes sense because the yield of culture from these patients will be high.

## 8.8 Data analysis and interpretation

Microbiologists who are familiar with the sensitivity and specificity of each of the tests used should interpret the results of AMR testing.

*Sensitivity* refers to the proportion of persons *with a disease* who are correctly identified by a screening test or case definition as having the disease, when compared with a defined gold standard.

*Specificity* refers to the proportion of persons *without a disease* who are correctly identified by a screening test or case definition as not having the diseases, compared with a defined gold standard.

Results of resistance testing should be reviewed annually (quarterly if feasible). It is important to ensure that the data are complete and patterns are generally consistent from year to year.

If a big change is noted in review of data, this should be investigated to determine whether the change is due to real shifts in resistance patterns or problems in the laboratory. Further investigations may be needed if such shifts are noted, and it may be useful to expand the sample beyond the number previously collected each month, or to increase the number of sites where susceptibility testing is performed, until the problem is identified.

The appearance of new resistant strains should be reported as soon as possible to a WHO collaborating centre. The centre will assist in confirming the finding and determine if inves-

tigation is needed. Data on resistance should be reviewed carefully in preparing updated treatment guidelines and in revising the country's list of essential drugs.

## 8.9 Disseminating results

Data on gonococcal resistance should be distributed nationally at least once a year, ideally using charts and graphs similar to those shown in Figures 4 and 5, to clarify data.

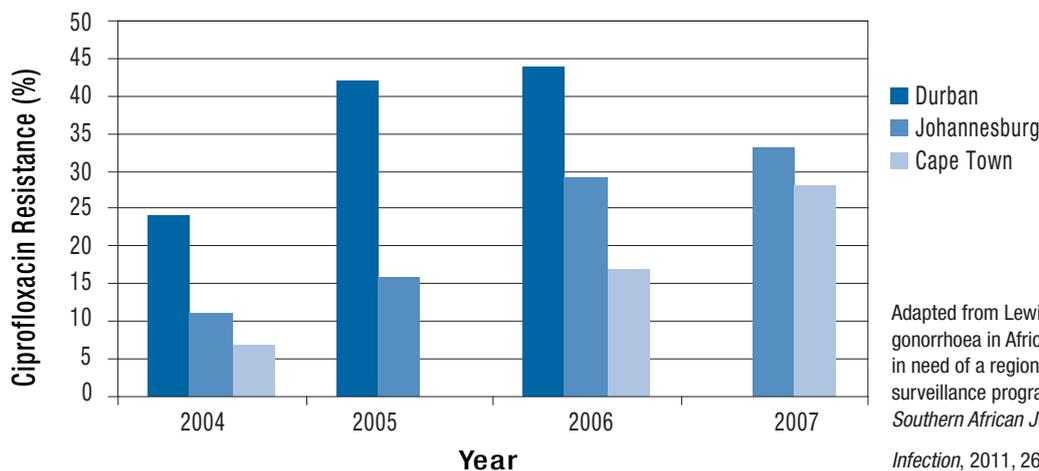
Reports should summarize the proportion of isolates that were found to be resistant to the antimicrobial agents, and results should be stratified by sentinel site. It may also be useful to summarize the proportion of isolates that were of intermediate sensitivity. Reports should include:

- the sex (and ideally age) of patients
- the clinic setting where the patients were tested (for example, STI clinic, clinic for female sex workers or clinic for long-distance truck drivers), and changes that have occurred in the sentinel sites over time
- all available demographic and behavioural data.

This information can assist in the interpretation of test results, particularly if certain sites are attended by patients whose previous therapies have failed. Such patients are more likely to have resistant strains.

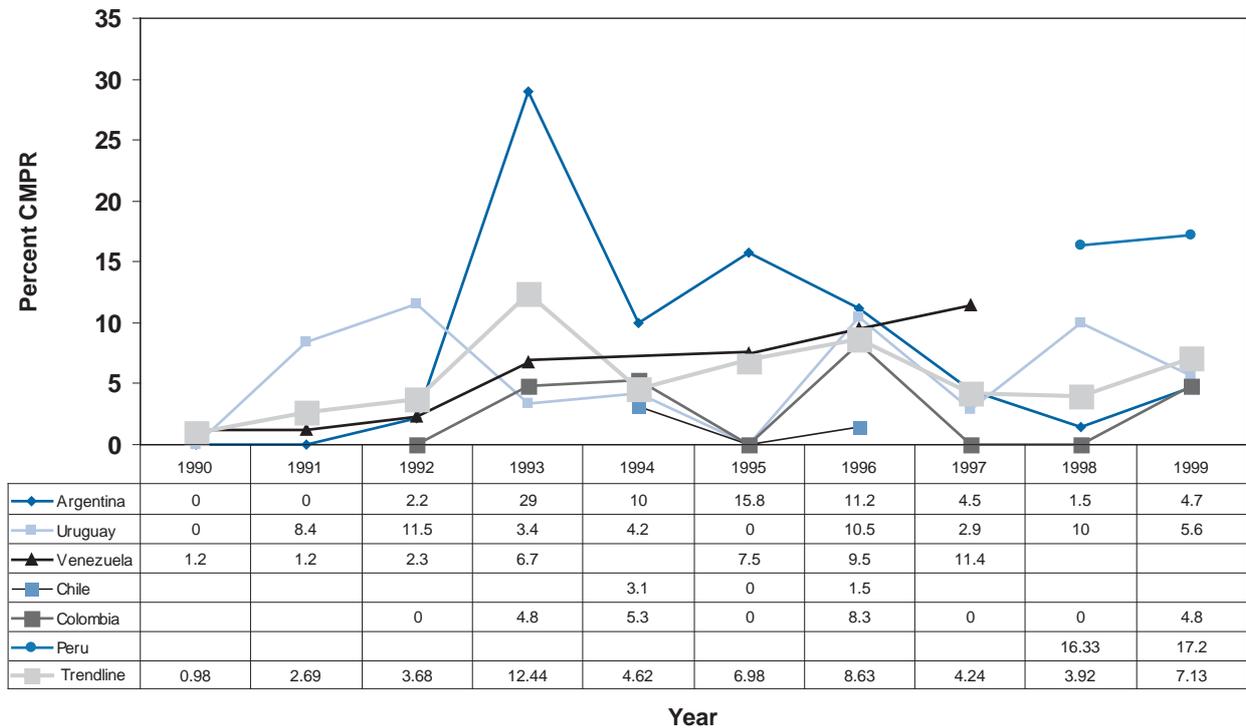
Where it is possible to systematically collect demographic and behavioural data on patients in the sample, it may be possible to provide a detailed description of the characteristics of infected patients.

**Figure 4**  
**Gonococcal resistance to ciprofloxacin in three South African cities, 2004–2007**



Adapted from Lewis DA. Antimicrobial-resistant gonorrhoea in Africa: an important public threat in need of a regional gonococcal antimicrobial surveillance programme. South Africa. *The Southern African Journal of Epidemiology and Infection*, 2011, 26(4):215–220 (17).

**Figure 5**  
**Chromosomal penicillin resistance (CPMR) in *Neisseria gonorrhoeae* in Latin America**



Adapted from Jo-Anne R. Dillon. Challenges in the Control of Gonorrhoea in South America and the Caribbean: Monitoring the Development of Resistance to Antibiotics. *Sexually Transmitted Diseases*, February 2006, Vol. 33, No. 2, p.87–95.

The assessment of AMR should be performed at least once a year. When feasible, it is best to sample isolates on an ongoing basis rather than during only one month or quarter per year. An example would be to test 20 isolates per month at each sentinel site throughout the year. Ongoing sampling makes it more likely that newly emerging resistance or large changes in patterns of resistance will be detected early. If trends in susceptibility are to be reliably monitored over time, variations in the sentinel sites and sampling procedures should be minimized.

The results of gonococcal AMR monitoring should be disseminated to key stakeholders such as health-care providers/clinicians who provide STI care (private and public), the ministry of health, national guidelines committee, national medical associations, donor agencies and UN agencies.

## 9. Dissemination and communication of surveillance results

Surveillance is data collection for action. Effective and timely public health responses depend upon the ability of health systems to provide reliable and timely information for action. Often, health-care providers collect STI data because they have been asked to do so by public health officials, but these surveillance data are rarely utilized to monitor trends in STIs, to review treatment guidelines and recommend suitable antimicrobials for treatment, review and plan for training of health-care providers or to advocate politicians and other authorities for more resources for STI control and prevention. Even STI data available from syphilis screening among pregnant women and blood donors that are available in most countries are rarely analysed, reported or used.

Dissemination of analysed surveillance data to health-care workers at all levels, from those who manage STI patients to those who actually collect and collate data is essential to make staff understand the purpose of collecting data. It also helps motivate staff to be more diligent with data collection if they realize and understand that they are playing an important role in STI control and prevention in their country.

National STI programmes should develop and implement a plan to effectively communicate STI surveillance data. If resources permit, it would be useful to seek the services of those experienced in health communications to design materials that concisely summarize and effectively communicate the data to all the stakeholders. The surveillance unit of the national STI programme is responsible for this activity and should guide the material development.

STI surveillance data should be disseminated to:

- the national STI programme manager;
- the national AIDS programme manager;
- provincial and district medical officers;
- health-care providers at primary health-care level including private providers;
- laboratories participating in STI surveillance;
- ministry of health officials responsible for STI/HIV programmes;

- other public health agencies;
- NGOs providing STI services;
- donors;
- UN agencies, for example, WHO, UNFPA, United Nations Children's Fund (UNICEF), World Bank.

### 9.1 Types of reports

Surveillance data may be communicated in the form of a report. The following types of reports could be used to communicate data to the relevant stakeholders:

- annual STI surveillance reports, with case numbers, rates and trends by geographical areas and demographic variables, and prevalence data by population;
- fact sheets, based on the data provided by the system, with tables and graphs that can be posted at health department offices and clinics, and provided in response to ad hoc enquiries; guidelines; and technical manuals;
- regular newsletters to clinicians, laboratory personnel and others, which may include brief reports of surveillance data along with updated information on patient management;
- press releases that highlight disease burden and trends, and can be used as part of public information campaigns;
- educational material such as charts and posters developed using the data provided by surveillance case-reports;
- verbal feedback during meetings and supervisory visits;
- electronic media such as publication of summary data on a website.

National STI programmes should also include a system for feedback from the health-care providers and institutions that participate in STI surveillance, as this would assist the STI programme to review its surveillance activities and make the necessary changes to improve the system.

## 10. Evaluation of surveillance

Each country needs to periodically assess its STI surveillance system so that it continues to reflect the national STI control priorities, remains efficient and takes advantage of opportunities for the integration of activities. If the evaluation indicates that the system is functioning unsatisfactorily, new surveillance methods and techniques that improve the efficiency of the system could be considered and included in the process for strengthening the surveillance system.

During an evaluation, it is important to determine whether:

- the surveillance objectives are being met;
- surveillance data are used for action;
- surveillance has had an impact at district, regional and national levels.

### 10.1 Key points for evaluating STI surveillance systems

The evaluation should begin with identification of all STI surveillance activities, categorizing them by component (e.g. case-reporting, assessment of syndromic etiologies, AMR monitoring and prevalence assessment and monitoring) and by syndrome or disease.

