

## **PRINCIPLES OF TUBERCULOSIS CONTROL.**

**Tuberculosis as a global problem. WHO promoted TB control measures - DOTS and Stop TB strategies.**

### **Principles of Tuberculosis Control**

The highest priority in any tuberculosis control program is the prompt detection of cases and the provision of short-course chemotherapy to all tuberculosis patients under proper case-management conditions, including directly observed therapy. In addition, in low-prevalence countries with adequate resources, screening of high-risk groups (such as immigrants from high-prevalence countries, migratory workers, prisoners, the homeless, substance abusers, and HIV-seropositive persons) is recommended. TST-positive high-risk persons should be treated for latent infection. Contact investigation is an important component of efficient tuberculosis control, a great deal of attention has been given to the transmission of tuberculosis (particularly in association with HIV infection) in institutional settings such as hospitals, homeless shelters, and prisons. Measures to limit such transmission include respiratory isolation of persons with suspected tuberculosis until they are proven to be noninfectious (i.e., by sputum AFB smear negativity), proper ventilation in rooms of patients with infectious tuberculosis, use of ultraviolet irradiation in areas of increased risk of tuberculosis transmission, and periodic screening of personnel who may come into contact with known or unsuspected cases of tuberculosis. In the past, radiographic surveys, especially those conducted with portable equipment and miniature films, were advocated for case finding. Today, however, the prevalence of tuberculosis in industrialized countries is sufficiently low that "mass miniature radiography" is not cost-effective.

### **DOTS strategy**

In high-prevalence countries, many tuberculosis control programs have made good progress in reducing morbidity and mortality during the past decade by adopting and implementing the DOTS strategy promoted by the WHO. DOTS means - Directly Observed Treatment, Short-course. This strategy consists of:

1. political commitment with increased and sustained financing;
2. case detection through quality-assured bacteriology (starting with microscopic examination of sputum from patients with cough of >2–3 weeks' duration);
3. administration of standardized treatment, with supervision and patient support;

4. an effective drug supply and management system;
5. a monitoring and evaluation system, with impact measurement (including assessment of treatment outcomes—e.g., cure, completion of treatment without bacteriologic proof of cure, death, treatment failure, and default—in all cases registered and notified).

In 2006, the WHO indicated that, while DOTS remains the essential component of any control strategy, additional steps must be undertaken to reach the 2015 tuberculosis control targets set within the United Nations Millennium Development Goals.

Thus, a new **"Stop TB Strategy"** with six components has been promoted:

1. Pursue high-quality DOTS expansion and enhancement.
2. Address HIV-associated tuberculosis, MDR tuberculosis, and other special challenges.
3. Contribute to health system strengthening.
4. Engage all care providers.
5. Empower people with tuberculosis and communities.
6. Enable and promote research.

As part of the fourth component, new evidence-based International Standards for Tuberculosis Care, focused on diagnosis, treatment, and public health responsibilities, have recently been introduced for wide adoption by medical and professional societies, academic institutions, and all practitioners worldwide.

## **12.2. Evaluation of National Tuberculosis Program. Basic, intermediate and national level of management. NTP in Belarus.**

### **EVALUATION OF A NATIONAL TUBERCULOSIS PROGRAM**

Each National Tuberculosis Program should establish objectives for its activities, keeping in mind the ultimate goals of reducing deaths, disease and infection. Evaluation of the program's activities provides an indication of how well these objectives have been achieved. The evaluation is based on the records kept in each district; evaluation is always made by "cohort analysis" which signifies that all patients recorded in a register within a specified calendar quarter are accounted for within the analysis (no patients are "conveniently" left out).

## **12.3. Epidemiological indices (tuberculosis morbidity and mortality rate, disease incidence and prevalence, drug resistant TB and HIV-TB surveillance).**

The extent of tuberculosis and its evolution over time defines its epidemiology. Epidemiology provides the basis for public health practice needed to control the disease. Various epidemiological indices are employed that differ in complexity.

*Mortality* – the number of deaths caused by the disease has traditionally defined the extent of the tuberculosis epidemic. Mortality is expressed as the number of tuberculosis deaths per unit of population (usually 100000) and per unit of time (usually per year). However, this information is not reliably collected in most countries where tuberculosis is common.

