

Guidelines for HIV Surveillance among Tuberculosis Patients

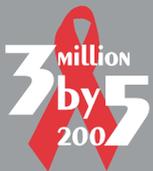
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GUIDELINES FOR HIV SURVEILLANCE AMONG TUBERCULOSIS PATIENTS

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List of abbreviations

AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ELISA	enzyme-linked immunosorbent assay
HIV	human immunodeficiency virus
IPT	isoniazid preventive therapy
IUALTD	International Union Against Tuberculosis and Lung Disease
KNCV	Royal Netherlands Tuberculosis Association
NAP	national AIDS programme
NTP	national tuberculosis programme
SGS	second generation surveillance
TB	Tuberculosis
TB/HIV	TB and HIV infection
UAT	unlinked anonymous testing
VCT	voluntary counselling and testing (for HIV)
WHO	World Health Organization

Summary

These guidelines are addressed to the managers of national tuberculosis programmes (NTP) and national AIDS programmes (NAP), those people responsible for HIV surveillance, and public health decision-makers at national and sub-national level. They form part of the TB/HIV series of documents produced by the Stop TB Department in the World Health Organization and also of the “Second Generation Surveillance” (SGS) series.

The main objective of these guidelines is to provide a framework for the methods to be used for measuring HIV prevalence among tuberculosis patients and to encourage implementation of HIV surveillance.

Surveillance of HIV among TB patients is being increasingly recognized as important, as the HIV epidemic continues to fuel the global TB epidemic. In many countries, HIV prevalence in TB patients is a sensitive indicator of the spread of HIV into the general population. Information on HIV levels in TB patients is essential to respond to the increasing commitment to provide comprehensive HIV/AIDS care and support, including antiretroviral therapy (ART), to HIV-positive TB patients.

The first edition of these guidelines, published in 1994, detailed one specific approach to determining HIV prevalence – through cluster sampling and unlinked anonymous seroprevalence surveys. The increasing availability of routine HIV testing and counselling as an entry point to HIV/AIDS care for TB patients has highlighted the need for updated and broader guidelines.

WHO’s “3 by 5” initiative, to reach 3 million HIV-infected people with antiretroviral therapy by the end of the year 2005, will further increase demand for HIV testing among TB patients and for knowing the size of the burden of HIV associated TB. HIV testing is the entry point for ART delivery, and this applies equally to patients with TB. Reliable HIV surveillance systems for TB patients and large-scale access to HIV testing and counselling services are cornerstones for effective TB/HIV collaboration.

This document outlines the three main methods for HIV surveillance among TB patients: data from the routine testing of TB patients for HIV; sentinel surveillance; and periodic (special) surveys. Selecting the appropriate surveillance strategy will depend on the existing surveillance system, the underlying HIV epidemic status in a country, and the status of ART implementation, as well as the overall TB situation. This document provides an overview of the principal issues to be considered by countries in strengthening their existing surveillance systems or developing new systems and increasing their utility.

At all levels of an HIV epidemic (low-level, concentrated, generalized), routine HIV testing data – when available – should be used for surveillance purposes. These data can be calibrated by periodic (special) or sentinel surveys. In countries where HIV prevalence among TB patients is unknown, a seroprevalence survey should be undertaken as part of the initial assessment of the situation.

WHO recommends the following HIV surveillance methods, which vary according to the level of the HIV epidemic:

1. All countries with a generalized HIV epidemic (HIV prevalence consistently >1% in pregnant women) should aim to ensure that HIV counselling and testing are actively promoted and offered to all TB patients. Whenever possible, this should be done in conjunction with the provision of ART. The data obtained in this way can form the basis of a reliable surveillance system where high coverage (>80%) of testing among TB patients is achieved. One of the best systems for capturing this information is through a computerized TB notification system, which also captures information on HIV status.

Periodic (special) surveys or sentinel surveys are also recommended, to calibrate the results of routine testing.

2. In countries with a concentrated epidemic (HIV prevalence consistently >5% in at least one defined subpopulation, e.g. intravenous drug users (IDUs); sex workers (SWs), men who have sex with men (MSM), and <1% in pregnant women in urban areas), data from routine HIV counselling and testing of all TB patients should still form the basis for the surveillance. If this system is not yet in place, periodic (special) surveys or sentinel surveys are suitable alternatives.
3. In countries with a low-level HIV epidemic (HIV prevalence has not consistently exceeded 5% in any defined subpopulation) and where HIV testing is not routinely offered to TB patients, periodic (special) surveys (at intervals of 2–3 years) or sentinel surveys should be conducted among TB patients.

Periodic sentinel serosurveillance for HIV in general is usually conducted among pregnant women (as a proxy for the general population) or among population groups with high-risk behaviour, depending on the level of the epidemic. This surveillance is useful for monitoring the trends in HIV prevalence and can identify, at an early stage, areas where routine HIV counselling and testing of individuals with tuberculosis should be undertaken.

HIV tests other than on serum or blood – principally on gingival secretions – are available and being further developed (for example for sputum testing). WHO recommends that further work be done to improve the sensitivity, specificity and therefore the positive predictive value of HIV test on sputum. Until such further work is reported HIV testing using sputum is only advisable if the HIV prevalence among TB patients is anticipated to be at least 10%.

It is intended to pilot these guidelines in several sites around the world in 2004. This will permit evaluation of their feasibility and answer questions regarding sputum-based HIV testing under different conditions.

1. Introduction

1.1 Background

The HIV epidemic has increased the global tuberculosis burden and focused attention on the need to strengthen links between TB and HIV/AIDS programmes in order to tackle these public health emergencies more effectively. In response to this situation, the World Health Organization has developed an expanded strategy aimed at reducing the burden of HIV-related tuberculosis through close collaboration between the TB and HIV/AIDS programmes (1). This multifaceted strategy comprises interventions targeted against TB, including intensified case-finding and preventive treatment, as well as interventions against HIV, including counselling, provision of condoms and antiretroviral therapy (ART).

As the HIV/AIDS and TB epidemics have progressed, surveillance has become widely recognized as a critical activity in understanding the trends of the epidemics and in enabling sound strategies to be developed for responding to them (2). Surveillance of HIV among TB patients is increasingly seen as important, as the HIV epidemic has continued to fuel the TB problem and as new solutions have emerged to tackle this developing situation.

WHO first published guidance on surveillance of HIV among TB patients in 1994, detailing a specific approach to determining HIV prevalence rates in this population group (3). The 1994 edition of the guidelines were produced by a group of experts from around the world and were based on experience from surveillance systems that had worked well in countries of sub-Saharan Africa. They outlined the methodology underlying an unlinked, anonymous, seroprevalence survey of HIV infection among adult patients with newly diagnosed TB.

Some countries have undertaken surveys based on the 1994 guidelines and generally reported the guidance to be useful. However, the methods outlined in the 1994 document detailed a single specific approach to surveillance; while surveys using that approach continue to have a specific role, many countries are now undertaking surveillance using alternative methods. In particular, HIV prevalence data on TB patients are increasingly available from health care delivery settings, where HIV testing is being routinely promoted and offered.

The changing epidemiological situation, combined with the emergence of new knowledge, technologies, treatments and strategies for tackling the TB/HIV problem, highlights the need for updated and broader guidelines that reflect these changes.

1.2 Rationale for surveillance

Surveillance is a “system for collecting information needed for advocating, designing, planning and evaluating public health action” (4). The overall objective of any communicable disease surveillance system is to collect, analyse and disseminate accurate epidemiological data (5). Surveillance should contribute to a better understanding of the magnitude of the problem and provide reliable, timely and cost-efficient information for action.