Initially, each component (case-reporting, etc.) should be evaluated separately, and within each component, separate attention given to each reported syndrome or disease.

After evaluating each component, an overall assessment should be performed that identifies components that need to be strengthened, gaps, and areas of duplication and activities that can be dropped.

### 10.2 Systems evaluation

To evaluate the STI surveillance system, the system description is important and should include the following:

- the staff and organizations involved
- the flow of information
- tools used for data collection, analysis and dissemination
- mechanisms for transfer of data
- the frequency of reporting and feedback
- quality control

The evaluation should address the following questions:

- what is the population being monitored?
- who is responsible for reporting a case?
- what data are collected on each case and who is responsible for collecting them?
- how are data collected and entered into the surveillance system?
- are data elements coded in a standard manner?
- if there are multiple administrative levels represented in the system, how are the data transferred from one level to another?
- are privacy and confidentiality guidelines in place?
- how is information stored?
- what format is used to store information?
- are data-quality checks done?
- what type of documentation is available?
- how is the surveillance system maintained and who is responsible for system maintenance?
- who analyses the data?
- how are data analysed and how often?
- are there tabulations, analyses and reports?
- how are the reports disseminated, to whom and how often?
- has there been any feedback?

### 10.3 Monitor the quality of the surveillance system

An important indicator of a quality-reporting system is measurement of its timeliness and completeness. When reports are sent and received on time, the possibility of a prompt and effective response is greater. Completeness of reporting describes whether all the reporting sites have reported as expected. If reports are late, or not submitted, the aggregated information for the district (or region or centre) will not be accurate.

A monitoring tool such as a record of reports received may be used to monitor the timeliness and completeness of reporting. The record of reports received should be used to:

- measure how many reporting sites submitted reports for a given period;
- identify which reporting sites have reported;
- measure how many reports were submitted on time.

## 11. Enhanced surveillance for STIs

When the core components of the STI surveillance system have been established and found to be of good quality, additional approaches could be selected for “enhanced surveillance” of STIs. Enhanced surveillance builds on the foundation described above, with the objective to provide more comprehensive and improved quality information. It includes studies to support special initiatives and issues that are not addressed in sufficient detail through the core components described above.





## Annex 1: Case definitions for selected sexually transmitted infections and syndromes

### *Genital ulcer disease*

An ulcer (a visible break in the skin) on the penis, scrotum or rectum in men, and on the labia, vagina, cervix and rectum in women.

Genital ulcer disease syndrome can be caused by syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale or genital herpes.

### *Urethral discharge*

A discharge in men (with or without dysuria), seen at the urethral meatus, with or without milking/expressing the urethra.

Urethral discharge syndrome is commonly caused by *Neisseria gonorrhoeae* or *Chlamydia trachomatis*; other infectious agents associated with urethral discharge syndrome include *Mycoplasma genitalium*, *Ureaplasma urealyticum* and *Trichomonas vaginalis*.

### *Vaginal discharge*

An abnormal vaginal discharge with change in the quantity, consistency, colour or odour (with or without vulval itching or burning).

Vaginal discharge syndrome is commonly caused by trichomoniasis, bacterial vaginosis and vulvovaginal candidiasis; it is less frequently caused by gonococcal or chlamydial cervical infection.

### *Lower abdominal pain in women*

Pain in the lower half of the abdomen. If accompanied by abnormal vaginal discharge, marked pelvic tenderness and cervical motion tenderness with or without fever, it is suggestive of pelvic inflammatory disease.

### *Anorectal infections*

Infections of the external anus and anal canal involving stratified squamous epithelium (for example, human papillomavirus, herpes simplex virus, and syphilis).

### *Urethritis*

Inflammation of the urethra characterized by dysuria and urethral discharge with microscopic evidence of more than five white blood cells per high-power field.

### *Proctitis*

Inflammation caused by infections from the dentate line to the rectosigmoid junction (for example, gonorrhoea, chlamydial infections, HSV).

### *Gonorrhoea*

#### **Probable**

Microscopic demonstration of Gram-negative intracellular diplococci in a sample from the endocervix or urethra or rectum

#### **Confirmed**

Isolation by culture of oxidase positive, Gram-negative intracellular diplococci confirmed by sugar utilization or demonstration of *Neisseria gonorrhoeae*-specific DNA in a clinical specimen (from the endocervix, urethra, rectum or pharynx) by a properly evaluated nucleic acid detection test.

### *Chlamydia trachomatis infection (genital)*

A positive culture, direct fluorescent antibody test or antigen detection test for *Chlamydia trachomatis*, or demonstration of *Chlamydia trachomatis*-specific DNA from a urethral, cervical, vaginal or urine sample by a properly evaluated nucleic acid detection test

### *Chancroid*

Infection caused by *Haemophilus ducreyi* characterized by painful genital ulceration and inflammatory inguinal adenopathy confirmed by identification of *Haemophilus ducreyi* by culture or nucleic acid test in ulcer exudate

## Genital herpes

### Probable

A history of one or more previous episodes of similar genital lesions or blisters

### Confirmed

A positive culture or demonstration of HSV-specific DNA by nucleic acid tests in blister/ulcer exudate

## Syphilis, primary and secondary

### Probable

An illness with ulcers (primary) or mucocutaneous lesions (secondary) and a reactive serologic test (non-treponemal or treponemal). Primary syphilis lesions may occur on sites other than in the anogenital area.

### Confirmed

Demonstration of *Treponema pallidum* in clinical specimens by dark-field microscopy, DFA-TP, nucleic acid test or equivalent methods

## Syphilis, latent

No clinical signs or symptoms of syphilis and (1) a reactive non-treponemal and treponemal test in a patient with no prior syphilis diagnosis; or (2) a non-treponemal test titre demonstrating fourfold or greater increase from the last non-treponemal test titre in a patient with a prior syphilis diagnosis

Latent syphilis may be further characterized as *early latent*, if there is evidence that the infection was acquired within the previous 24 (or 12) months, and *late latent*, if there is evidence that the infection was acquired earlier.

## Lymphogranuloma venereum

Infection with L1, L2, or L3 serovars of *Chlamydia trachomatis*, characterized by genital lesions, suppurative regional lymphadenopathy or haemorrhagic proctitis

## Granuloma inguinale

A slowly progressive ulcerative disease of the skin and lymphatics of the genital and perianal area, caused by infection with *Calymmatobacterium granulomatis*.

## Trichomonas vaginalis infection

The presence of typical trichomonads by microscopy of a wet mount of genital swabs or urine from women or the presence of typical trichomonads detected by cervical smear or isolation by culture of *Trichomonas vaginalis* or demonstration of *Trichomonas vaginalis*-specific DNA from a urethral, cervical, vaginal or urine sample by a properly evaluated nucleic acid detection test

## Bacterial vaginosis

A condition in which the normal bacterial flora in the vagina is disrupted and replaced by an overgrowth of *Gardnerella vaginalis*, *Bacteroides*, *Mobiluncus*, and *Mycoplasma hominis*. It is sometimes accompanied by an abnormal vaginal discharge, odour, pain, itching or burning.

## Candidiasis

Infection with overgrowth of *Candida* spp. (example, *Candida albicans*, *Candida glabrata*) in the vagina, presenting with pruritus, abnormal discharge and erythema, confirmed by the presence of pseudohyphae on a wet mount or Gram stain smear, or a positive culture for *Candida*.

## Scrotal swelling

Acute-onset unilateral testicular pain and swelling, often with tenderness of the epididymis and vas deferens.

## Cervicitis

Cervical inflammation that is not the result of infection with *Neisseria gonorrhoeae* or *Trichomonas vaginalis*. Cervical inflammation is defined by the presence of one of the following criteria:

- mucopurulent secretion (from the endocervix) that is yellow or green when viewed on a white, cotton-tipped swab (positive swab test);
- induced endocervical bleeding (bleeding when the first swab is placed in the endocervix).

## Anogenital warts

An infection characterized by the presence of visible, exophytic (raised) warty growths on the internal or external genitalia, perineum or perianal region.

## *Ophthalmia neonatorum*

### **Probable**

Unilateral or bilateral conjunctivitis in a neonate (within 4 weeks of delivery).

### **Confirmed**

Unilateral or bilateral conjunctivitis in a neonate (within 4 weeks of delivery) with an ocular specimen that is positive for *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

## Annex 2: Sample size determination

Sample sizes required to detect a change (decrease or increase) in seroprevalence rates at a specific site between two survey periods are shown in the Table A1. For example, if the baseline prevalence is 20%, a sample size of 197 is required to detect a 50% decrease in prevalence (from 20% to 10%) between two periods.

**Table A1**

**The sample size required for determining a significant change between two proportions<sup>a</sup>**

Baseline prevalence (%)	Sample size for specific percentage change								
	10%	20%	30%	40%	50%	60%	70%	80%	90%
1	145 800	34 000	14 000	7290	4280	3000	2070	1459	1060
5	28 000	6550	2800	1500	903	585	400	282	204
10	13 000	3200	1350	718	432	280	190	135	97
15	8500	2030	850	457	275	178	122	86	62
20	6000	1425	612	326	197	128	87	61	44
25	4500	1090	463	247	149	97	66	46	33

With a power of 80% (beta = 0.80) and a significance level of  $P < 0.05$ .

<sup>a</sup> Adapted from UNAIDS/WHO Working Group on Global HIV/AIDS/STI Surveillance. *Guidelines for conducting HIV sentinel serosurveys among pregnant women and other groups*. Geneva, World Health Organization, 2003 (UNAIDS/03.49E) (19).

## Annex 3: STI recording and reporting forms

### Tally sheet for STI cases based on syndromic diagnosis

Name of health-care facility

Dates: From

To

Syndromic diagnosis	Number of cases by sex and group															Total
		Males							Females							
		0-4	5-14	15-19	20-29	30-39	40-49	50+	0-4	5-14	15-19	20-29	30-39	40-49	50+	
Urethral discharge	0000	0000	0000	0000	0000	0000	0000									
	0000	0000	0000	0000	0000	0000	0000									
	0000	0000	0000	0000	0000	0000	0000									
Genital ulcers	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
Vaginal discharge		0000	0000	0000	0000	0000	0000	0000								
		0000	0000	0000	0000	0000	0000	0000								
		0000	0000	0000	0000	0000	0000	0000								
Lower abdominal pain (women)		0000	0000	0000	0000	0000	0000	0000								
		0000	0000	0000	0000	0000	0000	0000								
		0000	0000	0000	0000	0000	0000	0000								
Inguinal bubo	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
Acute scrotal swelling	0000	0000	0000	0000	0000	0000	0000									
	0000	0000	0000	0000	0000	0000	0000									
	0000	0000	0000	0000	0000	0000	0000									
Neonatal conjunctivitis	0000		0000													
	0000		0000													
	0000		0000													
Other STI	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000
Total																

For every STI patient, cross one “0” vertically in the appropriate cell according to syndrome, sex and age like this Ø.

Cross only at the first visit for the current episode. Do not cross for the follow-up visit for the current episode.