Tuberculosis is the cause of an estimated 2.8% of deaths in the world in all age groups — and 26% of avoidable deaths in developing countries.

Practical point: tuberculosis kills more young people and adults than any other infectious disease; someone dies of tuberculosis every 10 seconds.

*Morbidity* - tuberculosis morbidity is expressed by two main indices: prevalence and incidence.

*Disease prevalence* is the number of cases of disease present in the community at any given point in time per unit of population (usually 100000).

Prevalence can be determined only by surveys conducted on representative samples of the general population. These surveys are costly and difficult, but have been conducted in certain countries to monitor the epidemiological trend of tuberculosis.

*Disease incidence* is expressed by the number of cases of a disease newly occurring over a specific period of time (usually one year) per unit of population (usually 100000).

An estimation of incidence is obtained from notifications of new cases. The estimation is in exact because not all cases that occur during the year are diagnosed, and those that are diagnosed are not always notified. The incidence of tuberculosis cannot be accurately estimated by notification of cases; in general estimations of incidence based on notified cases is lower than the real incidence, as only 30–60% of cases are notified in many countries. The notified cases are usually specified by type (i.e. pulmonary tuberculosis, smear-positive or smear-negative, extrapulmonary). The incidence of tuberculosis can also be predicted from estimates of the incidence of tuberculous infection. This is reliable only in regions that do not have a high incidence of HIV.

**Table 12.1 – Epidemiological variables and parameters of tuberculosis**

Variables or indicators:	
<u>Mortality rate</u>	the number of deaths due to tuberculosis per 100000 population per year
<u>Morbidity rate</u>	

Prevalence	the number of cases at a given moment per 100000 population
Annual incidence	the number of new cases in one year per 100000 population
<u>Infection</u>	
Prevalence	the percentage of the population infected at a given moment
Annual incidence	the percentage of the population newly infected in one year

- a smear-positive case remains infectious for an average of 2 years (in the absence of treatment, during the natural course of the disease, the prevalence is estimated to be twice the incidence)

- in one year, 25% of untreated cases die — this is the case-fatality rate: the annual number of deaths is four times lower than the prevalence and two times lower than the incidence

All of these parameters are affected by the application of National Tuberculosis Programs, and especially chemotherapy.

### **Gender distribution**

While females often predominate among tuberculosis cases in those under 20 years of age, there is a predominance of males among all notified tuberculosis cases and among those dying from tuberculosis in most countries. Among women, tuberculosis kills more women than any cause of maternal mortality.

### **HIV-TB**

Tuberculosis is one of the most common diseases among HIV-infected persons worldwide. In some African countries, the rate of HIV infection among tuberculosis patients reaches 70–80% in certain urban settings. A person with a positive TST who acquires HIV infection has a 3–13% annual risk of developing active tuberculosis. A new tuberculosis infection acquired by an HIV-infected individual may evolve to active disease in a matter of weeks rather than months or years. TB develops in HIV-infected hosts at a yearly rate of 8 % by either of the two pathogenic mechanisms: endogenous reactivation or exogenous reinfection.

Thus the principle points of the HIV epidemic impact are following:

1. All of the parameters are affected by the HIV epidemic.
2. The risk of developing tuberculosis is 10 times higher in an HIV-positive individual than in a seronegative individual living in the same conditions.
3. The case-fatality rate is higher for HIV-positive tuberculosis patients than for HIV-negative patients.

### ***Impact on morbidity***

Individuals with HIV and tuberculosis co-infection have a much greater risk of developing active tuberculosis disease than the general population. In countries with

high tuberculosis prevalence, tuberculosis is an early manifestation of HIV infection and presents in the majority of cases as smear-positive pulmonary tuberculosis. Extra pulmonary tuberculosis, particularly tuberculosis pleurisy, lymphadenitis and pericardial tuberculosis, is more common in HIV-positive individuals. The annual risk of developing active tuberculosis disease for co-infected patients is on average 10% (between 5% and 15%). In countries with high numbers of co-infected patients, there has been an increase in the overall number of tuberculosis cases because HIV infection occurs in the age groups in which the majority of individuals already have tuberculous infection.