Surveillance activities for HIV usually refer to the intentional collection of data – through surveys, for example. However, it is increasingly recognized that surveillance systems can also make use of data deriving from other activities. For example, HIV data from prevention of mother-to-child transmission (PMTCT) programmes are increasingly used for surveillance purposes, although they can be liable to bias, if, for example, those most likely to be infected refuse to be tested. Data from voluntary counselling and testing (VCT) services or blood banks may also be useful in certain circumstances, although they are subject to even more important biases, if, for example, VCT services are preferentially attended by those at risk of HIV infection, or blood banks specifically exclude those at risk.

Surveillance systems for measuring HIV prevalence among TB patients have a variety of specific objectives, which are likely to vary between countries according to the different needs and demands existing in the countries (Box 1).

Box 1. Objectives of surveillance of HIV prevalence among tuberculosis patients in different HIV prevalence settings¹

All HIV prevalence settings

- To inform the targeting of resources and the planning of activities for people with HIV and TB and for monitoring the effectiveness of these activities.
- To increase political, professional and civil society awareness of the situation.
- To assess the need for collaboration between HIV/AIDS and TB programmes on formulation and implementation of a joint TB/HIV strategy.
- To provide information on the HIV/AIDS epidemic and its impact on TB patients.
- To quantify the need for providing ART to TB patients.

Concentrated or generalized HIV epidemic state

- To assess the impact of the HIV epidemic on the TB situation.
- To monitor the effectiveness of joint strategies aimed at reducing the TB/HIV burden.

Low-level HIV epidemic state

- To alert TB and HIV/AIDS programmes to a potential HIV problem so appropriate changes can be made to programmes, such as the institution of more systematic surveillance methods or the development of joint strategies.

¹Classified according to the WHO definitions (low level – HIV prevalence has not consistently exceeded 5% in any defined subpopulation; concentrated – HIV prevalence consistently >5% in at least one defined subpopulation, and <1% in pregnant women in urban areas; generalized: – HIV prevalence consistently >1% among pregnant women) outlined in *Guidelines for second generation HIV surveillance*. Geneva, World Health Organization and Joint United Nations Programme on HIV/AIDS, 2000 (WHO/CDS/CSR/EDC/2000.5 & UNAIDS/00.03E).

1.3 Challenges to surveillance

The main challenges to any type of surveillance may be categorized as ethical, organizational and/or financial.

➤ Ethical

A major challenge to any HIV surveillance system is the ethical issues related to HIV testing, which have been widely debated in the published literature and are complex. The main ethical problem with regard to surveillance of HIV among TB patients concerns the use of unlinked anonymous or “blinded” methods, especially in the context of increased access to ART. Unlinked anonymous testing refers to the taking of blood or other specimens for other purposes, stripping the left-over part of the specimen of all identifying markers and testing it for HIV infection without the consent of the individual concerned (6). These methods are used in periodic (special) and sentinel surveys to help control for the participation bias that may result when people refuse to have their blood tested.

Testing without informed consent, for the purpose of surveillance, has generally been considered ethical if it is not only anonymous but also unlinked, so that all identifiers are removed from specimens, making it impossible to link test results to a particular individual. However, blinded HIV prevalence surveys have always provoked considerable controversy (7), particularly in economically developed nations including the Netherlands, the United Kingdom and the USA (8).

The high rates of HIV infection among TB patients in many countries and the improving prospects for care of HIV-infected individuals have led some to challenge the ethical validity of unlinked anonymous methods. A further problem concerning the use of these methods in TB patients relates to the collection of samples. In HIV surveillance, unlinked anonymous methods usually rely on blood samples collected for other purposes, e.g. syphilis testing among pregnant women (4;9). A problem with blinded seroprevalence surveys among TB patients is that blood is often not routinely sampled and has to be specially collected for the purpose of the survey. This has led to debate about whether these methods should be used in such settings (8), and has prompted consideration of the possible alternative of testing sputum samples.

The main ethical proviso relevant to HIV surveillance among TB patients is that, whenever blood is drawn *exclusively* for the purposes of unlinked anonymous surveillance, the fully informed consent of each individual subject should be obtained, even though the number of refusals may compromise the initial rationale of such methods – the elimination of participation bias. In addition, all subjects included in unlinked anonymous seroprevalence surveys should have access to voluntary counselling and testing for HIV infection.

Individual countries should weigh up the advantages and disadvantages of using unlinked anonymous testing in the light of any local issues and the available ethical guidance from the WHO that is currently under revision.

➤ Organizational and/or financial

Current communicable disease surveillance systems vary markedly between countries, and systems that work well in some countries may fail to meet the needs and demands of others. An understanding of a country's specific needs and demands is important, and surveillance systems should be tailored accordingly.

There is often a general lack of understanding among senior health policy-makers of the importance of surveillance as a planning and evaluation tool, which results in low priority for surveillance activities and insufficient investment in the infrastructure necessary for an effective surveillance system (4). A specific problem of surveillance for monitoring HIV prevalence among TB patients is that, as an activity which bridges the HIV/AIDS and tuberculosis programmes, it may suffer from falling between the two programmes, with neither programme fully aware of its importance or willing to fund or accept responsibility for this surveillance.

A considerable challenge to the establishment and maintenance of communicable disease surveillance systems in many countries is the lack of skilled epidemiology personnel. Staff working in the field often have insufficient training and may be ill informed of the purpose of surveillance activities. Feedback to staff involved in surveillance activities is often inadequate, which may lead to their becoming demotivated and to the system functioning poorly.

A problem with many of the current HIV surveillance systems among TB patients is that they reflect more the access of patients to health care services than the true occurrence of HIV within the overall tuberculosis population. The bias introduced through differential access and through patients' reluctance to be tested for HIV, may be a particular problem for surveillance systems that rely on data from HIV routinely testing services. Problems also often exist around collecting data from the private sector, with data from private services often omitted from surveillance systems leading to under-representation of all those who use these services (10).

2. Methods for HIV surveillance among tuberculosis patients

This section describes the main methods that should be used in the surveillance of HIV among tuberculosis patients and provides recommendations for the appropriate method mix for individual countries according to their HIV epidemic state.

2.1 An overview of different surveillance methods

The three main surveillance methods for measuring the prevalence of HIV infection among TB patients are summarized in Box 2.

Box 2. Different surveillance methods for measuring the prevalence of HIV infection among tuberculosis patients			
Surveillance method	Periodic (special) surveys	Sentinel methods	Data from routine care
Description	Cross-sectional HIV seroprevalence surveys among a sample of TB patients within a country. Surveys should include all newly registered TB cases, but for ease countries may choose to focus on a sub-group of patients, such as adult cases with smear-positive disease.	Includes TB patients as a sentinel group as part of the general HIV sentinel surveillance system. A predetermined number of TB patients are routinely tested at selected sentinel sites; testing is performed in a regular and consistent way. As with surveys, all TB cases should be included, but for ease countries may chose to focus on a sub-group of patients, such as adult cases with smear-positive disease.	Data collected from routine care of TB patients who are tested for HIV on voluntary and confidential basis. With increasing levels of HIV in the general population, countries should aim to test all TB patients for HIV. Countries with a generalized HIV epidemic state should aim to ensure that HIV testing is actively promoted and offered to all TB patients.
Key objectives	<ul style="list-style-type: none"> • This method should be used where the prevalence is previously unknown. It aims to provide TB programmes with rough point prevalence estimates of HIV infection among TB patients, as part of the initial assessment of the situation. • This information may alert TB programmes to a potential HIV problem and enable programmes to make appropriate changes, which may include the institution of more systematic surveillance methods. • This system may also be used in countries with established surveillance systems based on data from routine patient care, to corroborate prevalence estimates. • The system may also be used in resource-limited countries with underdeveloped surveillance systems where HIV prevalence in the general population may be high but the institution of more systematic methods of surveillance is not possible. 	<ul style="list-style-type: none"> • This surveillance method aims to provide more systematic information that will indicate point prevalence estimate of HIV among TB patients as well as identifying trends. • This information is of value for designing, implementing and monitoring public health programmes for prevention and control of TB. • These regular prevalence estimates can also be used to identify, at an early stage, areas where HIV testing programmes directed to the individual should be developed. 	<ul style="list-style-type: none"> • The objective is to provide information that is of value for designing, implementing and monitoring public health programmes for prevention and control of TB.