If the patient comes for another episode of STI, cross again. Work out the total at the end of each month; calculate the total horizontally and vertically. One sheet is usually enough for one month. However, add more sheets if necessary.

## Tally sheet for STI cases based on etiologic diagnosis

Name of health-care facility

Dates: From

To

Etiologic diagnosis	Number of cases by sex and group														Total
	Males							Females							
	0-4	5-14	15-19	20-29	30-39	40-49	50+	0-4	5-14	15-19	20-29	30-39	40-49	50+	
Syphilis	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Gonorrhoea	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Lymphogranu- loma venereum	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Non-gonococcal urethritis	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Chancroid	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Trichomoniasis	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Pelvic inflammatory disease (women)	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Bacterial vaginosis (women)	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Candidiasis	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Genital herpes	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Granuloma inguinale	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Genital wart	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Neonatal conjunctivitis	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Other STI	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	0000	
Total															

For every STI patient, cross one "0" vertically in the appropriate cell according to syndrome, sex and age like this Ø.

If the patient comes for another episode of STI, cross again. Work out the total at the end of each month; calculate the total horizontally and vertically. One sheet is usually enough for one month. However, add more sheets if necessary.

Cross only at the first visit for the current episode. Do not cross for the follow-up visit for the current episode.

## STI report based on syndromic diagnosis

Country \_\_\_\_\_ Period of report: \_\_\_\_\_ Date of report: \_\_\_\_\_

Syndromic diagnosis	Number of cases by sex and age group (years)														Total
	Males							Females							
	0–4	5–14	15–19	20–29	30–39	40–49	50+	0–4	5–14	15–19	20–29	30–39	40–49	50+	
Urethral discharge															
Vaginal discharge															
Genital ulcer															
Lower abdominal pain (women)															
Scrotal swelling															
Inguinal bubo															
Neonatal conjunctivitis															
Total															

1. This report of STI should be based on syndromic diagnosis.
2. Only new cases diagnosed during the period should be reported.
3. The report should include data from all treatment facilities, public and private.
4. The report should be forwarded quarterly and annually.

### Results of serological test for syphilis

Persons tested	During this period	Cumulative for this year	Remarks		Remarks
	Number tested	Number +ve	Number. tested	Number +ve	
Blood donors					
Pregnant women					
STI patients					
Others					
Total					

## STI report based on etiologic diagnosis

Country

Period of report:

Date of report:

Etiologic diagnosis	Number of cases by sex and age group (years)														Total
	Males							Females							
	0-4	5-14	15-19	20-29	30-39	40-49	50+	0-4	5-14	15-19	20-29	30-39	40-49	50+	
Syphilis															
Gonorrhoea															
Lymphogranuloma venereum															
Non-gonococcal urethritis															
Chancroid															
Trichomoniasis															
Pelvic inflammatory disease (women)															
Bacterial vaginosis (women)															
Candidiasis															
Genital herpes															
Granuloma inguinale															
Genital wart															
Neonatal conjunctivitis															
Other STI															
Total															

1. This report of STI should be based on etiologic diagnosis.
2. Only new cases diagnosed during the period should be reported.
3. The report should include data from all treatment facilities, public and private.
4. The report should be forwarded quarterly and annually.

### Results of serological test for syphilis

Persons tested	During this period	Cumulative for this year	Remarks		Remarks
	Number tested	Number +ve	Number. tested	Number +ve	
Blood donors					
Pregnant women					
STI patients					
Others					
Total					

## Clinic-based STI register

SW register (to adapt) <name of clinic> <name of organization> <date>

Demographics (complete all)			Visit (tick 1 or more)				Syndrome (tick 1 or more)						Treatment (tick 1 or more)						Prevention/ Screening (tick 1 or more)				Lab/other needs (optional)										
ID Number	Sex (M, F, T)	Age (years)	1st clinic visit	Check-up	Syndrome	Partner referral	Follow-up	VCD	GUP	LAP	UD	ARD	Other	none	Rx1	Rx2	Rx3	Rx4	Rx5	Rx6	Counsel	Condoms	Partner treat	Referral	Next visit	RPR/VDRL	VCT	IUD HR	Comments				
1																																	
2																																	
3																																	
4																																	
5																																	
6																																	
7																																	
8																																	
9																																	
10																																	
11																																	
12																																	
Fill in date once per day	Indicate if:		1st clinic visit					VCD = vaginal cervical discharge							Rx1 = cervicitis, UD, ARD or presumptive treatment																		
Start new page each day ID numbers from cards	Check-up							GUD = genital ulcer							Rx2 = vaginitis treatment																		
Sex/gender	Syndrome							LAP = lower abdominal pain							Rx3 = GUD treatment																		
	Partner referral							UD = urethral discharge							Rx4 = GUD (herpes) treatment																		
	Follow-up for previous STI (within 2 weeks)							ARD = anorectal discharge							Rx5 = LAP treatment																		
															Rx6 = UD 2nd-line treatment (adapt if using STI packs)																		

## Annex 4: UNAIDS/WHO recommendations for core surveillance in different epidemic settings<sup>a</sup>

	HIV surveillance	STI surveillance	Behavioural surveillance and population size estimation
Low level	<ol style="list-style-type: none"> <li>1. HIV advanced infection reporting</li> <li>2. HIV case-reporting</li> <li>3. Facility or community-based HIV sentinel surveillance for key population at higher risk of HIV exposure</li> </ol>	<ol style="list-style-type: none"> <li>1. STI case-reporting</li> <li>2. Facility or community-based STI sentinel surveillance for key population at higher risk of STI exposure</li> <li>3. Antenatal clinic syphilis surveillance</li> </ol>	<ol style="list-style-type: none"> <li>1. Mapping-based size estimation of high-risk groups</li> <li>2. Biobehavioural surveys of key population at higher risk of HIV and STI exposure (e.g. biological and behavioural surveys (BBS) or integrated biological and behavioural surveys (IBBS))</li> </ol>
Concentrated	<ol style="list-style-type: none"> <li>1. HIV advanced infection reporting</li> <li>2. HIV case-reporting</li> <li>3. Facility or community-based HIV sentinel surveillance for key population at higher risk of HIV exposure</li> <li>4. ANC sentinel surveillance for HIV</li> </ol>	<ol style="list-style-type: none"> <li>1. STI case-reporting</li> <li>2. Facility or community-based STI sentinel surveillance for key population at higher risk of STI exposure</li> <li>3. Antenatal clinic sentinel surveillance for syphilis</li> </ol>	<ol style="list-style-type: none"> <li>1. Mapping-based size estimation of high-risk groups</li> <li>2. Biobehavioural surveys of key population at higher risk of HIV and STI exposure (e.g. BBS, IBBS) and inclusion of biological markers in highest-priority sites where feasible</li> </ol>
Generalized	<ol style="list-style-type: none"> <li>1. HIV advanced infection reporting</li> <li>2. HIV case-reporting</li> <li>3. Facility or community-based HIV sentinel surveillance for key population at higher risk of HIV exposure</li> <li>4. Antenatal clinic sentinel surveillance for HIV</li> <li>5. General population surveys (with behavioural and biological markers, including STI)</li> </ol>	<ol style="list-style-type: none"> <li>1. STI case-reporting</li> <li>2. Facility or community-based STI sentinel surveillance for key population at higher risk of STI exposure</li> <li>3. ANC sentinel surveillance for STI</li> </ol>	<ol style="list-style-type: none"> <li>1. Characterization and size estimation of high-risk groups including profile of general population with multiple/concurrent sexual partners</li> <li>2. Biobehavioural surveys of risk behaviours, HIV and STI of key population at higher risk of HIV and STI exposure, especially proxy groups for general population with multiple/concurrent sexual partners</li> </ol> <p>Repeated behavioural surveys in groups considered to engage in high-risk behaviour for HIV infection</p> <p>Repeated risk-behaviour surveys in the general population with a focus on young people</p>

In all three epidemic states, STI surveillance serves as:

- an early warning system for HIV infection and emergence of HIV in new groups or new geographical areas
- an evaluation tool for HIV-prevention programmes

Adapted from *Guidelines for second generation HIV surveillance: an update*. Geneva, World Health Organization, 2011 (6).

## Annex 5: Recommended list of existing surveillance documents relevant for some technical aspects of STI surveillance

### List of surveillance technical guidance documents available

Title	Year	Topic
UNAIDS/WHO Working Group on Global HIV/AIDS/STI Surveillance. <i>Guidelines for second generation HIV surveillance: an update: know your epidemic (6)</i> , ISBN 978 92 4 150582 6	2013	Update on methodologies for conducting Second Generation HIV Surveillance
UNAIDS/WHO Working Group on Global HIV/AIDS/STI Surveillance. <i>Guidelines on estimating the size of populations most at-risk to HIV (9)</i> ISBN 978 92 4 159958 0	2010	Update on methodologies for estimating the size of most at risk populations
UNAIDS/WHO Working Group on Global HIV/AIDS/STI Surveillance. <i>Guidelines on surveillance among populations most at risk for HIV (20)</i> ISBN 978 92 4 150137 8	2011	Update on methodologies for conducting HIV surveillance among most at risk populations
UNAIDS/WHO Working Group on Global HIV/AIDS/STI Surveillance. <i>Evaluating a national surveillance system (21)</i> , ISBN 978 92 4 150137 8	2011	How to assess and evaluate HIV surveillance systems and adapt them to the needs of countries

# Annex 6: WHO informal consultation on STI surveillance guidance and laboratory support for improving surveillance systems for STIs, 31 January to 1 February 2008, Geneva, Switzerland

## Topics for group work

### Topic A I

1. Using the criteria from the plenary, discuss:

- which STIs (and sequelae) should be considered essential for STI surveillance, taking into account:
  - the rationale for each infection
  - geographical settings
  - population groups
  - linkages with other existing health interventions/programmes
- which of the commonly used STI syndromes should be part of a national STI surveillance system, taking into account:
  - the rationale for each syndrome included and excluded
  - geographical settings
  - populations

2. At which level of the health-care system:

- should each syndrome be monitored;
- should each specific infection be monitored (for example, syphilis, chlamydia, HPV, gonorrhoea, HSV, lymphogranuloma venereum, chancroid).

3. Are there any other reproductive tract infections, like bacterial vaginosis, to be recommended for surveillance? Give the rationale for inclusion and exclusion.

4. Diagnostic methods for STI surveillance (we suggest the use of a matrix to facilitate your discussion):

- which laboratory tests can be recommended for STI surveillance for each condition?
- is there any need for standardization for purposes of comparability between programmes and countries (i.e. case definition or interpretation)?

### Topic B I

1. Discuss approaches for STI surveillance (e.g. population-based screening, antenatal clinic clients) and settings in which they are most appropriate:

- data source, setting, populations, frequency, etc.

2. For the purpose of public health decision-making, how can data gathered by syndromic reporting be reconciled with data gathered by laboratory-based methods?

3. What should be the standard (core) data elements and optional (additional) data elements for STI surveillance?

4. How can the surveillance data be better linked to action?

5. Highlight challenging ethical, legal and rights issues to be addressed in guidance for STI surveillance. Propose action points to try and resolve them (e.g. chlamydia surveys in adolescents under the age of majority, school-based surveys, etc.).