In countries with low tuberculosis prevalence, tuberculosis is not the principal opportunistic infection observed, as HIV infection occurs in population groups that have not previously been infected by the tubercle bacillus.

### ***Impact on mortality***

Tuberculosis that occurs in AIDS- and HIV-positive patients can be cured using the treatment regimens prescribed for all tuberculosis patients. However, the proportion of patients who die while on treatment is higher, but this is often due to conditions unrelated to tuberculosis.

## **ORGANIZATION OF CASE-FINDING.**

**The passive case-finding of patients presenting with symptoms suggestive of tuberculosis (suspects). Smear-positive individuals identifying. Collection of sputum samples.**

The organization of tuberculosis case-finding should enable the sources of infection in the community (i.e. those with pulmonary tuberculosis) to be identified. The most effective method is passive case-finding, which consists of identifying pulmonary tuberculosis patients from among those who present to the health services of their own accord. **The main objective of case-finding is to identify smear-positive pulmonary tuberculosis patients, who are the most potent sources of infection.** These patients are found among adults (individuals aged over 15 years), as tuberculosis in children is rarely smear-positive and smear-negative patients rarely transmit disease, even if they are positive on culture.

The system used to evaluate patients presenting with symptoms suggestive of tuberculosis (suspects) is often likened to a *funnel* with a series of filters that identify smear-positive cases among symptomatic individuals:

The top of the *funnel* represents all adult patients presenting to the health care services. This number depends on the accessibility of the health services and the degree of confidence in the health system.

- The first filter is the clinical examination: among patients presenting with general symptoms, the staff working at the primary level of the health services must identify those with respiratory symptoms. On average 10–15% of adults presenting to the general health services have respiratory symptoms.

- The second filter is also a clinical examination: this distinguishes patients who have symptoms of less than 3 weeks' duration, who most probably have acute respiratory infection. Among those with longer duration of symptoms are not only tuberculosis patients but also patients with chronic lung disease. Of all patients presenting to the health services with respiratory symptoms, 10–25% have a long-term or chronic condition. Tuberculosis patients most frequently have symptoms of at least 3 weeks (distinguishing them from those with acute respiratory infection) but usually of less than one year (distinguishing them from those with asthma or other chronic lung conditions). These patients are termed “tuberculosis suspects”.

- The third, bacteriological, filter is indispensable, as it is the only means by which the most potent sources of infection can be identified. At least three smear microscopy examinations are performed to detect tuberculosis in all those individuals designated “tuberculosis suspects” after passing through the previous filters.

### **The role of radiography and tuberculin skin test in case-finding.**

Chest radiography is not widely used in high prevalence countries, as X-ray facilities are frequently not available in the primary health services and the skills required to correctly interpret them are not present at that level. Furthermore, chest radiography is not necessary for detecting smear-positive patients; it is useful mainly for diagnosing pulmonary tuberculosis in patients whose smear examinations are negative. However, chest X-ray provides early case finding which is most important for individual healing prognosis. Thus routine X-ray, if available, is the most effective method of finding smear-negative active TB cases. TST is not value in adults due to impossibility to identify active TB disease but it remains to be effective in children as provides possibility to identify the moment of getting first infected and high risk groups.

### **Tuberculosis register. Categories of TB patients for registration on diagnosis.**

Tuberculosis register is kept in each basic management unit

By keeping the tuberculosis register up to date, the main case-finding indicators can be determined for each unit, each year:

1. *The total of all newly notified cases, corresponding to all patients recorded in the register at the time of commencing treatment.*



2. *Classification of smear-positive pulmonary tuberculosis cases by their status at the time of notification:*

- new cases;
- relapses;
- failures;
- return to treatment after default.

When the program is poorly run there will be a high rate of previously treated patients, as the patients are not cured. As the NTP becomes better organized, the proportion of re-treatment cases will fall and most patients will be new cases.

3. *Classification of new pulmonary tuberculosis cases by bacteriological status:*

- smear-positive pulmonary tuberculosis,
- smear-negative pulmonary tuberculosis.

4. *Site of disease:*

- pulmonary tuberculosis;
- extrapulmonary tuberculosis.

Depending on the country, extrapulmonary tuberculosis represents 15–35% of all tuberculosis cases. This figure varies depending not only on the situation, but also on the technical ability to diagnose extrapulmonary tuberculosis.