Advantages	<ul style="list-style-type: none"> • Simple. • No major investment in infrastructure needed. • Established method. • With representative sampling, may provide reliable estimate of HIV among TB patients. • Can be helpful in indicating possible sources of bias in surveillance based on sentinel methods or data from routine care of patients. 	<ul style="list-style-type: none"> • Fairly simple and inexpensive method. • Good information on trends. • Focuses on easily accessible patients. • Often part of a well established HIV sentinel system. 	<ul style="list-style-type: none"> • The testing and reporting of HIV among tuberculosis patients are important in individual case management and provide the opportunity for co-infected patients to benefit from collaborative prevention and care programmes • Public health advantages from the HIV prevention activities that can be associated with large-scale HIV counselling and testing programmes • The system that offers greatest benefit to patients. • Provides tangible evidence of the presence of the HIV epidemic and may, depending on the completeness of the reporting, provide a basis for estimating the burden of HIV-related disease and the demand for health care • If testing widely available and uptake is high, data may provide reliable HIV prevalence estimates among TB patients
Disadvantages	<ul style="list-style-type: none"> • Provides poor information on trends if undertaken infrequently. • May be expensive and time-consuming • Problems with the inclusion of smear-negative TB patients who may have complicated diagnostic pathways. • Problems in obtaining sample for testing if it is not one that is routinely taken. • Ethical issues concerning unlinked anonymous methods. • Sample sizes may be too small for detailed analyses. • Representativeness of sample often questionable; may be open to selection bias. • Has been found to provide inconsistent results in countries with poor testing procedures and inadequate quality control. 	<ul style="list-style-type: none"> • Representativeness of sentinel sites may be insufficient. • Lack of a consistent sampling frame may lead to biased estimates of trends. • Problems with the inclusion of smear-negative TB patients who may have complicated diagnostic pathways. • Ethical issues concerning unlinked anonymous methods. • Problems concerning who has responsibility for the system. • Has been found to provide inconsistent results in countries with poor testing procedures and inadequate quality control. • Representativeness of sample often questionable; may be open to selection bias. 	<ul style="list-style-type: none"> • Necessary infrastructure for the surveillance system may be complex and time-consuming and expensive to maintain. • May provide biased estimate if HIV testing rate is low. • Completeness often affected by the quality of the reporting itself, health-seeking behaviour and the availability of testing. • May reflect more the access to health care services than the true occurrence of HIV among TB patients. • Has been found to provide inconsistent results in countries with poor testing procedures and inadequate quality control

➤ Periodic (special) surveys

Periodic (special) seroprevalence surveys have been the main surveillance method for measuring HIV prevalence among TB patients for many countries around the world (11–17). Well conducted, cross-sectional seroprevalence surveys can provide TB programmes with sufficiently precise point prevalence estimates of the HIV prevalence among TB patients (18, 19). In settings where the prevalence was previously unknown, they are useful as part of the initial assessment of the situation. These surveys are also useful in resource-poor countries with underdeveloped surveillance systems, where HIV prevalence in the general population may be high but the institution of more systematic methods of surveillance is not possible. Periodic (special) surveys can also be used to corroborate from other surveillance methods.

Prevalence surveys are a well established surveillance method and can be undertaken relatively simply compared with other methods of surveillance. They obviate any need for the major investment in infrastructure that other surveillance methods may require. However, they can still be time-consuming and expensive and, if they are not undertaken using appropriate methods, the results may be subject to bias. Where possible, countries should aim to undertake surveys using unlinked anonymous testing (UAT) and appropriate methods for sampling and calculation of sample size.

In most countries, however, this may not be feasible because of the unavailability of left-over blood samples that could be used for UAT. Where UAT cannot, for whatever reason, be conducted without informed consent, it should be undertaken with informed consent (9). Alternatively, the survey could be conducted using linked anonymous testing, in which case all identifiers of the blood specimen of the TB patient consenting to an HIV test are removed and replaced with a specimen code, which enables only the patient to get back the result of the HIV test linked on presentation of this specimen code (2).

Since the samples should be composed principally of newly diagnosed TB cases, surveys conducted over short time periods (2–3 months) – to avoid the same individuals being included in the study population more than once – provide a “point prevalence” estimate. These surveys provide local programmes with a useful snapshot and may be undertaken as part of an initial assessment of the problem. In some circumstances, it may take longer to recruit large enough samples to give statistically meaningful results; the estimate then obtained is a “period prevalence”, measured over a stated time period (6).

Ideally, periodic (special) surveys should be repeated after an interval of 2–3 years. There is little distinction between prevalence surveys, which use a consecutive sample of patients from specific health care settings and are undertaken regularly and in consistent manner, and the methods of sentinel surveillance outlined in the next section.

➤ Sentinel surveillance

For surveillance of HIV among TB patients, some countries use the sentinel surveillance methods outlined in the WHO guidelines (20). However, very few reports of the results from these methods have appeared in the published literature (19).

The sentinel surveillance system was developed specifically to collect information on HIV prevalence, based on the measurement of HIV infection in pregnant women and other groups from whom blood is usually drawn for purposes other than HIV testing (9, 10). The WHO guidance describes sentinel surveillance as the system by which “specific sites and population

groups are selected; a predetermined number of persons are routinely tested, and testing is performed in a regular and consistent way” (9, 18).

When conducted properly, sentinel surveillance should be fully integrated into the normal activities of health care facilities and should aim to not disrupt day-to-day activities at these sites (22). Indeed, the testing of TB patients for surveillance at “sentinel sites” should be undertaken as part of the routine work at these sites and similar procedures should be followed for each survey to ensure consistency (9, 20). Like special surveillance, sentinel surveillance is based on unlinked anonymous methods, using blood specimens that have been collected for other purposes and stripped of all identifying markers. In most countries, however, as for periodic (special) surveys, this may not be feasible because of the unavailability of left-over blood samples. In countries where UAT without informed consent cannot be conducted, it should be undertaken *with* informed consent (9). Alternatively, the survey could be conducted using linked anonymous testing, as described above for periodic surveys.

Sentinel sites are generally selected “because they provide access to populations that are of particular interest” or because they are considered “representative of a larger population” (6). One of the problems with sentinel surveillance methods, however, is determining how representative these sentinel sites are. In interpreting the results from sentinel methods, it is important to estimate first the extent to which the people tested are representative of the sentinel population from which they are drawn and second the extent to which the sentinel population is representative of the general TB population.

If sentinel sites are not selected through probability-based sampling methods, the results can be confidently applied only to the selected populations and sites surveyed (22). However, when data from many different sentinel populations and sites are considered together, they may provide a reasonable overview of the situation in a particular country.