## Distribution of the participants per each small group

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## Appendix 1: A brief guide to sampling and laboratory requirements for conducting gonococcal antimicrobial susceptibility surveillance

### Background and rationale

Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* (*N. gonorrhoeae*) presents a significant challenge to controlling gonorrhoea.

An effective antibiotic for programmatic treatment or use in a standard treatment regimen is defined by the World Health Organization (WHO) as one that cures 95% or more cases presenting from the local community general population. That is, at a level of AMR of 5% or more, an antibiotic should not be used in a standard treatment regimen. This level of antibiotic effectiveness is needed to help control disease and prevent morbidity arising from complications of gonococcal infection (1–6). In key populations with a potential to transmit infection more frequently or to many sex partners, such as sex workers and men who have sex with men (MSM), a level of resistance to an antimicrobial agent of 1% or more should be sufficient to consider its substitution.

Data from many existing programmes indicate AMR rates of 50% or more to some antibiotics, such as the quinolones and penicillins. Additionally, resistance to certain adjunctive treatments such as tetracyclines and azithromycin is also common. Further, AMR and, in several countries, treatment failure, is now documented when the most potent oral cephalosporin (cefixime) is used, which is the recommended and preferred treatment in many countries, and the first gonococcal strain with high-level resistance to ceftriaxone, most probably related to a treatment failure, has been characterized in detail (7–10).

At the population level, surveillance of AMR in *N. gonorrhoeae* is key to the monitoring of local, regional and international trends in AMR, which can help inform and shape public health policy. Comparisons between antimicrobial susceptibilities of gonococci isolated in different geographical areas provide information about the distribution and temporal spread of resistant isolates. Thus, changes in recommended antimicrobial therapies can be anticipated, and surveillance can be enhanced to guide timely changes in these therapies at the local level.

### Objectives

The principal objective of the monitoring exercise is to determine the antimicrobial susceptibility of *N. gonorrhoeae* to the current treatment regimens in the local setting or country, in order to optimize treatment of gonorrhoea in that setting or country.

A second objective is to participate in the wider Gonococcal Antimicrobial Surveillance Programme (GASP) of WHO to determine the antimicrobial resistance/susceptibility of *N. gonorrhoeae* in all WHO regions, in order to detect the emergence of AMR and its spread.

### Methods

*(Men with urethral discharge are often selected for sampling because of the relative ease of collection, higher yield of positive cultures and lower cost. Studies need not be limited to this group, and preferably samples also from women, MSM and especially extra-genital sites (preferably pharyngeal) can be included. However, the following descriptions are based on sampling from the male urethra.)*

Samples of urethral-discharge specimens will be collected from men presenting at designated sites over a specified period in time.

### Monitoring population and eligibility

Eligibility criteria:

- males with visible urethral discharge (pus), whether they come for a first visit or a follow-up visit.

Exclusion criteria:

- men complaining of dysuria without visible signs of urethral discharge.

### Monitoring sites and sample size

The number of monitoring sites used will depend on the likely number of attendees at each site. At least initially, it is best to keep these at a minimum to reduce costs, but not at the expense of a sample that is more representative. A target of approximately 100 *N. gonorrhoeae* isolates at least should be sought in the monitoring period. If the determined resistance level to a specific antibiotic is between 3% and 10%, it is recommended to enhance the surveillance.

(A smaller number only may be obtainable for a pilot study. It may provide some useful and indicative data that suggest the need for an expanded study.)

### Sampling procedures

Consecutive men with signs of urethral discharge should be included in the monitoring exercise. Specimens should be labelled with a code number (*there may be a need for consent form in some settings or countries*).

### Specimen collection at the STI clinics

Urethral pus should be collected by a member of the health-clinic staff, onto a swab, and immediately inoculated onto selective and enriched gonococcal medium culture plates labelled with the patient code, date and time of collection. The swab can also be placed in an appropriate transport medium for transport to the laboratory for inoculation on culture plates.

The clinic site where the material was obtained and the date and time the specimen was obtained need to be recorded. Ideally, as much basic clinical and patient demographic data as possible should be collected, i.e. age, sex, sexual orientation, type of sexual partner (female or male sex worker, MSM, etc.).

The plates should be placed immediately into a humidified incubator with a carbon dioxide (CO<sub>2</sub>) source (*laboratory in close proximity*), or into a suitable transport system for sending to the laboratory.

Transported plates will need to reach the microbiology laboratory by a specified time. It should be noted that culture plates will need to be examined at 24 and 48 hours' incubation. As such, laboratories may have to work with cultures for 48 hours after swab collection. This may have implications for weekend overtime and opening hours for the laboratory.

Plates can be kept for a maximum of 4 hours at room temperature before incubation.

The specimen may be transported in an insulated box (without ice), to the laboratory (to avoid extreme heat exposure during travel). A transportation log showing the number of plates sent and received needs to be kept and signed as received.

### Symptomatic treatment

Every male patient with a complaint of urethral discharge, whether or not included into the *N. gonorrhoeae* monitoring, should receive antibiotic treatment according to national STI management guidelines and directly administered by the staff, if possible. Patients should be counselled and requested to refer their sexual partners to the clinic for treatment, in accordance with the national guidelines. In addition patients may be provided a condom demonstration and free condoms, according to local policy.

### Specimen processing and culture at the laboratory

When the plates inoculated in the clinics reach the laboratory, they should be cross-streaked to obtain isolated colonies and placed in the incubator. Control plates should also be used.

Incubated plates should be examined for possible growth of *N. gonorrhoeae* at 24-hour intervals for a minimum of 48 hours. Presumed colonies of *N. gonorrhoeae* will be Gram stained (Gram-negative diplococci) and presumptively identified using this and the oxidase reaction (rapid oxidase positive). Again, suitable controls should be used.

Definitive identification procedures should be employed if possible. A suitable system is a rapid carbohydrate utilization test – these tests are quite inexpensive. After identification, *N. gonorrhoeae* colonies should be subcultured to a suitable storage material, for 24–48 hours at 35–37°C, again with control plates.

The colonies are then *either* tested on site for AMR *or* stored for later testing *or* stored for shipping and testing elsewhere.

Documentation should be made of where antimicrobial susceptibility testing will be conducted.

The minimum inhibitory (in vitro) concentrations (MICs) of the antimicrobial agents currently utilized for treatment of *N. gonorrhoeae*, as well as, possibly, antimicrobial agents proposed for future use nationally should be determined, following agreed standard methods and interpretations, and using and recording quality-control procedures and findings.

Ideally, WHO reference control strains (11) should be used for each batch of tests (or if there are too many tests daily, the controls should be used on a regular basis). The number of

strains used will depend on the antibiotics tested and concurrent use of other internal control procedures (see Appendix 4). The reference controls may be requested from the regional WHO GASP reference laboratories or the WHO collaborating centres for STIs.

The laboratory testing for antimicrobial susceptibility should participate in the external quality assessment surveys (EQASs) conducted by the WHO regional reference laboratory or WHO collaborating centres.

## Training

### Collection of samples

The health-care staff of the selected sites may need to be instructed on the selection of eligible males, urethral pus collection, inoculation onto media plates, labelling, and storage and transport of inoculated plates to transport media/systems.

### Microbiological procedures

The microbiology laboratory staff may need training in various aspects of *N. gonorrhoeae* microbiology, depending on their experience and prior training.

## Data management and use of results

The laboratory data will be used to:

- determine the level of *N. gonorrhoeae* susceptibility to a number of selected antimicrobial agents in the country;
- determine the level of *N. gonorrhoeae* susceptibility to a number of antimicrobial agents in the wider region.

One hundred gonorrhoeae isolates would provide the following information:

- if a high proportion (more than 30–50%) of *N. gonorrhoeae* is resistant, it will be reliably detectable in a sample of this size. Conversely, if there is zero or very low resistance (less than 1–2%) to an agent in a sample of this size, it is likely, but not certain, that resistance is below the critical level of 5%. In this instance, it is suggested that monitoring be continued intermittently and that reports of any treatment failure be monitored. If the resistance level is at an “intermediate level”, (3–10%), it will be necessary to undertake enhanced surveillance to verify the true level of resistance.

## Selected monitoring sites list and characteristics

Site code number	Names of selected sites	Supporting laboratory	Estimated number of <i>N. gonorrhoeae</i> isolates realistically collectable in (x) months	Comments
01				
02				
03				
04				
05				
06				
07				
08				
09				
10				
11				
12				
13				

## Laboratory materials and equipment needed for collecting gonococcal isolates

The following materials will be required

- swabs
- gloves
- CO<sub>2</sub> incubator/candle jars
- plates of *N. gonorrhoeae*-selective agar media for initial isolation and non-selective agar medium for subculture
- plastic bacterial inoculation loops and needles
- Gram stain reagent
- microscope with magnification ×400 to ×1000
- microscope slides
- immersion oil
- oxidase tests
- species-confirmatory test
- labels
- laboratory markers
- control strains

For storage/preservation methods for *N. gonorrhoeae*, see Appendix 2.

## Selection of growth media

Some systems require the use of animal blood, usually horse blood, which may be difficult to obtain in many settings. Bovine blood is also suitable but sheep and goat blood less so. Haemoglobin containing media are sometimes available. *Human blood should not be used in bacteriological growth media*, for several reasons:

- it may contain inhibitory substances not found in animal blood sources, either in the form of natural or acquired immune mechanisms or antibiotics. This will affect the outcome of AMR testing, by an unquantifiable amount:
- there are significant health hazards for laboratory staff, such as acquiring bloodborne viruses.

AMR testing requirements will depend on the test method chosen and the growth media available.

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## Appendix 2: Strategies for improving sample sizes, transport and preservation of *Neisseria gonorrhoeae* for antimicrobial resistance testing

### Low availability of isolates of *N. gonorrhoeae* for AMR testing

New approaches are needed to ensure availability of *Neisseria gonorrhoeae* (*N. gonorrhoeae*) cultures for antimicrobial resistance (AMR) testing.

Historically, gonococcal isolates for AMR testing and surveillance were obtained from laboratories using culture-based methods for diagnostic purposes. The two roles of diagnosis and AMR testing were closely linked.

Changes over time in the diagnosis of gonorrhoea suggest that this approach is not sustainable if a supply of gonococcal isolates is to be maintained in sufficient numbers for AMR testing and surveillance. Two major factors account for this difficulty:

- the widespread *introduction of syndromic management* approaches, particularly in resource-constrained settings, has resulted in a considerable decline in the number of *N. gonorrhoeae* isolates that have been cultured for diagnostic purposes. Many laboratories formerly functioning at a high level no longer perform culture for gonococci, and basic skills have been lost;
- nucleic acid amplification assays (NAATs) have been rapidly replacing culture-based methods for diagnosis of gonorrhoea, particularly in well-resourced settings. These tests are generally reliable for most sexually transmitted infections (STIs), including *N. gonorrhoeae* and can be used in remote settings to provide an understanding of what is causing the local syndromes. However, currently, NAATs for *N. gonorrhoeae* cannot reliably supply AMR data and so research for development of genetic AMR testing methods is essential.