5. *The age and sex distribution of smear-positive pulmonary tuberculosis cases* provides an indication of the age groups mainly affected by the disease and its evolution over time.

6. *The notification rate of new smear-positive tuberculosis cases per 100000 population (based on annual estimates of population size).*

The indicators used for new cases can also be used for newly notified relapses. All of the information necessary for performing these evaluations is noted in the Tuberculosis Case Notification Register if it is properly kept up to date. This why it is so important to keep the register correctly and to train the health staff to update it.

Quarterly case-finding reports are prepared by each basic management unit and kept at a **national level**. This centralization allows case-finding to be reviewed at intermediate and national levels for each of the basic management units. The rate of notified smear-positive pulmonary tuberculosis can thus be determined at national and intermediate levels as well as at the level of the basic management unit.

## **ORGANIZATION OF TREATMENT**

The basic management unit, generally located in the main urban center of the district, is responsible for organizing the treatment of all of the tuberculosis patients in the area. Organization of patient treatment requires the application of adapted

organizational measures so as to ensure that treatment is directly observed at least during the initial phase and that patients comply with their treatment until cure.

Tuberculosis can be cured only if the drugs are taken regularly. The choice of the place of treatment depends on two factors: the **state of the patient**, and the ability of the health staff to **provide treatment to patients**.

### **During the initial phase of treatment**

During the initial phase of treatment, which always contains rifampicin, the patient must take the drugs in front of the health worker who is responsible for verifying that the patient **swallows all of the prescribed drugs every day**.

- If the patient lives, or can be housed, near a basic management unit, he or she can attend every morning to take the drugs.
- If the patient lives near a health post with staff who are trained and acknowledged to be capable by the district coordinator, treatment can be entrusted to this health post, but the follow-up of the patient must continue to be done by the basic management unit and systematic and regular visits must be made to the health post by the unit coordinator.
- If directly observed treatment can not be provided on an out-patient basis, or if the state of the patient requires it, the patient should be hospitalized during the whole of the initial phase of treatment.

Nevertheless, the application of outpatient-based directly observed treatment is not always easy:

- **In urban areas**, especially in big cities, there are often too few health care insitutions, or they are poorly distributed and are not always able to provide correct patient management. These difficulties are further enhanced in some countries by the HIV epidemic and the rapid increase in the numbers of patients needing to be cared for by each center.

- **In rural areas** the distances that patients need to travel in order to reach a basic management unit are sometimes too long or difficult (remote areas, bad weather, lack of transport or transport too costly for the patient).

Patients for whom directly observed treatment cannot be provided on an outpatient basis must be hospitalized throughout the initial phase of treatment. Hospitalization is a costly way of providing treatment, and alternative local solutions have already been identified in many countries: short-term renting of a room in the city, or accommodation in a shelter created for this purpose.

Supervised treatment refers to helping patients to take their TB medications regularly and to complete TB treatment. It is also meant to ensure that the providers give proper care and are able to detect treatment interruption. One example of treatment supervision is recording each dose of anti-TB drugs on the patient's treatment card. A treatment supporter observing intake of every dose ensures that a



TB patient takes the right anti-TB drugs, in the right doses, at the right intervals. Regular supervision and support help to maintain frequent communication between the patient and a health worker or treatment observer; this provides more opportunities for TB education, identification and resolution of obstacles to treatment, and early identification of non-adherence – allowing interventions to return the patient to the prescribed treatment. Regular supervision also allows the prompt detection and management of adverse drug reactions and clinical worsening of TB.

Supervised treatment should be carried out in a context-specific and patient-friendly manner.

### **Monitoring of TB patients during treatment - sputum conversion, clinical and chest X-ray monitoring.**

It is important to monitor all TB patients, adults and children, during treatment.

Bacteriological monitoring is readily available only for patients with sputum smear-positive PTB. These are usually adults and sometimes older children.

#### **Monitoring of patients with sputum smear-positive PTB:**

- **At the end of the initial phase** sputum conversion is observed in most cases. If the patient is still smear-positive the initial phase should be prolonged by 1 month.
- **At the end of the 4th month** for 6-month regimens, and at the end of the 5<sup>th</sup> month for 8-month regimens.
- **During the last month** (at the 6th or 8th month, depending on the regimen).

