

# DESIGNING STD SURVEILLANCE SYSTEM IN THE TROPICS

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## **Introduction**

### *The global burden of sexually transmitted diseases (STDs)*

STDs are a major cause of morbidity throughout the world. The World Health Organization has estimated that in 1995 there were 333 million cases of curable STD (gonorrhoea, chlamydia, syphilis, and trichomoniasis infections)<sup>1</sup>. Although the incidence of bacterial STDs has declined in many developed countries, incidence and prevalence rates of STDs in developing countries remain high.

The consequences of STDs are most severe for women and children. In high prevalence areas, these diseases rank second as a cause of healthy life lost in women aged 15 to 45 years, after maternal morbidity and mortality (not including HIV)<sup>2</sup>. Untreated chlamydial and gonorrhoeal infections can lead to acute pelvic inflammatory disease and its complications which include infertility, ectopic pregnancy, and chronic pelvic pain. Human papillomavirus infections have been strongly associated with cancer of the uterine cervix.

There are also the well-known effects of STDs on the foetus such as spontaneous abortion, stillbirth, prematurity, and congenital syphilis. Another important sequela of untreated infection is ophthalmia neonatorum, a result of *N. gonorrhoeae* or *C. trachomatis* ocular infection during delivery.

STD control is important not only to prevent these consequences, but also because of the relationship of STDs with HIV infection and transmission. Numerous studies have shown that both ulcerative and non-ulcerative STDs facilitate HIV transmission<sup>3-8</sup>. Therefore, STD control is now recommended as an important way to enhance HIV prevention efforts. In a community-based, randomised trial in the Mwanza Region, Tanzania, STD syndromic treatment resulted in a 42% reduction in HIV incidence<sup>9</sup>. Furthermore, as HIV and other STDs share the same behavioural risk factors, behavioural interventions to control the former will have beneficial consequences on the latter.

STD surveillance can be coordinated with HIV surveillance activities. First, ongoing activities in each area can be used to provide data about the other (for example, performing syphilis testing in HIV serosurveillance sites or performing HIV testing in selected populations that are routinely screened for syphilis). Second, according to the pattern of the HIV epidemic in a country, STD surveillance activities can be modified to better target and evaluate the impact of HIV prevention programs. These concepts are discussed further below.

### *Importance of STD surveillance*

Despite its importance, surveillance data on STDs have been scarce and those that have been available are problematic and cannot be used to accurately assess the global STD situation. An improved STD surveillance program aims to:

- evaluate the magnitude and regional distribution of STD, i.e., the prevalence and incidence rates;
- identify trends in infection rates;
- identify groups with high incidence and prevalence of disease;

- define aetiologies of STD syndromes;
- monitor antibiotic resistance;
- establish realistic outcome objectives for prevention programs;
- define resources that are necessary and advocate for support; and
- evaluate effectiveness of control programmes over time.

Accurate STD surveillance information is necessary to develop activities to interrupt STD transmission, to prevent their complications, and to reduce HIV transmission. A major question, however, is how to design an STD surveillance program.

## **Alternatives for STD surveillance**

### *Universal case-reporting*

Systems of universal case-reporting rely on the collection and reporting of data by health care providers throughout the country. A system of universal reporting can be useful to the extent that it provides information on the whole population and not only on a sample. Also, it makes use of the existing infrastructure for communicable disease surveillance. However, universal case-reporting can yield information of limited quality on the true disease burden since its reliability depends on the extent to which patients seek health care (especially important for STD), on consistent use of case definitions, on the validity and completeness of case-reports, and on quality of diagnostic methods. Frequently, there is no accurate information on population-level denominators, making the interpretation of data even more difficult. Even countries with well-organized health care systems have high rates of under diagnosis and under reporting of STDs.

However, universal case-reporting data can be very useful to the extent that they are a source of information on which health care providers (and, in some countries, laboratories) are diagnosing STDs. Sites that are not reporting, or where reporting has suddenly declined, should be contacted to determine if the decline is due to lack of drug availability, lack of trained personnel available to diagnosis STDs, or if it is only a problem of submitting case-reporting forms. Data from a system of universal reporting can be made even more useful if they are compared with other sources of information (e.g., prevalence surveys).

### *Sentinel sites and populations*

In a sentinel-site case-reporting system, selected clinical sites report STD cases on a regular basis. Selection of sentinel sites (or "enhanced surveillance sites") make it possible to work more intensively with designated clinics to systematically collect data and to obtain high quality information. If the cost of these surveillance activities is minimized, this activity may be integrated into existing services.