Thus, there is a need to modify approaches to culture to obtain adequate numbers of gonococci. In many settings, obtaining *N. gonorrhoeae* isolates for AMR testing needs to be considered separately from diagnostic procedures based on culture, which, in any event, is in decline.

### Recommendations for increasing the availability of gonococcal isolates for AMR testing

#### *Use of “targeted” culture*

This means that resources for culture are focused in areas where a high yield of isolates is likely. In settings where syndromic management is the main diagnostic approach, urethral specimens from men with urethral discharge could be cultured (effective in all settings and already used in a number of national surveillance programmes). In settings where Gram staining is performed as the main diagnostic test, samples showing Gram-negative intracellular diplococci could be timely cultured. In settings where NAATs are the main diagnostic tests, samples that are NAAT positive for *N. gonorrhoeae* could be promptly cultured. Ideally, the patient should not have been administered any antibiotics in the last three days.

It has been shown previously that a high yield of *N. gonorrhoeae* can be obtained by timely culture of the first-void urine of those with a positive NAAT (see [www.icngco.org](http://www.icngco.org) and go to “Sampling and other methods”). That is, if there is a positive NAAT for *N. gonorrhoeae* in a first-void urine, if that urine is cultured within 24 hours, it can yield viable gonococci in between 30% and 70% of specimens (depending also on urine attributes).

#### *Maintaining N. gonorrhoeae cultures or nucleic acid for testing, storage and/or transport*

In many programmes, *N. gonorrhoeae* is cultured in peripheral centres and then stored and transported to a larger facility for testing. Loss of viability of *N. gonorrhoeae* isolates is a continuing problem that may seriously deplete the number of these isolates available for testing. The following describes techniques for storing and transporting *N. gonorrhoeae* cultures. Less commonly, gonococci that are no longer viable, e.g. due to power failures causing loss of refrigeration or incubator capability, can now be tested for some forms of resistance by molecular methods using

nucleic acid extracted from the dead gonococci. This technology is currently in development and is expensive, and close contact between the peripheral and reference centres is required to make it possible.

Various storage methods may be used for maintaining the viability of *N. gonorrhoeae* cultures for prolonged periods and for transporting them over long distances under extreme conditions. Reference strains (e.g. World Health Organization (WHO) reference strains for quality assurance (1) of designated categories of susceptibility, which are supplied to network participants, should also be maintained by the participating laboratory, and participants may also like to store certain clinical isolates of interest or use them for referral. The following methods are recommended for either long-term storage (or transportation to other centres):

- preservation of bacteria on chocolate agar slopes;
- preservation of bacteria by deep freezing (−70°C);
- preservation of bacteria by freeze-drying (lyophilization);
- preservation of bacteria in liquid nitrogen (not described in the present Appendix, which focuses on peripheral laboratories).

### Maintaining viable *N. gonorrhoeae* on chocolate agar slopes for storage and transport

A pure culture of the gonococcus to be stored is heavily inoculated onto a 3 ml volume chocolate agar slope in a polycarbonate (plastic) screw-top Bijou (5 ml volume) bottle and incubated with the screw cap loosened for a minimum of 24 hours in a CO<sub>2</sub>-enriched atmosphere or until visible growth is present on the agar surface. Sterile liquid paraffin is then used to completely fill the agar slope, the screw cap lid is fully tightened and the Bijou bottle slope is then stored at 37°C until the *N. gonorrhoeae* are tested or forwarded elsewhere (2, 3). When the gonococci are required for testing, a sterile bacteriological loop is inserted through the paraffin overlay to remove the bacterial growth. When this is inoculated onto a fresh agar plate and streaked, globules of paraffin will also be present. However, after incubation for 48 hours, gonococcal colonies are readily discernible and can be subcultured for appropriate examination. The original paraffin-overlaid slope can be returned to storage for further use, but special care must be taken at the initial inoculation to use a pure culture and to ensure that, when sampled, the slope is not contaminated.

The location of strains should be recorded, as should details of access to the slopes!

### Notes

- Polycarbonate (plastic) bottles, not glass, must be used.
- Larger-volume containers may also be used, e.g. 30 ml MacCartney bottles, but these should also be polycarbonate and will require larger volumes of bacteriological media and paraffin, and occupy more storage space.
- The storage temperature should be 37°C, not room temperature; otherwise loss of viability will occur.
- For transport, lower temperatures may not affect viability for transit times of up to 5 days.
- Loss of plasmids may occur on long-term storage.
- It is suggested that familiarity with the system be obtained by both distributors and receivers of the slopes, before the system is implemented.
- Fully viable gonococci have been recovered after 9 months with this system in 100% of cases, but there are no data on viability beyond this period.
- Paraffin may be sterilized in large batches, e.g. 200 ml placed in a hot air oven at 180°C for 2 hours.

### Maintaining viable *N. gonorrhoeae* frozen at −70°C (NOT −20°C) for storage and transport

Storage at −70°C in a nutritious suspending medium, such as nutrient broth containing 20% glycerol, is an efficient means of storing bacteria, particularly *N. gonorrhoeae*, for a relatively long-term period and has proven to be one of the most successful ways of storing a large number of strains in a minimal amount of space. In addition, retrieval of the frozen isolate is relatively simple and quick.

### Materials and methods

- Storage temperature: −70°C.
- Nutrient broth plus 20% glycerol: 80 ml nutrient broth; 20 ml glycerol.
- Sterilize by autoclaving at 121°C for 15 minutes. The medium used is distributed in 1.0 ml volumes in small test tubes and stored at 4°C to 8°C prior to use.
- *Preparation of bacterial suspensions:* a heavy inoculum of the bacteria (obtained from a fresh pure subculture) is made in 1.0 ml nutrient broth with glycerol. Using the same pipette, the suspension is mixed well before being transferred to a labelled cryovial, and placed in a documented position in a labelled cryostorage box at −70°C.

- Documenting the location of strains: this should be completed, as should details of access to the vials.

### Notes

- Long-term storage at  $-20^{\circ}\text{C}$  is less effective, as fluctuations of temperature occur around  $-20^{\circ}\text{C}$  freezing systems when they are accessed, which materially affects strain viability.
- These frozen bacterial suspensions may be shipped to other centres if packed in dry ice. The transportation time should be minimal, so that the frozen cultures reach their destination before the dry ice has evaporated.
- Retrieving the culture from  $-70^{\circ}\text{C}$ : remove the cryotube from the freezer and do not allow it to thaw. Using the tip of a sterile Pasteur pipette, gently remove a small sample of the frozen bacterial suspension and transfer it to an appropriate *N. gonorrhoeae* agar growth medium. Use a loop to streak the inoculum for single isolated colonies and incubate the culture plate. Return the cryotube immediately to the freezer.

### Maintaining viable *N. gonorrhoeae* by freeze-drying (lyophilization) for storage and transport

This option is rarely available at peripheral centres and details of the procedures are not provided here. It is more usual for laboratories in peripheral centres to receive freeze-dried cultures from reference laboratories for use as quality control strains (7) or as part of an external quality assurance system (EQAS). However, the lyophilized strains may need to be stored at the peripheral laboratory before testing; this should be in the dark, but room temperature is satisfactory. Directions for resuscitation of the freeze-dried strains should accompany their dispatch.

Storage in liquid nitrogen is another option, but is not described for use in peripheral centres.

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# Appendix 3: Criteria for defining cases of treatment failure in gonorrhoea that are attributable to antimicrobial resistance in *Neisseria gonorrhoeae*

## 1. Background

The most important manifestation of antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* is undoubtedly treatment failure. Treatment failure may occur sporadically (1, 2) or cause outbreaks (3) or smaller clusters (4, 5), as AMR strains emerge or are introduced into a population. Treatment failure due to AMR may also occur endemically at low rates if inadequate treatments continue to be used (6). Recognition of treatment failures and early intervention to identify and control an outbreak is important for both individual patients and their sexual partners. Public health perspectives are also most relevant, in that treatment failures result in increases in disease rates and morbidity and costs (7–9).

However, what may at first appear to be clinical treatment failure may actually be due to circumstances other than antibiotic resistance, most commonly reinfection following successful treatment. Failure to comply with treatment, especially where multidose treatments are employed; inadequate dosing (6); use of low-quality antimicrobials; or cases where only an unsatisfactory clinical history is available are other examples of sources of possible confusion in defining the presence of a “true” treatment failure, i.e. one that is due to AMR.

From a laboratory perspective, the examination of *N. gonorrhoeae* obtained from cases of presumed treatment failure can be highly instructive. Laboratory evaluation of *N. gonorrhoeae* isolates from these cases can, in certain circumstances, exclude the possibility of treatment failure, or in others confirm that it was a possibility (see Section 2.1 point 4, below). It is also very important to fully examine the *N. gonorrhoeae* from probable treatment failures in instances where the failure is thought to be due to lack of efficacy in a previously satisfactory treatment regimen or to a possible emergence of resistance to a newly introduced antibiotic. Invaluable insights into resistance mechanisms, the relevance of existing minimum inhibitory concentration (MIC) breakpoints and the spread of resistant gonococci may be obtained. In these cases, every effort should be made to store

the isolate(s) concerned and, as appropriate, forward them to relevant centres for full characterization of their resistance genes and other features.

This appendix sets out clinical and laboratory criteria and requirements for defining, *in an ideal way*, probable and possible treatment failure in gonorrhoea due to antibiotic-resistant *N. gonorrhoeae* in an individual case. It also describes the need for laboratory involvement and how this may be applied and organized in relation to the detection of new and emerging AMR in *N. gonorrhoeae*. However, it must be recognized that all criteria cannot be fulfilled in all settings and situations, but it remains exceedingly valuable to also define treatment failures as much as possible (using all available information) in these settings and situations. Accordingly, the ideal way to define a treatment failure in gonorrhoea needs to be slightly adjusted and adapted to the actual, local setting.

The wider public health aspects of investigation of possible cases of treatment failure are not dealt with in this appendix, and require close epidemiological, clinical and laboratory liaison and collaboration. Other aspects of clinical management, such as partner notification and counselling, are also beyond the scope of this appendix. However, additional clinical data from sexual partners may clarify relevant issues (see Section 2.1, point 1, below), and Section 4 refers to additional investigations on samples from sexual partners that may be relevant to a wider investigation.