➤ Data from routine patient care

In some countries, particularly those where HIV prevalence in the general population is high, HIV testing of TB patients for diagnostic purposes is becoming more routine. As treatment and care options for HIV infection increase, diagnostic testing of TB patients for HIV in an “opt out” fashion (i.e. routinely testing TB patients for HIV unless they decline to be tested) will be done increasingly in such settings.

Data from the routine care of TB patients form the basis of information for surveillance in several countries. Although systems for recording this information are often still crude, progress towards more systematic approaches reduces the need for data from specific surveys or sentinel methods. In Côte d’Ivoire, for example, the national tuberculosis programme (NTP) has developed and implemented a free, voluntary and confidential HIV counselling and testing programme for all newly diagnosed TB patients, which provides continuous sero-surveillance data (23). Uptake of testing is good, with 92% of those counselled consenting to testing; although coverage of the country remains incomplete, valuable epidemiological inferences have been drawn from the data.

In a few countries, data on HIV status are collected on the TB register or on the TB notification form. In the United States, for example, where there has been electronic reporting of individual TB cases since 1993, the TB case report has been expanded to include additional information on TB risk factors, including HIV status (24).

Cross matching, which is undertaken using a combination of identifiers such as date of birth and sex, aims to enhance the completeness of the two systems, “leading to a more valid appraisal of the overlap of the two interrelated epidemics” (25). Although problems have been noted in terms of differences in the definition of an active TB case, these differences are not considered to detract substantially from a good match. Some efforts have been made to cross-match between systems manually, because of the relatively small databases involved, but electronic matching using carefully selected parameters is used in most circumstances for logistic reasons (25, 26).

Data from routine patient care may be collected by a variety of different methods. The main features of these different methods and their strengths and weaknesses are outlined in Annex 3. In general, the methods used to capture data from routine care will depend largely on the existing TB and HIV/AIDS programmes in a country, as well as on available resources for surveillance activities. However, data should be based on the routine reporting of all individuals with TB who test positive for HIV and should include patients with TB tested for HIV for diagnostic reasons as well as those who attend VCT services. One of the best systems for capturing this information is through a computerized TB notification system that also captures information on HIV status. The capture of data through other methods, such as the use of VCT registers, may provide extremely biased estimates of HIV prevalence among TB patients, because only a subset of all TB patients is likely to attend VCT, generally those who are younger and less sick.

➤ Special studies

Data gathered from special studies can provide useful information to supplement general surveillance data from other sources. Such studies usually focus on subgroups of the population, which limits their generalizability. An example is the pathology study undertaken in Zambia that focused on children who had died from acute respiratory infections (27). Post-mortem investigations of these children looked for the presence of HIV and TB infections, among others. Many similar studies have been undertaken in other African countries, including Côte d’Ivoire (28).

A few studies have investigated the relationship between HIV infection and the outcomes of TB treatment, such as the development of drug resistance (11, 29, 30). Some of these studies have used cohort survey methods.

2.2 Surveillance methods in different HIV prevalence settings

The framework suggested in Boxes 1 and 2 and in Table 1 is intended to be flexible in relation to identifying the system that may be suitable for a particular country. Countries should be encouraged to develop systems that best fit their particular needs and demands and that build upon any strengths within their HIV/AIDS and TB programmes and their communicable disease surveillance systems. However, as detailed in the framework, the methods used to provide estimates of the number of people with TB who are co-infected with HIV should vary with the underlying **HIV epidemic state**, as well as with the type and quality of existing surveillance systems.

Table 1. Flow table for selection of surveillance method

Criteria	Recommended HIV surveillance methods
Generalized HIV epidemic state (HIV prevalence consistently >1% among pregnant women).	Data from routine HIV testing of TB patients <i>and</i> Periodic (special) or sentinel surveys to calibrate the data from routine HIV testing
Concentrated HIV epidemic state (HIV prevalence consistently >5% in at least one defined sub-population, e.g. IDUs, SWs, MSM; HIV prevalence <1% in pregnant women)	Data from routine HIV testing of TB patients <i>or</i> Periodic (special) or sentinel surveys in the administrative areas where HIV level unknown (routine data not yet available). Such surveys can also calibrate the data from routine HIV testing.
Low-level HIV epidemic state (HIV prevalence has not consistently exceeded 5% in any defined sub-population, e.g. IDUs, SWs, MSM)	Periodic (special) or sentinel surveys

➤ **Surveillance in countries with a generalized HIV epidemic state**

All countries with a generalized HIV epidemic state should aim to ensure that HIV testing is actively promoted and offered to all TB patients. The data available from these initiatives can form the basis of a reliable surveillance system that achieves high coverage (>80%) of testing among TB patients.

The strength of data from such systems depends on the methods used to capture them as well as on the uptake of testing by TB patients. If the uptake is poor and data from this system are considered incomplete or unrepresentative, countries may wish to collect corroborative surveillance information through the periodic (special) surveys (undertaken every 2–3 years) or sentinel surveys.

In resource-limited countries, where the HIV and TB burden in the general population may be high but the institution of more systematic surveillance methods is not possible, tailored periodic (special) or sentinel surveys should be undertaken. The results, providing the estimates of HIV prevalence among TB patients, should encourage the routine offer of HIV counselling and testing for all TB patients. In such settings, small special surveys of new adult TB cases should be undertaken using convenience methods of sampling (see section 3.4) and may, for ease, focus on smear-positive pulmonary cases.

➤ **Surveillance in countries with a concentrated HIV epidemic state**

In countries with a concentrated HIV epidemic state, HIV testing and counselling of all TB patients should form the basis for surveillance. If this is not yet in place, periodic (special) surveys or sentinel surveys are suitable alternatives.

Sentinel surveillance methods are particularly useful for monitoring national trends, which is important if the underlying HIV epidemic state is rapidly evolving: they can identify, at an early stage, areas where HIV tests and TB screening programmes directed towards the individual should be developed.

➤ **Surveillance in countries with a low level HIV epidemic state**

Both periodic (special) and sentinel surveys can be used in countries with a low-level epidemic state. Special surveys have a specific role in all countries where the prevalence of HIV among TB patients has not been previously estimated. Surveys based around the methodology outlined in the 1994 WHO guidelines, using representative sampling methods and appropriate sample sizes, can provide accurate estimates of the burden of HIV on the TB epidemic and are an essential part of the initial assessment of the situation. This information may alert TB programmes of a potential HIV problem and enable them to make appropriate changes, which may include the institution of a more systematic surveillance system. Periodic (special) surveys should be repeated at intervals of 2–3 years.

➤ **Additional surveillance methods**

Additional methods may also be considered useful in obtaining information on HIV prevalence among TB patients. Firstly, many studies are undertaken using tuberculosis patients for research and planning purposes, in which blood is often drawn. These studies provide an opportunity for the samples to be also used for unlinked anonymous HIV testing (6). Ideally the results of such testing should be correlated where possible with existing data or results from sentinel sites or prevalence survey sites so that the data sets can be compared. Second, in countries with well established vital registration systems, death certificates may provide further information about deaths of patients who were co-infected, which can be used to supplement data gathered by other surveillance methods. Finally, some countries may also consider corroborating data obtained through standard methods with information collected from reviews of hospitals', and laboratories' data and lists of persons receiving medications (4).

3. Methodological issues

3.1 Initial situation assessment

Before a surveillance protocol is formulated, a detailed situational analysis should be undertaken. This may include the following questions:

- Analysis of current system for HIV and TB surveillance – is there a system for monitoring the prevalence of HIV infection among TB patients and/or TB among HIV-positive people? If so, what is the system?
- Are systems for linkage between HIV and TB reporting databases possible or available?
- What is the prevalence of HIV infection in the general population and/or among at-risk population groups (IDUs, SWs, MSM, prisoners)?
- What is the prevalence of TB in the general population and/or among at-risk population groups (e.g. IDUs, prisoners) and is the information reliable?
- What laboratory capacity is currently available for diagnosing TB and HIV infections?
- To what extent are services available for those seeking HIV testing and counselling?
- To what extent are services available for TB patients seeking HIV testing and counselling?
- To what extent is there appropriately trained staff to conduct the surveillance?