Ideally, sentinel case-reporting sites should be chosen to obtain some representation of the whole population attending clinical services. Sites should be selected in most geographic areas (urban and rural), include different types of clinics where STDs are usually seen (primary health care, general outpatient departments, specialized clinics, private and public sectors), and which can provide reliable information on the overall clinic population (denominators). Even if some of these conditions cannot be met but the data are collected consistently, they may be of some use.

If patterns of clinic attendance (including overall numbers and types of patients) do not fluctuate substantially over time, data collected from these sites may be used to monitor trends in numbers of STD cases, in proportions of clinic attendees with STDs, and in types of STDs. However, if this

condition is unlikely to be met, or if placing emphasis on sentinel case-reporting sites detracts from efforts to integrate STD care more broadly into primary health care, it may be preferable to strengthen the universal reporting system rather than to use scarce resources for sentinel-site case reporting.

It is well known that many patients with STDs do not seek health care from clinicians, and self-treat their infections using drugs they have obtained from pharmacies. Others may receive treatment from traditional healers. Ideally, pharmacies should also be included in sentinel surveillance in order to make data more representative; however, the feasibility and utility of this approach have not yet been demonstrated. Another approach may be to perform special surveys to estimate how many patients with STD do not reach the formal health care system.

For monitoring STD prevalence (an activity distinct from case-reporting), among the most important sentinel populations is pregnant women, seen either at antenatal clinics or examined at delivery. Although pregnant women at these sites can be quite representative of women in the general population, as they are seeking health care for reasons unrelated to STD symptoms, data obtained on this population does have biases. Women with reduced fertility are under represented; infertility is an important consequence of untreated STD. In some settings, pregnant women who have multiple sex partners may be less likely to seek clinic-based care than those who only have stable partners. In addition, women who are consistently using condoms are less likely to become pregnant (and thus will not be presenting for care at these sites).

It is especially important to obtain data on STD prevalence among female sex workers, and other persons at high risk. This is especially important as part of basic surveillance activities because limited data are being collected. Findings of high STD prevalence in persons at high risk can serve as a warning signal regarding the general population. Other sentinel populations that can be used for assessing STD prevalence include blood donors, military recruits, and factory workers. Their representativeness depends on the socio-cultural characteristics of each group.

### *Special surveys*

Universal case-reporting and sentinel surveillance activities can be used to provide data on trends in incidence and prevalence of disease (this will be discussed below). However, when further information is needed, additional STD surveillance related data need to be obtained. Among the most important supplement activities include monitoring of *N. gonorrhoeae* resistance and studies of proportional distribution of aetiologies associated with each major STD syndrome.

### *Syndromic and etiologic reporting*

In most countries, laboratory examinations for diagnosing STDs are not widely available. Diagnostic and therapeutic decisions are made syndromically, therefore case reports should also be syndromic. This approach is feasible since it is rapid, does not depend on laboratory confirmatory examination nor on specialized staff, and can yield useful information. Case-reporting of syndromes characterized by symptoms which present acutely (e.g., urethral discharge and genital ulcer disease) can be used to monitor trends in STD incidence.

Countries (or even isolated sites) that have sufficient resources to routinely identify etiologic agents of STDs should do so. If a country has the capacity to report only some cases etiologically, syndromic and etiologic reports should be reported separately. Most developing countries however will not be able to report cases etiologically.

### *Basic and advanced STD surveillance activities*

Basic STD surveillance activities are used to obtain the minimum data necessary to evaluate the STD situation within a country, despite lack of resources. Countries with enough resources (human and/or financial) may also perform advanced STD surveillance activities.

Basic STD surveillance activities include case reporting of genital ulcer disease and urethral discharge (universally or at sentinel sites); congenital syphilis case reports (universally); syphilis prevalence in pregnant women attending antenatal clinics or seen at delivery (at sentinel sites); and studies of gonococcal resistance and aetiology of STD syndromes in only a few sites.

Vaginal discharge cases may also be reported to assist in health services management and pharmaceutical distribution; however, vaginal discharge syndrome is too non-specific to be a useful measure of STD incidence or prevalence, and need not be recorded for these purposes.

According to the stage and type of HIV epidemic some modification of STD surveillance activities is recommended. In order to prioritise HIV/AIDS surveillance activities it has been proposed that countries be categorized according to their HIV epidemic stage: low-level (few cases of AIDS, low HIV prevalence (<5%) in high risk groups), concentrated (high HIV prevalence in high risk groups but low prevalence in the general population) or generalized (>5% HIV prevalence in the general population, with increasing equalization of HIV prevalence between urban and rural areas).