## 2. Considerations, confounders and laboratory contributions to the confirmation of antibiotic treatment failure in gonorrhoea that is due to antibiotic resistance

### 2.1 Considerations and important (ideal) criteria for defining treatment failure in gonorrhoea

1. A thorough and detailed clinical history is essential to any consideration of a possible treatment failure. Arguably, the most common reasons for exclusion of a case of putative treatment failure as one of probable treatment failure are:

- the admission by the patient of additional unprotected sexual contact(s) following the initial (primary) treatment;
  - the likelihood, from the wider clinical history, such as from named sexual partners, of further post-treatment exposures not otherwise disclosed;
  - the possibility of non-compliance with the treatment regimen. Compliance should not be a problem in clinics with a “directly observed treatment” strategy, but such an approach is not always universally applied;
  - the possibility that pharmacokinetic issues, such as decreased absorption of drug with/without food, concurrent medications, or failure of an antibiotic to disperse from an intramuscular injections site, may also contribute to treatment failure that is not attributable to AMR.
2. *This clinical history may be very difficult to obtain, especially if the putative case attended several other/unidentified practitioners rather than receiving sequential care at a single centre, or if self-obtained treatment was administered by the patient. The important and relevant clinical data that are needed in these cases include:*
- the date of exposure(s);
  - the drug type(s) and dose(s) administered for both primary and adjunctive treatment;
  - the possibility of any further contacts following treatment and their number and timing in relation to receipt of any antibiotic treatment;
  - the use or lack of use of condoms during these contacts.
3. *Re-isolation of N. gonorrhoeae was obtained within a reasonable time frame: 3–14 days (see also below for possible reasons for a longer duration for re-isolation). If effective treatment is given, gonococci are difficult, if not impossible, to cultivate post-treatment, e.g. 24 hours after treatment, suggesting that follow-up for proof of cure by culture after 24 hours in clinical trials of new antibiotics for gonorrhoea may be acceptable (10). If only nucleic acid amplification tests (NAATs) can be used, the test of cure (TOC) should be sampled after 2 weeks.*
4. *Laboratory parameters are useful in excluding, but less so in confirming, a possible treatment failure. Pre- and post-treatment isolates should be tested and be indistinguishable on laboratory testing when compared by a reliable and highly discriminatory genotypic method. The results of this investigation do not distinguish between failed treatment and reinfection with the same subtype from the same or another source.*
- However genotypic differences between the original isolate and that from a test of cure (TOC) culture mean that the case is almost certainly one of reinfection.
- Note:* comparisons of isolates obtained from identified sexual contacts and the index case by the same means are also relevant for similar reasons.
5. *There may be differences in MICs between pre- and post-treatment isolates in treatment failure. It is crucial to perform antibiogram determinations; however, these are less helpful as distinguishing markers between pre- and post-treatment isolates. These methods have a low ability to discriminate gonococcal strains and, for some antibiotics, resistance to the treatment drug may arise during treatment, with resulting differences in MICs (11).*
6. *Infrequent use of TOC cultures may distort estimates of treatment failures. TOC cultures are not routinely performed, except when patients return or re-present with symptoms following treatment (9). Accordingly, performance of more frequent TOC is recommended (see also comments 8 and 9 below).*
7. *The detection of gonococcal nucleic acids after successful treatment can occur for prolonged periods (up to one to two weeks has been suggested). It is crucial to recognize this, if NAATs have to be used for TOC.*
8. *Assessment of possible failed treatment for gonorrhoea that is based on symptomatic assessments alone is problematic. Symptoms may persist for some time post-treatment, or else improve only slowly due to the presence of other untreated coinfections transmitted with the N. gonorrhoeae. That is, the persistence of symptoms after treatment for gonorrhoea may be due to reasons other than failure to eliminate N. gonorrhoeae. These*

organisms may include *Chlamydia trachomatis* (*C. trachomatis*), *Mycoplasma*, *Ureaplasma* and *Trichomonas* and other as-yet unidentified agents.

9. *Infections, especially those at extra-genital sites such as the pharynx and rectum, are often asymptomatic; diagnostic testing of these sites is suboptimal, and pharyngeal gonorrhoea in particular is more difficult to treat.* Pharyngeal infection in particular has been recognized as a likely reservoir for infection that is often not sought or detected (12). Although asymptomatic clinically, pharyngeal infection is associated with a higher risk of disseminated gonococcal infection (13).

Protocols for sampling from extra-genital sites appear to differ widely according to clinic practice and attitude, patient history, sexual orientation, cost or perceived cost and available resources (14). In most countries, diagnosis is still highly dependent on culture-based approaches that are not always available or fully reliable. No NAATs for detection of *N. gonorrhoeae* in extra-genital sites have been approved by the Food and Drug Administration of the United States of America, and many NAATs suffer severe limitations, especially regarding specificity, when used to diagnose gonorrhoea in these sites (15), so that proper molecular microbiological testing protocols that truly verify gonococcal infection must be used. It is standard laboratory practice to retain clinical samples such as swabs or first-void urines used in NAATs when a positive test result is obtained. In cases of putative treatment failure, this clinical material should be appropriately stored and retested as required. Nucleic acid extracted from these samples may also be stored and used in subsequent examinations, but it is preferable to undertake a re-extraction process from the original sample for any further testing.

10. *Use of dual antibiotic therapy at first presentation complicates the assessment of possible treatment failures in gonorrhoea.* Dual antibiotic therapy, which includes that for *C. trachomatis*, is standard practice in most syndromic management approaches to male urethritis and is also included in most etiologically based systems when *N. gonorrhoeae* is diagnosed or reasonably suspected prior to initial treatment, e.g. on a positive Gram stain.

The antibiotics most often administered for suspected concomitant *C. trachomatis* infection are azithromycin in a 1 g statim oral dose, or tetracyclines given orally over 10 days. Both drugs have anti-gonococcal activity that may supplement the primary gonococcal treatment if it is inadequate or otherwise ineffectual. Thus, programmatic cotreatment given in conjunction with an ineffectual primary treatment may mask emerging resistance and the possibility of treatment failure if single drug therapy was to be used.

11. *Dual treatment may be suppressive rather than curative, so that recrudescence of symptoms in true treatment failure may occur.* High-level resistance to both components of this dual therapy has been documented. In the case of prolonged tetracycline cotreatment, this therapy may be suppressive rather than curative, so that on completion of treatment, a recrudescence of symptoms may occur that may be confused with reinfection, in the absence of a careful clinical history and close examination of pre- and post-treatment isolates (1, 6, 9).
12. *The likelihood of treatment failure is more difficult to detect but more likely to occur at sites other than the male urethra.* Point 9 above suggests that diagnostic testing facilities for often-asymptomatic gonococcal infection at extra-genital sites are underutilized, and also mentions that the testing itself at these anatomical sites may be less sensitive than for infections of the male urethra.

Additionally, *N. gonorrhoeae* is more difficult to eradicate at extra-genital sites and from the female endocervix. In an analysis of many efficacy studies, Moran (16) did not agree with the above contention, except for pharyngeal gonorrhoea. However Moran's analyses were mostly derived from efficacy studies performed before or shortly after the release of each antibiotic. That is, the evaluations of treatments were mainly of infections caused by fully sensitive gonococci (i.e. fully sensitive to the just-released antibiotic also known as "wild-type" organisms lacking any phenotypic or genetic alteration). After use and misuse of any agent, MICs rise, and differences in cure rates only then become apparent, but studies to compare rates of cure at different sites over time since drug release are rarely, if ever, performed.

### 3. Application of these considerations and ideal criteria for the assessment of possible or probable treatment failure in gonorrhoea due to antibiotic resistance in *N. gonorrhoeae*

#### 3.1 Probable treatment failure: ideal requirements for definition of a case

Taken together, the above considerations mean that conditions listed next are ideally required in order to argue convincingly that a *probable* case of treatment failure exists.

There is an unambiguous and documented history that:

- provides relevant details of the original sexual partner(s) (exposure and time to original clinical presentation);
- indicates that no further instances of unprotected sexual contact have occurred post-treatment;
- the original drug administered (primary treatment) is known, as is the dose and route of administration, and preferably the origin of the drug, e.g. proprietary or generic;
- the primary treatment is known to have been administered and there are no known possible pharmacokinetic interferences or drug interactions;
- any adjunctive treatment given before, with or after the primary treatment is also known and documented as above;
- the primary diagnosis of gonorrhoea was confirmed and the isolate is available for examination;
- a TOC culture was performed (within an acceptable time frame – see Section 2.1 point 3, above) on the follow-up presentation, *N. gonorrhoeae* was isolated and the isolate is available for further examination as required

*Note:* NAAT testing has limitations additional to those that normally apply to diagnostic testing with these assays (15) (see 7 above). Further, the other mandatory investigations performed on culture (see bullet points below) at present cannot be undertaken with molecular methods.

- the original isolate and that from TOC culture are indistinguishable when compared by a reliable and highly discriminatory genotypic method;
- the MIC determinations, preferably performed at the same time, for the antibiotic used were obtained by a reliable method using proper controls on the original and TOC isolates;

- the MIC values obtained for the TOC culture are consistent with those likely to be obtained from a treatment failure – a fully sensitive isolate (“wild-type” MIC) would suggest that the treatment failure was due to causes other than resistance;
- after retreatment, a further TOC culture is negative.

#### Note

Even when all the above *ideal* criteria are fulfilled and the case is regarded as one of “true” treatment failure involving an organism with a raised MIC to the antibiotic(s) used, it is still possible that other factors may be involved. Ideally, if treatment failure occurs due to newly emerged resistance to recommended treatment, the genetic resistance determinants in the AMR gonococcal isolates should also be elucidated.

Criteria for defining “possible cases” of treatment failure may be applicable to obtain presumptive or adjunctive information of interest. Table A2 provides a suggested algorithm for classification of cases investigated.

### 4. Laboratory requirements and considerations

Cases of possible antibiotic treatment failure in gonorrhoea are of considerable importance, but the verification of such an event requires close public health, clinical and laboratory collaboration.

Isolates from a probable case of treatment failure provide important data in relation to laboratory methods for detection of the emergence of new forms of resistance to new and existing antibiotics and a means to identify their wider spread. Clarification of events and mechanisms surrounding any possible resistance to newly introduced or current first-line drugs are of great importance from a public health perspective. Such an event may represent the initial manifestation of a form of resistance that would ultimately lead to the withdrawal of a major therapeutic group. For example, the 1970s saw the emergence and rapid spread of plasmid-mediated penicillinase-producing *N. gonorrhoeae*. If a similar event occurred with gonococci acquiring a cephalosporinase or chromosomal resistance to the third-generation extended-spectrum cephalosporins that are now widely used as first-line treatment, this would be catastrophic for treatment and disease control. This is not a hypothetical event. Recent emergence of chromosomal resistance to third-generation

extended-spectrum cephalosporins and resulting in treatment failure has been documented (2, 9, 17–20). Detailed examination of the isolates from these cases has provided significant insights into the resistance mechanisms involved (2, 9, 20–24). Gonococci naturally develop new forms of resistance to existing drugs and it is important to identify the genetic resistance determinants, because the development of molecular methods of AMR detection is crucial and is dependent on this information. However, molecular AMR testing only detects resistance mechanisms that are already known, but not newly emerging ones. This makes it imperative that culture-based AMR surveillance be strengthened globally in order to keep in step with *N. gonorrhoeae*. The isolates from treatment failures are also useful in helping to define proper laboratory criteria for the detection of these “resistant” organisms (3).

The optimal test procedures to establish a probable case of antibiotic treatment failure in gonorrhoea where this was due to AMR are set out in Section 3 and Table A2. However, in practical terms, it is unusual to have pre- and post- treatment isolates available in such cases (1, 6, 15, 19, 20, 25). More

commonly, only post-treatment cultures are available, but when accompanied by unambiguous clinical data, these can also be extremely useful for the purposes outlined above. Thus, in an instance where possible treatment failure has occurred, every effort should be made for the laboratory to perform a culture-based examination of the relevant clinical material to confirm the diagnosis, store the isolate and perform the tests described above (see Section 3), or alternatively have them performed elsewhere in a reference laboratory (see Appendix 2 for options for storage and transport of isolates).