➤ Indicators to be used for surveillance and information needed for the indicators

The point or period prevalence of HIV infection among TB patients (see case definition, Box 3) is the main indicator to be measured by the surveillance methods described.

What should be measured? The proportion of registered TB patients which is HIV-positive. The people responsible for the surveillance system at country level should define the numerator and denominator as well as the surveillance time-scale according to the method used (Box 2).

The proportion of TB diagnosed among HIV-positive people should be measured in countries where the surveillance system is based on the capture of data obtained from routine HIV/AIDS care (see Annex 3).

3.2 Case definitions

The case definition for TB patients who are co-infected with HIV should integrate the two current standard reporting criteria for TB and HIV infections. The standard case definition for HIV infection is given in the *WHO recommended surveillance standards (31)*, and the international case definitions for TB in the WHO Treatment of tuberculosis guidelines for National programmes, 2003 (32), and summarised in Box.3.

Box 3. WHO recommended case definitions for tuberculosis and HIV infection.

HIV infection

- **Clinical description:** there is no clinical description; diagnosis is based on laboratory criteria.
- **Confirmed case:** a laboratory-confirmed case

Laboratory criteria:

1) For surveillance purposes – HIV-positive serology (enzyme-Linked immunosorbent assay {ELISA}); confirmation by a second serological test (ELISA or simple/rapid assay based on a different antigen preparation and/or a different test principle) is necessary only in settings where estimated HIV prevalence is known to be <10%.

2) For diagnostic purposes – in low-level countries (HIV prevalence has not consistently exceeded 5% in any defined population), a third test or confirmatory test (Western Blot) may be necessary if the second ELISA is indeterminate.*

Tuberculosis

- **A case of tuberculosis:** a patient in whom tuberculosis has been bacteriologically confirmed, or has been diagnosed by a clinician.
Note: Any person given treatment for tuberculosis should be recorded.
- **A definite tuberculosis case:** a patient with culture positive for the *Mycobacterium tuberculosis* complex. (In countries where culture is not routinely available, a patient with two sputum smears positive for an acid-fast bacillus is also considered to be a “definite” case).

* Based on current WHO recommendations. Revised WHO recommendations will be available by end of 2004.

3.3 Population under surveillance

➤ Eligibility criteria

Ideally, all newly registered patients with TB according to the standard international case definition (Box 3) should be considered for surveillance. However, if periodic (special) surveys or sentinel methods are used and resources are limited, countries may choose to focus only on adult patients with smear-positive pulmonary TB, as diagnosis in this group of patients is generally easier and quicker to confirm and the patient pathway likely to be less complex. Indeed, for these reasons, most of the published surveys have included only smear-positive cases, and there is limited information on HIV infection rates among children with TB in the published literature (33). Countries where resources are scarce and the HIV epidemic state is either low or concentrated may also choose to include only patients between the ages of 15 and 59 years.

➤ Exclusion criteria

Where possible, relapse cases should be excluded from surveillance systems because of the risk of surveying the same patient twice, unless they are identified as such and the results are analysed separately (3). However, relapse cases may be included – and need not be identified as such – if surveillance is based on survey methods and these surveys are undertaken over a short period of time, ideally less than 2–3 months.

3.4 Sampling

As a statistical method to form a group of patients to be tested sampling should be used only for periodic (special) or sentinel surveys. When HIV counselling and testing are routinely offered to all TB patients, there is no need for a specific sampling method – the size of the sample would be exhaustive.

➤ Sample size

The sample size necessary to provide a reasonably accurate estimate of prevalence should be calculated before any survey is undertaken. The calculation should use standard techniques, based on the expected prevalence and using appropriate levels of precision. Annex 5 outlines the main steps that should be taken in calculating a sample size for surveys. The STATCALC feature in the EpiInfo software also provides a user-friendly sample size calculator for calculating specific sample sizes, which some may find easier to apply.

The minimum sample for any survey should generally exceed 150 patients. However, surveys undertaken in resource-poor settings with high TB prevalence may limit sample size to 150 adult patients (expected prevalence of 10–20% with a 5% error margin). In such circumstances, new TB cases should be selected on a consecutive basis, from a range of representative institutions involved in the treatment of TB patients (rural and urban area), over the period of time necessary to reach the sample size.

➤ Sampling procedure

Ideally, representative sampling methods should be used wherever a population sample is used to estimate prevalence in the wider population. The following three main sampling methods are used to select individuals for inclusion in the sample (22):

- **Simple random sampling.** Each TB patient in the population being sampled has an equal probability of being selected. This method requires the use of random number tables, or some other method of generating random numbers, to identify patients for inclusion in the sample.
- **Systematic sampling** The initial patient who meets the eligibility criteria is randomly selection, after which every “*n*th” (e.g. 5th) eligible patient is selected until the predetermined sample size is reached.
- **Consecutive sampling.** Every patient who meets the eligibility criteria at a particular site is selected until the required sample size is reached or until the survey period is over.

In practice, random or systematic sampling methods can be logistically complex and expensive, and most surveys use consecutive sampling methods at a few selected sites. Where random selection procedures are not feasible, and sampling methods of convenience are used, patients should be tested under standardized conditions; if only a limited number of diagnostic centres are used, care should be taken in extrapolating the results to the wider population.

More reliable prevalence estimates for a population may be obtained if “cluster” sampling methods are used, with “clusters” of patients from different diagnostic centres in the country being randomly selected; the “clusters”, rather than single persons, are used as sampling units (3). This method, which is described in the 1994 guidelines, is simpler than random selection methods for individual patients; it consists of testing all eligible patients on a consecutive basis in each of the randomly selected clusters until the required cluster size is reached.

For sentinel surveillance, sentinel sites should be selected. once the sample size has been calculated. Choice of these sites should take into consideration their geographical coverage, the type of population (urban and rural) and the number of TB patients seen at each specific site. Other criteria that should be taken into consideration include the willingness of the staff at each site to participate and cooperate in surveillance, and access to a reliable laboratory capable of performing HIV tests.

Experience from the field has indicated that, where sentinel surveillance or surveys are carried out, it is often advantageous to concentrate resources on a few selected sites with the required minimum managerial and technical capacity to produce reliable data (4). The eventual goal should be to extend the number of sites to a broad geographical distribution, depending upon the availability of staff and financial and logistic resources.

In surveys and sentinel surveillance, experience has also shown that it is more practical if staff are instructed to begin and end surveillance activities on certain fixed dates (22). The duration of the sampling will vary according to the clinic capacity and the number of patients seen in the clinic who meet the eligibility criteria. Ideally, the sampling duration should be about 8 weeks, and should not exceed 12 weeks. To allow sufficient time for data collation, analysis, interpretation, and report writing and dissemination, surveys should not be repeated more than once a year (22).

3.5 Specimen selection

➤ Advantages and disadvantages of different specimens

Many different types of specimen can be used in HIV biological surveillance – whole blood, plasma, serum, oral fluids, sputum and urine. With the emergence of new HIV testing technologies, a number of prevalence surveys have been undertaken in countries around the

world using new technologies such as the Oraquick testing kit, which provides on-the-spot testing of saliva (34, 35). The choice of specimen for HIV testing depends on several factors, including the overall validity of the tests for each specimen, available resources and the logistics for surveillance activities within the country. It will also depend on underlying contextual factors such as national policy as well as the HIV epidemic state (22).