In countries with nascent and concentrated HIV epidemics, basic STD surveillance activities should include (at a minimum) assessment of syphilis, gonorrhoea, and chlamydia prevalence in persons at high risk. In countries with generalized HIV epidemics, these assessments should be done both in sentinel populations at high risk and in the general population (at least in pregnant women). Clearly, the expansion of data collection is limited by human and financial resources.

Advanced STD surveillance activities include etiologic case reporting; syphilis, chlamydia, gonorrhoea and trichomoniasis prevalence studies in sentinel populations; more accurate data about aetiological proportions for each syndrome (for example, HSV, chancroid, and syphilis testing on genital ulcers); and reporting of ophthalmia neonatorum.

We now focus on the details of basic STD surveillance activities.

## **Standards for basic STD surveillance**

### *Incidence monitoring*

Only urethral discharge and genital ulcer disease are considered useful for monitoring trends in STD incidence because of their acute, symptomatic onset, and their specificity for recently acquired infection with an STD agent. Persistent, asymptomatic and recurrent infections cannot be used to monitor trends in incidence (e.g., endocervical infection, genital warts, vesicular ulcers, latent syphilis).

### *Syndromic reporting*

Minimum data items - age, sex, date, residence, and reporting site.

### *Urethral discharge*

Case definition: Urethral discharge in men with or without dysuria. (This syndrome is most commonly caused by *N. gonorrhoeae* and *Chlamydia trachomatis*; other infectious agents associated with urethral discharge include *Trichomonas vaginalis*, *Ureaplasma urealyticum*, and *Mycoplasma* spp.)

The syndromic reporting of urethral discharge can be useful for monitoring trends in *N. gonorrhoeae* and *Chlamydia trachomatis* infections in men since these are usually acute, symptomatic and self-limited infections. Although these agents do cause asymptomatic infections, and other agents can cause urethritis, the high proportion of symptomatic cases due to these pathogens makes reporting of this syndrome useful for monitoring trends.

### *Genital ulcer disease*

Case definition: Ulcer on penis, scrotum, or rectum in men and on labia, vagina, or rectum in women, with or without inguinal adenopathy. (This syndrome can be caused by syphilis, chancroid, lymphogranuloma venereum, granuloma inguinale, or atypical cases of genital herpes.)

Since non-vesicular ulcers may be due to atypical cases of HSV (and because HSV lesions often are recurrences of a persistent infection that was acquired long before), non-vesicular genital ulcer disease is only a fair indicator of incident STD. In settings where patients are attending health services for reasons unrelated to STD symptoms (e.g., routine sex worker examinations), prevalence of genital ulcers may also be useful as one measure of STD prevalence.

As a large proportion of ulcers in women go unnoticed, case reports of genital ulcer disease are a much better indicator of STD incidence in men than in women.

However, it is worth emphasizing that even with under-detection of disease, these syndromic case-reports can be useful when other data on prevalence and incidence are lacking. Vaginal discharge  
Case definition: Abnormal vaginal discharge (indicated by amount, colour, and odour) with or without lower abdominal pain or specific symptoms or specific risk factors. (This syndrome is most commonly caused by bacterial vaginosis, vulvovaginal candidiasis, and trichomoniasis; it is less frequently caused by gonococcal or chlamydial infection.)

This syndrome is less useful as an indicator of STD than urethral discharge or genital ulcers because many etiologic agents associated with vaginal discharge are not sexually transmitted (*Candida albicans*, bacteria associated with bacterial vaginosis).

### *Aetiologic case-reporting*

As mentioned above, countries with enough resources or even isolated sites that have good laboratory infrastructure can report STD cases aetiologically. In order to report etiologically, it is important to stress that these data can only be useful if the quality of laboratory testing is certain. Therefore, for etiologic reporting, clinicians and laboratories must have sufficient material and reagents, trained staff, adequate specimen collection, and quality control. If this cannot be achieved, it is preferable to report syndromically. The only aetiological reporting that is considered a basic surveillance activity is reporting of congenital syphilis cases.