Close liaison with the public health authority, as well as the clinicians concerned, is essential. Wider epidemiological investigations such as tracing, examination and treatment of sexual partners are of extreme importance and may yield additional clinical information and clinical samples that are also positive for *N. gonorrhoeae*. These isolates should undergo the same typing and MIC determinations as the isolates from the index patient and should be carefully stored. Similarly, if NAAT testing was used in diagnosis of these partners, the clinical samples should also be stored if a positive assay has been reported.

**Table A2 Algorithm for determining possible cases of treatment failure**

Necessary criterion	Outcome and comment	
1. <i>Clinical history</i> : available and with all requisite details (see above)	<i>Yes: possible case</i> – apply criteria below	<i>No</i> : clinical details not available, unevaluable – <i>exclude as a case</i>
1a. <i>Clinical history</i> : available and with all requisite details except those for any post-treatment contact(s)		<i>No post-treatment contact history</i> – <i>doubtful case</i> ; apply criteria below
1b. <i>Clinical history</i> : available and with all requisite details except drug type(s) used and dose(s), including any adjunctive treatment		<i>No treatment identified</i> – <i>exclude as a probable case</i> ; MIC data may be useful
2. <i>Laboratory data</i> : primary diagnosis of gonorrhoea confirmed by laboratory tests, preferably including culture	<i>Yes: possible case</i> – apply criteria below	<i>No confirmation of diagnosis</i> , not useful – <i>exclude as a case</i>
3. <i>Laboratory data</i> : primary diagnosis of gonorrhoea confirmed by laboratory tests, original culture is available	<i>Yes: possible case</i> – apply criteria below	<i>No: remains a possible case</i> ; see below for investigation of repeat isolate
4. <i>Laboratory data</i> : diagnosis of gonorrhoea confirmed by laboratory tests on second visit	<i>Yes: possible case</i> – apply criteria below	<i>No confirmation of diagnosis</i> : not useful – <i>exclude as a case</i>
5. <i>Laboratory data</i> : culture obtained at second visit is available	<i>Yes: possible case</i> – apply criteria below	<i>No</i> – <i>remains a possible case only</i> ; no further investigation possible
6. <i>Laboratory data</i> : both first and second cultures are available and are indistinguishable by typing	<i>Yes: possible case</i> – apply criteria below	<i>No</i> : not a treatment failure – <i>exclude as a case</i>
7. <i>Laboratory data</i> : the MICs of the second isolate are raised, consistent with possible treatment failure	<i>Yes: probable case</i>	<i>No</i> : the MICs are those of a fully susceptible gonococcus – <i>doubtful case</i> ; seek other explanation
8. <i>Laboratory data</i> : retreatment and negative TOC obtained on second follow-up	<i>Yes</i> – no further investigation of individual case	<i>No</i> : positive culture again obtained; repeat above cycle

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## Appendix 4: Rationale and applications for the current (2008) World Health Organization panel of *Neisseria gonorrhoeae* for antimicrobial resistance surveillance for public health purposes and instructions for their use

### Background

Arguably the most significant application for antimicrobial resistance (AMR) testing for *Neisseria gonorrhoeae* is to optimize antibiotic treatment for gonorrhoea. Effective antibiotic treatment for gonococcal disease is defined as one that cures 95% or more of cases presenting from the local community general population, and is an essential component of integrated approaches for the control of gonococcal disease (1, 2).

AMR, manifested clinically as treatment failure, appeared in significant proportions of gonococcal populations following the introduction of penicillin treatment and has since emerged in all classes of relevant antibiotics. Resistant gonococci may also have a propensity for rapid spread and this attribute has accelerated the need for substitution of many formerly successful treatment regimens (1, 2). The process of optimizing treatment through continuing AMR surveillance is not only important for the welfare of the individual patient but is also pivotal for disease control and morbidity reduction at a public health level (1–6).

Formal surveillance of gonococcal AMR and modification of treatment options as required is conducted in several World Health Organization (WHO) regions; this has functioned continuously in the WHO Western Pacific Region since 1992 (7). The public health objective for this form of surveillance is to establish the proportion of phenotypically resistant strains present in a population, irrespective of the nature or level (expressed in numeric terms as the minimal inhibitory concentration (MIC)) of this resistance (1). Once the verified proportion of resistant strains reaches the “threshold for action” – defined as resistance in 5% of gonococci derived from patients presenting from the general population or more than 1% of gonococci from key populations with a potential to transmit infection more frequently or to many sex partners, such as sex workers and men who have sex with men (MSM) – changes in the treatment regimens should follow promptly (2–6, 8).

### Rationale for the use of reference cultures

For the data from AMR testing to result in any necessary changes in treatment regimens, there is a requirement for these data to be both epidemiologically sound and microbiologically valid (8). Gonococci are fastidious pathogens and AMR testing is consequently difficult. Further, the methods available for AMR determination may involve agar dilution, MIC testing, agar dilution “breakpoint” MIC screening, E-test MIC measurements or, commonly in resource-poor settings (9), antibiotic disc diffusion AMR testing.

All methods are capable of providing the necessary data, when performed with high-quality reagents, but are also prone to error and misinterpretation in the absence of suitable controls, or misinterpretation or misuse of interpretative criteria that accompany each test method. Additionally, variations in how these methods are used and the results interpreted are common, although often unavoidable due to reagent quality and lack of availability in many settings. This limitation of lack of universal availability of some key reagents means that uniform testing procedures cannot be achieved. Thus, this combination of unusual factors requires proper and rigorous internal and external quality-control procedures for AMR determinations in *N. gonorrhoeae* if the results of these determinations are to be compared and used for their intended purpose of optimizing treatment regimen composition. Reference cultures, when properly applied and used for their intended purpose, play a major role in these quality-control and quality-assurance practices (1, 2, 10).

### Applications of the reference panel in a public health context

The WHO reference cultures are used to ensure the continuing validity of microbiological examinations for AMR determination. Early studies (11) established that these differences in test procedures produced different numeric MIC values for the same strain when tested in different laboratories,

and that these differences were non-uniform over the range of MICs tested. Use of reference cultures was then recommended by a WHO working group, to enable valid comparisons of the in vitro data derived by the different studies (11). Through its collaborating centres, WHO has maintained a series of reference panels of gonococci for use as control strains in AMR testing of *N. gonorrhoeae*, for public health purposes and in external quality assessment survey (EQAS) programmes run by the WHO networks. With the continuing emergence and spread of new forms of AMR in gonococci, there is a need for continuous modification of the reference strain panels. This continuing need for such an approach was confirmed when recent international comparisons of AMR data in *N. gonorrhoeae* were compromised by several factors that produced different numeric MIC values for identical organisms, even when the same methods were supposedly used (12). This international group called for wider use and distribution of the WHO reference panel at a time when concerns about multidrug-resistant gonococci saw renewed calls for more and better-quality surveillance of AMR in *N. gonorrhoeae* (5, 13, 14).

The 2008 WHO reference panel of gonococci has recently been described in detail in terms of the phenotypic and genotypic characteristics of the component gonococci (10). The primary applications of these reference cultures are as internal controls in individual laboratories when undertaking AMR determinations and in network-wide proficiency testing and external quality-assurance exercises. These applications allow intra-laboratory validation of test results and assessment of trends in AMR over time, and inter-laboratory comparison of data in adjoining national or regional centres. Other applications over and above that for these specific public health purposes are also possible because of the full characterization, both phenotypic and genotypic, of these strains, but these applications are not further explored here.

### Uses of the test panel

All testing for AMR in *N. gonorrhoeae* should be performed by means of a recognized method, using high-quality reagents and antimicrobials of known potency, and with strict adherence to the interpretive criteria for that method (1, 2). The reference cultures are designed to allow determination of the susceptible/resistant phenotype, irrespective of the test method used and the MIC or other interpretative criteria used

by that method. This is achieved on a comparative basis. While different test methods will produce different numeric MIC values, when the reference cultures are used as controls in AMR testing, they will allow recognition of resistant gonococci when those strains examined provide a test profile identical to that of the reference culture (1, 2).

### Use of the panel for quality control

Full and complete attention should be given to the totality of quality-control procedures that apply to good laboratory practice as a whole, for growing and testing *N. gonorrhoeae* and antibiotic susceptibility testing. These include, but are not limited to, measuring and recording such parameters as results of tests of bacteriological media quality, monitoring of incubator temperature, humidity and CO<sub>2</sub> concentrations on a continuous basis, disc potency and antibiotic concentrations. The quality-control panel can be used as a biological indicator for some of these functions. However, the description of their use here is restricted to the applications for AMR testing, which is achieved by comparing the MICs or zone sizes of known resistant phenotypes (the panel strains) with the results of testing the unknown phenotypes in the test strains when the two groups are tested simultaneously under the same conditions.

Use of the whole panel as a quality-control procedure in every situation and for every test batch would be wasteful. The test panel comprises strains and strain combinations that can be used in different settings and as appropriate to the antibiotics in use in that setting. The gonococci from the reference panel have known susceptible/resistant phenotypes to those antibiotics recommended in current treatment guidelines (Table A3). However, there may be little need in some jurisdictions to test, for example, resistance to penicillins or quinolone antibiotics because of the very high and already known resistance levels that would preclude use of these agents. The focus for each laboratory or region should thus be on those agents of local relevance for the public health purpose of ensuring effective treatments. Consequently, Table A3 shows in bold type the primary applications for each panel strain in resistance determinations for individual antibiotics. The appropriate strains for testing in a particular setting can be selected on this basis. Tables A4–A8 provide examples of possible selections of control strains in settings with different requirements.

However, many gonococci are now resistant to multiple antibiotics. This means that, in theory, the number of control strains could also be reduced by selecting, for example, strains WHO K and L because of their multiresistant phenotype. However, these strains, while quinolone resistant, have a phenotype that is highly resistant (very high MIC) to this antibiotic group. If used as the standard control for quinolone-resistant gonococci, many strains that are resistant, but at a lower MIC level, would be regarded as susceptible. Strains WHO M and N are shown as the control strains for quinolone resistance because their resistance profile is close to that for the cut-off or “break point” value that defines resistance. Therefore, they should be used in preference for resistance phenotype determination for this group of agents.

If there is no correlation of the quality-control strain phenotype with that obtained in a test run, the test should be regarded as invalid and a review of test procedures initiated. This should include a review of all stages of all the test procedures. If problems are repeatedly found, or if the source of a problem cannot be identified, the reference laboratory or a WHO collaborating centre should be contacted for advice and assistance.

### *Use of the panel in external quality assurance systems*

The reference panel is also useful for EQASs, which should be an integral part of the activity of any surveillance network or programme. Failure of a laboratory to participate in an available EQAS would mean that data obtained in that laboratory are potentially unreliable and cannot be used for the purposes intended.

In EQASs, the reference panel is distributed, by the coordinating laboratory of a network, to other participants, and the components of the panel are tested as “unknowns”. Another dimension beyond that of simple proficiency testing is to test network and laboratory capacity on an ongoing basis, and for the reference laboratory to advise on any remedial measures that may be required. On this basis, it is best if the EQAS cultures are tested by participants as part of routine laboratory procedures, to ascertain if any fine tuning of their methodology is needed. It is best to accept that mistakes will be made, so that they can be corrected, rather than giving the EQAS cultures “special” attention. The most useful result in an EQAS for participation purposes is the actual result

obtained under routine examination conditions, not one that was obtained by repeat examinations and “special attention”.