The advantages and disadvantages of using the different types of specimen are clearly outlined in guidelines on HIV testing technologies produced by WHO and the Joint United Nations Programme on HIV/AIDS in 2001 (2). In addition, there are two further issues that are particularly relevant to the issue of HIV testing for surveillance among TB patients. An advantage of using sputum specimens is that sputum is routinely collected in most countries as part of the preliminary diagnostic investigations for all TB patients. In some settings, this may favour the testing of sputum specimens over blood samples, particularly if unlinked anonymous methods are followed. However, where HIV testing is undertaken for diagnostic reasons (i.e. the HIV test is linked to the patient), the current sensitivity and specificity of HIV tests favour the use of blood testing over sputum testing (35). Even when unlinked methods are used, the current sensitivity and specificity (93.5–97.1% and 99.7–100%, respectively) of sputum testing methods are still not sufficiently high to avoid having a relatively low positive predictive value (71.9%) in countries where the HIV prevalence levels are low (5%) (35).

Testing sputa is therefore worth doing only if HIV prevalence in TB patients is anticipated to be 10% or more. However, where this is the case, HIV testing of sputum, by avoiding the need for consent of patients, since the specimens are not taken exclusively for the purpose of HIV testing, may offset the potential bias of HIV testing on serum where patients will need to be asked for consent.

WHO recommends that further work be done to improve the sensitivity, specificity and therefore the positive predictive value of HIV test on sputum. Such work should be reported in sufficient detail to allow others to follow precisely the same procedures.

➤ HIV testing approaches

A detailed overview of HIV testing technologies and strategies has been recently published in guidelines produced by WHO and the Joint United Nations Programme on HIV/AIDS (2). Countries undertaking HIV surveillance of TB patients, irrespective of which surveillance methods are used, should ensure that these guidelines are strictly adhered to.

➤ Laboratory issues

Quality control measures for laboratories are a key consideration in relation to HIV testing. A system of internal and external quality control of laboratory procedures should be established in advance of any surveillance activity and should be based on the latest WHO guidelines for HIV testing (2).

Information on the collection of sputum samples from TB patients and the transport of these samples is provided in the WHO guidelines for the surveillance of drug resistance in tuberculosis (36).

3.6 Data management

➤ General

It is important that staff involved in data management are both motivated and carefully instructed in the task of data collection, collation and analysis, and that they are provided with the necessary facilities and materials for these activities (36). Experience has shown that the quality of information obtained from surveillance systems is dependent on health workers' understanding of the purpose and procedures of data collection and on the provision of regular feedback (4).

Training workshops for staff should ideally be held before the start of any surveillance activities. This training should always include a clear description of the rationale for the surveillance. Follow-up visits should be made to each location involved in surveillance activities to monitor progress and ensure that the appropriate procedures are being followed and that the data obtained are accurate (11).

The general principles of data management and analysis outlined in the first edition of these guidelines are still valid for surveillance systems based on periodic surveys and sentinel methods (3).

➤ Data elements

Quality rather than quantity of data should be the main consideration in the design of a prevalence study. To reduce the likelihood of errors and incomplete reporting, data management – which in many countries relies on a few individuals – should focus on the use of simple report forms that do not require multiple data transfers (4).

Countries that collect HIV data from routine care of TB patients should aim to develop standardized reporting forms for the entry of data into the national surveillance system (see Annex 1). Sentinel methods and periodic surveys should also aim to collect information in a simple way; an example of a data collection form that may be used for both of these systems is given in Annex 2.

➤ Confidentiality

Maintaining confidentiality in the transfer of information is essential. The security and confidentiality policies and procedures in countries should be consistent with recognized standards for the security of HIV/AIDS surveillance data (37). In general, standards concerning the use of HIV/AIDS data are more stringent than those for TB data. These confidentiality standards emphasize the importance of minimizing storage and retention of unnecessary or redundant paper or electronic reports. Names should be removed from surveillance records when they no longer serve the public health purpose for which they were collected. Records should be located in a secured area and electronic data should be protected by coded passwords and computer encryption, especially during data transfer.

➤ Quality

Experience with surveillance has shown that the basic capacity to undertake surveillance can be strengthened and sustained through systematic quality control of data collection procedures and laboratory testing (4). This may be achieved in part through strengthening the capacity of

central managers and reference laboratories for regular supervision, quality control and feedback.

The importance of reliable and reproducible HIV testing over time is widely recognized as an important component of any HIV surveillance activity (2). Continuous monitoring of the laboratory system through internal and external quality assurance is essential. There are clear guidelines for the quality assurance of HIV testing that should be adhered to, irrespective of which surveillance methods are used (2).

Surveillance systems should also establish clear standards for the quality of data. Ideally, data quality should be improved through the use of computerized systems that may use built-in error checks and be able to generate reports to highlight missing data (38). In the absence of computerized systems, data quality can be monitored through periodic examination of each of the steps in the collection, collation and analysis process.