- Minimum data items - age, sex, date of specimen collection, residence, and reporting site.
- For etiological report the following laboratory diagnosis should be included in the case definitions:

- Acquired syphilis - positive non-treponemal tests (RPR/VDRL) confirmed by treponemal tests (TPHA/FTA-Abs). (Syphilis should be reported by stage of disease).
- Chancroid - Positive culture for *Haemophilus ducreyi*
- Granuloma inguinale (donovanosis)- direct microscopy showing typical Intracytoplasmic inclusions (Donovan bodies)
- Lymphogranuloma venereum - positive culture for *Chlamydia trachomatis* or antigen detection test on a genital ulcer or from a lymph node aspirate.
- Gonorrhoea - presence of Gram negative diplococci within polymorphonuclear leukocytes (in men); or positive culture or antigen detection test for *N. gonorrhoeae* (in men or women).
- Chlamydia - positive culture or antigen detection test.
- Trichomoniasis - positive wet mount preparation of vaginal fluid or positive culture.
- Congenital syphilis - an infant born to a woman with untreated or inadequately treated syphilis at delivery.

Although congenital syphilis case-reporting will underestimate the impact of congenital syphilis (in part, because spontaneous abortions will be missed, and usually many stillbirths), it is important to collect these data because this is one of the most serious sequela of untreated STD. The case definition requires a positive syphilis serologic test of pregnant women at the time of delivery; ideally, a confirmatory treponemal test should also be performed on the woman, and the infant should be evaluated for clinical and laboratory evidence of congenital syphilis.

#### *Prevalence assessment*

Prevalence of persistent STD tends to be much higher than prevalence of acute symptomatic STDs. Often, these persistent STDs are in an asymptomatic stage (e.g., latent syphilis). Therefore, for prevalence assessment, laboratory testing is necessary. To gain insight into the burden of disease in the general population, prevalence is best measured by testing patients who seek health care for reasons unrelated to STD symptoms (primary health care, prenatal clinics, family planning clinics, military recruits, etc.).

#### *Syphilis in pregnant women*

Although it may be difficult to interpret non-treponemal tests and distinguish treated from untreated disease, syphilis screening is the only way to obtain data on syphilis prevalence. Pregnant women are fairly representative of women in the general population. All women attending sites for antenatal control or delivery should be tested for syphilis; where feasible confirmatory treponemal tests should also be performed. In this population it may also be possible to perform HIV counselling and testing.

The non-treponemal tests (VDRL and RPR) are a better indicator of recent infection than are treponemal tests (FTA-ABS, MHA-TP) because the non-treponemal tests usually become non-reactive after treatment, although this may take months or years. False-positive nontreponemal tests, and persistently positive non-treponemal tests are two factors that diminish the utility of syphilis serologic testing for monitoring of incidence or prevalence. However, most false positive results are at low titres, and use of a cut-off point (e.g., 1:4) may diminish this source of error. Once positive, the treponemal examinations can remain so for life; they are not useful as measures of syphilis incidence (although in adolescents, reactive treponemal test results may more likely reflect recently acquired infection).

*Other populations (for example, military recruits, blood donors)*

STD prevalence can also be assessed in other populations, such as blood donors, military recruits, factory workers, and students; however, in interpreting these data, it is important to assess the extent to which the population selected may be representative of the general population.

As a basic surveillance activity, countries with nascent and concentrated HIV patterns should evaluate prevalence of syphilis, gonorrhoea, and chlamydia in populations at high risk. Countries with generalized epidemics should also perform these studies in some general population groups. Countries with sufficient resources can perform these studies in all sentinel populations enrolled.

*Using sera from HIV prevalence studies to assess STD prevalence*

Many countries already have a sentinel HIV seroprevalence system. It may be possible for some of these sentinel sites to provide data on the prevalence of other STDs. Since sera are already obtained for HIV testing, syphilis serology can also be performed; however, syphilis serologic testing should be performed in an unblinded fashion, and treatment must be available.

*Assessment of aetiologies of urethral discharge, genital ulcers, and vaginal discharge*

If a country is reporting STD syndromes, it is essential that a few centres perform special studies on the proportion of pathogens associated with each major syndrome (urethral discharge, genital ulcer disease, and vaginal discharge). If pathogen distribution for each syndrome is known in a few sentinel sites and these sites are fairly representative of the general population, it may be possible to extrapolate this pattern to other areas. This is important both for syndromic case management (treatment) and for tracking trends in the aetiology of different syndromes.

*Monitoring antimicrobial resistance in *N. gonorrhoeae**

Centres that are well equipped should provide data on antibiotic resistance, especially gonococcal resistance. These data are not required for individual case management but are of the utmost importance for deciding on guidelines. Resistance must be monitored at regular intervals to evaluate antimicrobial susceptibility within a population. At a minimum, the less expensive and more commonly used antibiotics should be tested.

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