EQAS testing used in a setting should contain the strains from the reference panel relevant to the antibiotics used and resistance patterns that exist in the country or region. This may, however, vary widely, for example, between rural and urban areas, such that it may be necessary to include a wide spectrum of resistance phenotypes for testing in a network. In different EQAS exercises, the same strain should be included more than once, and preferably in triplicate, to test the intra-laboratory reproducibility of results.

EQAS panels are distributed at least once a year and more frequently in the early stages of the establishment of a network (up to four times a year), when new resistance is suspected or emerging, or when problems have been identified within a network. Results of EQAS testing should be kept confidential between the reference laboratory and the individual participant, to encourage “routine” assessment of strains and a collaborative approach to problem-solving. On occasion, an individual laboratory may also request or require additional strains for testing. Results should be returned confidentially to the reference laboratory to provide a detailed response, listing problems and solutions for the participant. It is helpful for this part of the EQAS to include in data returns to the reference laboratory the MIC values or zone sizes obtained, with the same data for the controls used. Many apparent “errors” result from transcription mistakes or erroneous interpretations of resistance criteria rather than any technical issue.

### *Other applications and considerations of the panel*

AMR surveillance and testing has many applications other than that for the public health purposes described in this document. The reference panel may be used to determine the levels of resistance, for example, high-level quinolone resistance, if so desired. Indicative MICs for one specific test method are provided in reference (10), but these values will often be slightly different in different test systems. Accordingly, the exact MICs provided in reference (10) are indicative and should be interpreted with caution. However, the identified resistance phenotypes (SIR-categorization – susceptible, intermediate, resistant) should be the same as per the principles outlined in the text. For the exact MIC of

each antibiotic and 2008 WHO reference strain (10), testing has to be performed in each laboratory, using its nominated and quality-assured method. It should be remembered that the accuracy of any MIC determination in agar plate dilution methods is plus or minus two times the dilution, and this should be factored in to any use of the panel strains in assessing MIC trends.

The reference panel strains have also been fully characterized for their resistance determinants as well as molecular epidemiological characteristics – see reference (10) for details. These known genotypic characteristics may be helpful for use as controls if molecular-based testing is undertaken.

## Conclusion

Details of different and valid test methods are available from a number of sources, such as the Clinical and Laboratory Standards Institute and The British Society for Antimicrobial Chemotherapy. It cannot be emphasized too strongly that, when testing AMR in *N. gonorrhoeae*, there are many potential pitfalls and that a recognized method must be adopted in its entirety and the interpretive criteria for that method applied precisely. Common errors in AMR testing arise from attempts to “adapt” methods because of reagent limitation, or to mistakenly apply or interpret test criteria and definitions. Poor-quality data are often worse than no data if they lead to unwarranted complacency about the utility of a treatment regimen or, alternatively, if they result in unnecessary substitution of an effective drug by a more expensive one. The use of 2008 WHO controls and participation in an EQAS is thus mandatory for WHO-based protocols, and the reference cultures are an essential part of the total quality-assurance process.

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Table A3 Resistance phenotypes of the 2008 WHO control strains F, G and K to P (10)

WHO control strain	Resistance phenotype application	Pen	Ceftr	Cefix	Cipro	Spec	Azith
WHO F	Pen S Cipro S	<b>S</b>	S	S	<b>S</b>	S	S
WHO G <sup>a</sup>	Pen DS Cipro DS TRNG	DS	S	S	DS	S	S
WHO K	CMRP QRNG HLR Ceftr DS Cefix DS	<b>CMRP</b>	<b>DS</b>	<b>DS</b>	HLR	S	S
WHO L	CMRP QRNG HLR Ceftr DS Cefix DS	<b>CRMP</b>	<b>DS</b>	<b>DS</b>	HLR	S	S
WHO M	PPNG QRNG R	<b>PPNG</b>	S	S	R	S	S
WHO N <sup>a</sup>	PPNG QRNG R TRNG	<b>PPNG</b>	S	S	<b>R</b>	S	S
WHO O	PPNG Spec R	<b>PPNG</b>	S	S	S	<b>R</b>	S
WHO P	Pen LS Azit R	LS	S	S	S	S	<b>R<sup>b</sup></b>

Primary applications for use in resistance phenotype determinations by each strain are shown in bold.

Azith = azithromycin; Cefix = cefixime; Ceftr = ceftriaxone; Cipro = ciprofloxacin, representative of fluoroquinolones; CMRP = chromosomally mediated penicillin resistance; DS = decreased in vitro sensitivity of unknown clinical relevance; HLR = high-level resistance well above normal break point; Pen = penicillin; S = sensitive; PPNG = penicillinase-producing *N. gonorrhoeae*; QRNG = fluoroquinolone-resistant *N. gonorrhoeae*; R = resistant at normal break point; Spec = spectinomycin.

<sup>a</sup> WHO strains G and N also manifest high-level plasmid-mediated tetracycline resistance (TRNG).

<sup>b</sup> In vitro azithromycin resistance is imperfectly correlated with clinical outcomes and varies with the dose of antibiotic used.

**Table A4**

One example of a “useful” selection of strains from the reference panel, in a setting where resistance to penicillin, quinolones, spectinomycin, azithromycin and third-generation, expanded-spectrum cephalosporins is under assessment

WHO control strain	“Useful” resistance phenotype
WHO G	<b>Pen DS</b> <b>Cipro DS</b>
WHO K <sup>a</sup>	<b>CMRP</b> <b>High-level QRNG not suitable for QRNG detection</b> <b>Ceftr DS</b> <b>Cefix DS</b>
WHO M	<b>PPNG</b> <b>Cipro R</b> <b>Close to QRNG breakpoint useful for QRNG detection</b>
WHO O	<b>PPNG</b> <b>Spec R</b>
WHO P	<b>Pen DS</b> <b>Azith R<sup>b</sup></b>

Primary applications for use in resistance phenotype determinations by each strain are shown in bold.

Azith = azithromycin; Cefix = cefixime; Ceftr = ceftriaxone; Cipro = ciprofloxacin, representative of fluoroquinolones; CMRP = chromosomally mediated penicillin resistance; DS = decreased in vitro sensitivity of unknown clinical relevance; Pen = penicillin; S = sensitive; PPNG = penicillinase-producing *N. gonorrhoeae*; QRNG = fluoroquinolone-resistant *Neisseria gonorrhoeae*; R = resistant at normal break point; Spec = spectinomycin.

<sup>a</sup> WHO K contains a mosaic PBP2.

<sup>b</sup> In vitro azithromycin resistance is imperfectly correlated with clinical outcomes and varies with the dose of antibiotic used.

**Table A5**

A suitable panel for use where third-generation, expanded-spectrum cephalosporins, spectinomycin and azithromycin susceptibility only is being assessed

WHO control strain	“Useful” resistance phenotype
WHO K <sup>a</sup>	<b>Ceftr DS</b> <b>Cefix DS</b>
WHO O	<b>Spec R</b>
WHO P	<b>Azith R<sup>b</sup></b>

Primary applications for use in resistance phenotype determinations by each strain are shown in bold.

Azith = azithromycin; Cefix = cefixime; Ceftr = ceftriaxone; DS = decreased in vitro sensitivity of unknown clinical relevance; Pen = penicillin; S = sensitive; PPNG = penicillinase-producing *N. gonorrhoeae*; R = resistant at normal break point; Spec = spectinomycin.

<sup>a</sup> WHO K contains a mosaic PBP2; consider use of WHO L also (see Table A6).

<sup>b</sup> In vitro azithromycin resistance is imperfectly correlated with clinical outcomes and varies with the dose of antibiotic used.

**Table A6**  
**A suitable panel for use where third-generation, expanded-spectrum cephalosporins and spectinomycin susceptibility only is being assessed**

WHO control strain	“Useful” resistance phenotype
WHO K <sup>a</sup>	<b>Ceftr DS</b> <b>Cefix DS</b>
WHO L <sup>b</sup>	<b>Ceftr DS</b> <b>Cefixime DS</b>
WHO O	<b>Spec R</b>
<p>Primary applications for use in resistance phenotype determinations by each strain are shown in bold.</p> <p>Cefix = cefixime; Ceftr = ceftriaxone; DS = decreased in vitro sensitivity of unknown clinical relevance; R = resistant at normal break point; Spec = spectinomycin.</p> <p><sup>a</sup> WHO K contains a mosaic PBP2.</p> <p><sup>b</sup> WHO L contains an A501V mutation in <i>penA</i>.</p>	

**Table A7**  
**A suitable panel for use where penicillin and quinolone susceptibility only is being assessed**

WHO control strain	“Useful” resistance phenotype
F	Pen S Cipro S
G	Pen DS Cipro DS
Ka	CMRP
M	PPNG Cipro R

Primary applications for use in resistance phenotype determinations by each strain are shown in bold.

Cipro = ciprofloxacin, representative of fluoroquinolones; CMRP = chromosomally mediated penicillin resistance; DS = decreased in vitro sensitivity of unknown clinical relevance; Pen = penicillin; S = sensitive; PPNG = penicillinase-producing *N. gonorrhoeae*; R = resistant at normal break point.

<sup>a</sup> High-level resistance to quinolones well above normal break point and not suitable for determination of quinolone resistance – see text.

**Table A8**  
**Antimicrobial susceptibility, to some lesser used antibiotics or those proposed for possible use (2), of the 2008 WHO *Neisseria gonorrhoeae* reference strains panel (10)**

Characteristics	WHO F	WHO G	WHO K	WHO L	WHO M	WHO N	WHO O	WHO P
Ertapenem (0.004 to 0.125) <sup>a</sup>	S (0.004)	S (0.008)	DS <sup>b</sup> (0.125)	DS <sup>b</sup> (0.064)	S (0.012)	S (0.008)	S (0.032)	S (0.008)
Kanamycin (8 to 32) <sup>a</sup>	S (16)	S (16)	S (16)	S (32)	S (16)	S (16)	S (16)	S (8)
Gentamicin (2 to 8) <sup>a</sup>	S (4)	S (4)	S (2)	S (8)	S (4)	S (4)	S (4)	S (4)
Rifampicin (0.125 to >32) <sup>a</sup>	S (0.125)	S (0.5)	S (0.5)	S (0.5)	R (>32)	R (>32)	S (0.25)	R (>32)

R = resistant at normal break point; S = sensitive.

<sup>a</sup> Resistance phenotypes based on MIC (mg/l) using E-test (10). The range of the MICs for each antimicrobial and the different strains are given in parentheses. Most importantly, however, the MICs provided should be interpreted with caution because these were derived using one specific method only and, accordingly, can differ slightly using other methods. However, the identified resistance phenotypes (SIR-categorization) should be the same as per the principles outlined in the text.

<sup>b</sup> DS = decreased susceptibility but clinical/laboratory correlates are insufficient to allow resistance phenotype designation.



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