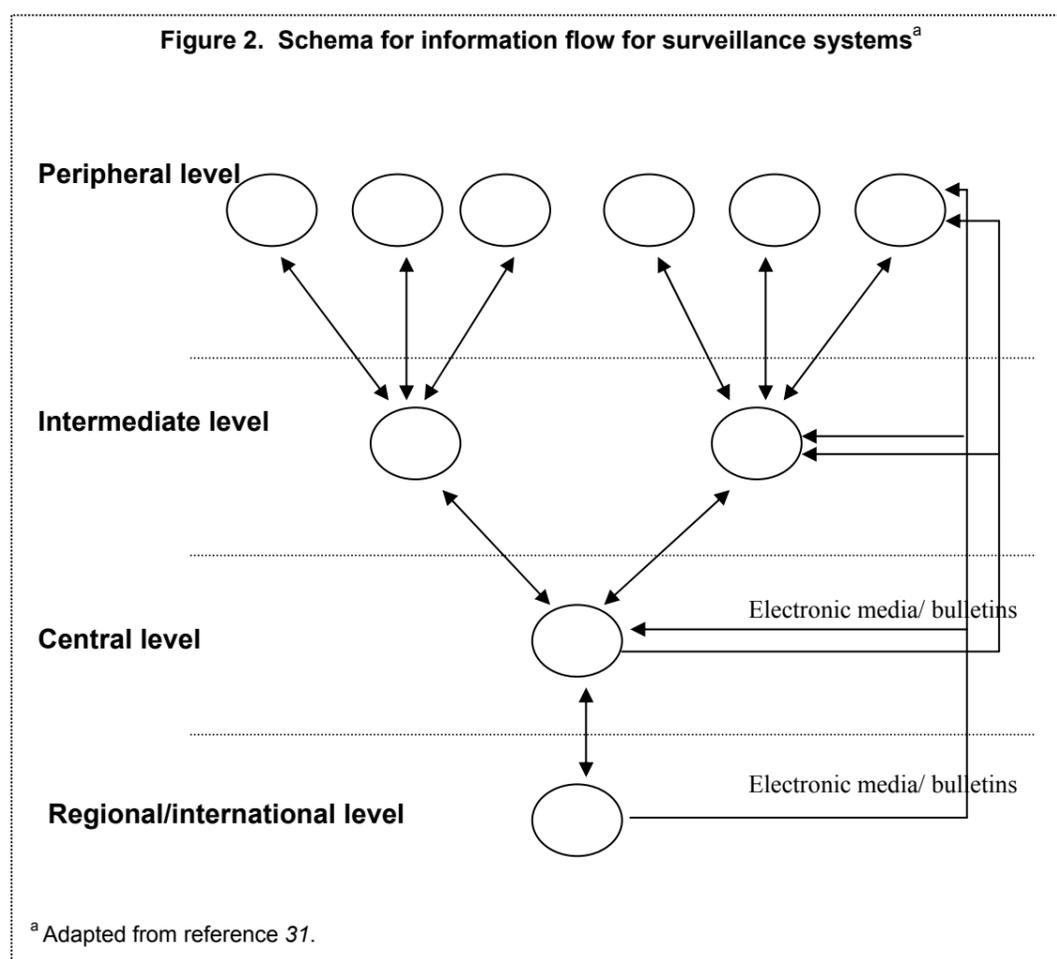
➤ Analysis and dissemination

Whatever surveillance system is in operation, it is important that countries develop a plan for data analysis, covering frequency of data analysis and methods for information dissemination. This should promote regularity and consistency (5). The frequency of data analysis will depend on the type of surveillance activity undertaken. In the case of periodic surveys and sentinel surveillance, data should be analysed, under the supervision of the survey coordinator, after completion of the survey period. In the case of surveillance based on data from routine care, data analysis should be undertaken at least yearly and on a more frequent basis, e.g. quarterly, if resources allow.

The development of skills in data management and of simple packages for statistics and data presentation should be supported. Surveillance data should ideally be entered into a computer programme, such as EpiInfo, that is able to undertake basic data analysis. Simple methods of data analysis should be used to determine the distribution of and associations between the key variables (5). Data collected using sentinel surveillance methods should be analysed separately for each sentinel site.

Dissemination of surveillance data to clinicians and to health centres and laboratories that have reported the data can help to increase timely, valid and complete reporting (38). It is increasingly recognized that feedback loops should be built into surveillance systems (31). Feedback may be through a variety of different media and the following types of reports should generally be considered when communicating surveillance data (31, 38):

- annual reports
- fact sheets
- Epi maps
- newsletters
- regular epidemiological bulletins, with tables and graphs showing trends and progress towards targets
- press releases.



Efforts should be made to ensure that the data generated are used at all levels (22). At a national level, TB and HIV/AIDS programme managers should use the surveillance data to guide, target, evaluate and demonstrate the need for programmes of TB/HIV care and prevention.

3.7 Programme responsibility

The NTP in each country should take responsibility for ensuring that surveillance of HIV among TB patients is undertaken. However, the programme responsible for actually carrying out the surveillance may vary between countries; in some circumstances the NAP and NTP may take joint responsibility for conducting surveillance activities. Whichever programme carries out the surveillance, interaction between the programmes, with respect to flow of information, should be clarified at a national level.

3.8 Resource considerations

The budget for surveillance will vary by country and is largely dependent upon how the surveillance activities fit into the existing infrastructure of the TB and HIV/AIDS programmes. It is important that the resource implications of the proposed system are fully identified. Some of the likely direct and indirect costs are outlined in Box 4.

Box 4. Direct and indirect costs of surveillance

Direct

- Specimen collection equipment
- Transport of specimens
- Specimen testing kits
- Laboratory staff time
- Staff travel costs
- Costs of data entry and analysis
- Dissemination of information (printing of reports, postage, presentations, etc.)

Indirect

- Investment of staff time at all levels in activities ranging from specimen collection to the overall coordination of surveillance activities

3.9 Evaluation

Surveillance systems based on routine patient care should be evaluated on a regular basis within the framework of the WHO protocol for the evaluation of epidemiological surveillance systems (39) (see Box 5).

Following the evaluation, a plan for strengthening surveillance should be developed, which identifies priorities for action within the context of the national TB and HIV/AIDS programmes.

Box 5. Key points for evaluating surveillance systems (38, 39)

- The evaluation should begin with clarification of the overall aims and objectives of the surveillance system.
- All surveillance activities should be identified and categorized in terms of the system's structure, process and outcome.
- The strengths and weaknesses of each component of the system should be assessed.
- Recommendations should be formulated for improving the performance of the system, identifying components that need to be strengthened, gaps, and areas of duplication and activities that can be dropped.

4. Implementation

A first step in ensuring successful implementation of surveillance activities and in improving these activities is advocacy for political support and funding at a national level. Effective surveillance is possible only if there is investment in the supporting infrastructure, in terms of human resources, laboratory support and logistics (40). As a second step, it is important that a multidisciplinary

surveillance team is established, to agree on the objectives of the system and clarify the roles and responsibilities of each of the team members.

Before setting up – or expanding – a surveillance system for monitoring HIV prevalence among TB patients, a number of issues should be addressed in a strategic plan of action and developed into a protocol (22). This plan should be developed and agreed by all members of the surveillance team and should include a budget covering all personnel and equipment requirements for the proposed activities.

One of the main considerations for this team, at an early stage, is a review of the need for surveillance. An assessment of existing surveillance activities should also be undertaken and the current epidemiological situation with respect to HIV and TB should be reviewed. This background preparation is essential and should help teams to identify the surveillance systems that are appropriate to their needs and the methods that should be used. Whichever type of surveillance system is selected, adequate attention should be paid to training and supervision in all areas and to quality assurance procedures for specimen processing and data collection and analysis.

A detailed step-by-step guide to setting up an HIV sentinel surveillance system has been developed by the WHO Regional Office for Africa in collaboration with the University of California and the United States Centers for Disease Control and Prevention (22). This guide may be easily adapted for countries undertaking periodic (special) HIV surveys among TB patients, and some of the general issues it identifies are relevant to any HIV surveillance system.

Annex 1

Minimum data requirements from tuberculosis clinic settings where patients are routinely tested for HIV (5).

Minimum data required for annual reporting from tuberculosis clinic settings to national level are:

Clinic setting:
 District/region in which clinic based:

Patient loads:

- Total number of TB patients per year.....
- Total number of TB patients tested for HIV per year.....

Age: Number of TB cases in the following age groups:
 [0–4] [5–14] [15–24] [25–34] [35–44] [45+]

Sex: Number of females: Number of males:

Clinical presentation:

Number of pulmonary cases:
 Number of extrapulmonary cases:

HIV test result:

Adult male (≥15)			Adult female (≥15)			Child (0-14) male			Child (0-14) female		
<i>n</i>	<i>N</i>	%	<i>n</i>	<i>N</i>	%	<i>n</i>	<i>N</i>	%	<i>n</i>	<i>N</i>	%

Adapted from *Third generation HIV/AIDS surveillance guidelines, WHO Caribbean, 2002.*

Annex 2

Sample data collection form for use in HIV prevalence surveys or sentinel surveillance among tuberculosis patients (3).

<u>Demographic data form*</u>	
Study site:	
Date of patient visit:	____ / ____ / ____ (dd/mm/yyyy)
Patient ID number:	
Age:	_____ (years)
Sex:	Male [] Female []
Clinical presentation:	Pulmonary [] Extrapulmonary []
If pulmonary:	Sputum smear-positive [] Sputum smear-negative []
(If relapse cases are included)	New [] Relapse []
.....	
<u>Laboratory form*</u>	
Patient ID number:	
Results test 1:	Positive [] Negative [] Doubtful [] Not done []
Results test 2: (if undertaken)	Positive [] Negative [] Doubtful [] Not done []

Adapted from World Health Organization. *Guidelines for HIV surveillance among tuberculosis patients*. World Health Organization; 1994. WHO document WHO/TB/94.180.