Routine monitoring of treatment response by CXR is unnecessary and wasteful of resources.

Clinical monitoring is the usual guide to treatment response for other TB patients. These include adults with sputum smear-negative PTB and extrapulmonary TB and most children.

### **Treatment outcome recording and “cohort analysis” of treatment results.**

#### **Recording treatment outcome**

At the end of the treatment course in each individual patient, the district TB officer should record the treatment outcome as follows:

<b>Cure</b>	patient who is sputum smear-negative in the last month of treatment and on at least one previous occasion
<b>Treatment completed</b>	patient who has completed treatment but does not meet the criteria to be classified as a cure or a failure
<b>Treatment failure</b>	patient who is sputum smear-positive at 5 months or later during treatment
<b>Died</b>	patient who dies for any reason during the course of treatment

<b>Defaulted (treatment interrupted)</b>	patient whose treatment was interrupted for 2 consecutive months or more
<b>Transferred out</b>	patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known

### How to evaluate the results of treatment

At the level of the basic management unit The treatment outcome of diagnosed patients is evaluated by **cohort analysis**. This analysis is based on the information recorded in the tuberculosis register. Certain indicators enable the progress of the NTP towards the global objective of a cure rate of 85% to be measured. They also highlight any weaknesses in the organisation of treatment, which can then be remedied. We will illustrate this analysis using the example of new smear-positive cases of pulmonary tuberculosis.

An early indication of treatment efficiency is provided by the rate of smear conversion: this is the proportion of smear-positive cases with negative smears at the end of the second month of short-course chemotherapy (or at the end of the third month in the case of re-treatment cases) out of all smear-positive cases registered for treatment.

Quarterly reports are completed separately for the various types of case (new smear-positive and re-treatment smear-positive cases; new smear-negative and extra-pulmonary cases are not usually evaluated). The treatment outcome of the cohort enables the following rates to be determined for a specified quarter. All outcomes can be determined for smear-positive cases; cure and failure cannot be considered outcomes where new smear-negative cases are evaluated.

Cured	This is the proportion of smear-positive cases who have completed treatment and who have at least two negative sputum smear tests (one of these during the last month of treatment), out of all new smear-positive cases registered for treatment.
Completed treatment	<p>This is the proportion of cases who have completed treatment, but for whom cure is not confirmed by two bacteriological examinations, out of the total number of cases registered for treatment.</p> <p><i>If this rate is high, the health center should do its best to provide proof of cure by bacteriologically testing patients who have completed treatment, most of whom are likely to have been cured.</i></p>

	<u>The success rate is obtained by adding together the cure rate and the completed treatment rate.</u>
Failure	<p>This is the proportion of smear-positive cases who remain or revert to being smear-positive 5 months or later after commencing the course of treatment, out of the total number of smear-positive cases registered for treatment.</p> <p><i>In a well-functioning NTP the failure rate should be lower than 5%.</i></p>
Defaulted	<p>This is the proportion of cases who have interrupted their treatment for 2 or more months, out of the total number of new smear-positive cases registered for treatment.</p> <p><i>This rate clearly reflects the quality of the organization of a tuberculosis control center, and should be less than 10% in an efficient NTP. When this rate is too high (more than 15%), the causes should be analysed and corrective measures should be taken.</i></p>
Transferred out	<p>This is the proportion of cases who have been transferred to another district (or to another province) during the course of treatment, out of the total number of cases registered for treatment, and whose results of treatment are unknown.</p> <p><i>Where results are obtained from the center where the patient continued treatment, these results should be entered for the patient instead of “transferred out”.</i></p>

Indicators of treatment outcome are useful to guide implementation and identify problems to be solved. Targets should be action-oriented, thus emphasis should be placed particularly on the proportion of cases who have defaulted or been transferred out.

The cohort analyses are sent to the intermediate and national levels, thus allowing the NTP to be analysed by basic management unit, intermediate level and for the whole country, for surveillance purposes and to improve the program. This analysis should aid, for example, in making the decision to improve patient management: closer supervision of certain basic units, creation of new treatment centers, and retraining of health staff. Cohort analysis performed on a regular basis allows the progress of the NTP to be measured over time.