*There are two main options for collating demographic and laboratory data (22). One option is to record demographic details and laboratory details on separate forms, enter data from these forms onto a computer, match centrally using the unique identifying number and merge into a single record. The other option is to record the data on the same form. The latter method is not ideal if unlinked anonymous methods are used, as an individual's identity number and the associated test results can be more easily disclosed.

Annex 3

Options for the capture of data obtained from routine care on HIV prevalence among tuberculosis patients

Option	Description	Advantages	Disadvantages
1. TB register	The TB register is a well established system that works well in most countries as an integral part of DOTS. The register could be altered to incorporate extra fields recording whether or not an HIV test had been done, and the results of any test undertaken.	<ul style="list-style-type: none"> Well established system that works well in most countries. Simple system. 	<ul style="list-style-type: none"> Confidentiality issues if HIV status is entered into a register that includes the patient's name. May be hard to change a system that is already established. Replacement of registers could prove costly and may take time.
2. TB notification form	System similar to the register: detailed information on each patient is collected and collated at national level through a formal, mandatory notification system. Notification form could be modified to include information on HIV status. System computerized where possible to enable cross-matching of data and revision of information. Computerization may take place at level of data input or nationally at level of data collation and analysis.	<ul style="list-style-type: none"> Detailed information collected, which could be used for variety purposes. Data could be corroborated with HIV surveillance systems through cross-matching of key variables. 	<ul style="list-style-type: none"> Confidentiality issues if HIV status is entered into a system that includes the patient's name If the notification is paper-based, the validity of the system depends on a patient having the test result at the time of the notification. Development of a computerized system, which would enable data to be linked, requires considerable investment.
3. Specific register for TB patients diagnosed with HIV	New register set up in the TB clinic setting for all patients diagnosed with HIV.	<ul style="list-style-type: none"> May provide reliable prevalence estimates if most patients with TB are tested for HIV. Easily identifiable cohort of patients who can be correctly identified for ART and treatments against opportunistic infections. 	<ul style="list-style-type: none"> Identifying the denominator may be difficult as patients with TB who are not tested for HIV, for whatever reason, are not included in the system. Duplication of registers, which may result in defective completion by hard-pressed staff.
4. Co-trimoxazole register	Paper-based co-trimoxazole register set up alongside TB register in TB clinic setting for all TB patients diagnosed with HIV. Primary purpose of register is to keep record of TB patients eligible for co-trimoxazole.	<ul style="list-style-type: none"> If most TB patients are referred for testing, the system may provide reliable estimates of HIV prevalence in these patients. Simple system that requires minimal infrastructure. 	<ul style="list-style-type: none"> TB patients who are not tested will not be captured by system. Problems of register "fatigue" and increased workload. Requires close collaboration between VCT staff and TB clinic staff.

5. IPT register	IPT register set up alongside VCT register for the main purpose of identifying patients who screen negative for TB and who are eligible for IPT. Register may contain details of all those who are screened for TB.	<ul style="list-style-type: none"> • System may work well if most patients who attend for VCT are screened for TB. • Simple system. • Low costs. 	<ul style="list-style-type: none"> • Will not capture data on TB patients who do not attend for VCT. • Requires close collaboration between VCT and TB clinic staff. • Problems of obtaining unbiased sample if not all patients who test positive for HIV accept offer of screening. • TB status may be determined some time after the patient is tested for HIV, which may cause difficulties in capturing data. • Problems of register “fatigue” and increased workload.
6. VCT register	VCT register for everyone who turns up for HIV testing through VCT settings. Information on TB status routinely collected.	<ul style="list-style-type: none"> • In most countries this is an emerging system that offers the opportunity of setting up a system for identifying HIV infected clients with TB. • Simple system. • Low costs. 	<ul style="list-style-type: none"> • TB status may be determined some time after the patient is tested for HIV, which may cause difficulties in capturing data. • Fails to capture patients who are tested for HIV outside the VCT system. • Problem of obtaining data from private VCT centres. • Relies on the commitment of a system that is set up primarily for benefit of HIV/AIDS programme. • Requires close collaboration between VCT and TB clinic staff.
7. Separate VCT register for patients with TB	Separate register set up alongside standard VCT register for known TB patients.	<ul style="list-style-type: none"> • System may work well when all TB patients are referred for VCT. • Simple system. • Low costs. 	<ul style="list-style-type: none"> • Problems of register “fatigue” and increased workload. • Problem of capturing data on people who are TB-free when they test positive for HIV through VCT but who subsequently develop TB. • Fails to capture patients who are tested for HIV outside the VCT system. • Requires close collaboration between VCT staff and TB clinic staff.

8. HIV/AIDS case notification form	Notification form: detailed information on each patient is collected and collated on a national level through a formal and mandatory system of notification. Notification form could be modified to include information on whether a patient has TB. Computerization of system would enable cross-matching of data and revision of information.	<ul style="list-style-type: none"> • Captures all HIV-positive individuals, including those outside the VCT system. 	<ul style="list-style-type: none"> • TB status may be determined some time after the patient is tested for HIV, which may prove difficult to capture. • Additional workload for those maintaining register who may fail to see benefit of capturing the data. • Relies on the commitment of a system that is set up primarily for benefit of HIV/AIDS programme.
9. Cross-matching of HIV and TB notification systems	Where a computerized surveillance system for HIV and TB patients exists, linkage of data through key variables can identify patients who are co-infected.	<ul style="list-style-type: none"> • Avoids need to set up new system. • Can be done relatively quickly and simply if appropriate resources are available. 	<ul style="list-style-type: none"> • Complex. • Requires sophisticated computer database packages. • Data analysts may have to be trained. • Data from two systems may require considerable "cleaning" before the matching process. • Unreliable data in two systems may result in problems when matching.

Annex 4

1994 WHO guidelines for HIV surveillance among tuberculosis patients

Corporate authors: WHO Tuberculosis Programme.
International Union against Tuberculosis and Lung Disease

Publication: Geneva, World Health Organization, 1994

Electronic access: http://whqlibdoc.who.int/hq/1994/WHO_TB_94.180.pdf

Annex 5

Sample size determination

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

Sample size required for determining a significant change between two proportions^a

Baseline prevalence (%)	Sample size for specific percentage change								
	10%	20%	30%	40%	50%	60%	70%	80%	90%
1	145 800	34 000	14 000	7 290	4 280	3 000	2 070	1 459	1 060
5	28 000	6 550	2 800	1 500	903	585	400	282	204
10	13 000	3 200	1 350	718	432	280	190	135	97
15	8 500	2 030	850	457	275	178	122	86	62
20	6 000	1 425	612	326	197	128	87	61	44
25	4 500	1 090	463	247	149	97	66	46	33

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

^a Adapted from reference 9.

To calculate sample size for values not shown in the table, the following formula can be used:

$$N = PQ / (E/Z)^2$$

where

N = the minimum sample size required

P = the maximum expected prevalence rate or expected population proportion

Q = $100 - P$

E = the margin of sampling error tolerated

(Note: In general a sampling error of greater than 5% is not acceptable)

Z = the centile of the standard normal distribution.

If the confidence level chosen is 95%, $Z = 1.96$; if another confidence level, e.g. 99%, $Z = 2.58$.

For example:

If a country is undertaking an HIV prevalence survey among TB patients where the expected HIV prevalence rate among these patients (P) is 20%, Q will be $100 - 20 = 80$; and if the margin of error chosen is 5, the minimum sample size is $80 \times 20 / (5/1.96)^2 = 246$.

If at the end of this survey, an HIV prevalence rate of 18.5% is observed, the real prevalence among the TB patients is between 14% ($18.5\% - 5\%$) and 24% ($18.5\% + 5\%$) within a 95% confidence interval.

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