4. Diagnosis and Laboratories

Introduction

There are three components relating to diagnosis and laboratories:

- Functional network of quality laboratory services
- Health facility staff with an appropriate clinical suspicion for TB among their patients
- Use of laboratory services by clinicians and accurate diagnosis and classification of TB cases, especially of those cases that are not smear positive.

Laboratory Services

Laboratory services should be the cornerstone of a TB control program. They are clearly identified as one of the elements of the DOTS strategy, yet the public health laboratory network has traditionally been a neglected component in TB control activities, and this network remains one of the weakest links in many NTPs.

Any discussion or assessment of the laboratory's role in TB control should go beyond the technical aspect of performing smears. The following aspects should be considered:

- To what extent is the national laboratory a part of the NTP, and what is its role in decision-making regarding laboratory issues?
- Does the national reference laboratory belong to a supranational reference laboratory for culture examination and drug susceptibility testing?
- Has a needs assessment for laboratory services been conducted, examining human and capital resources?
- Is there a strategic plan for laboratory improvement, including a budget that considers the needs identified?
- Is there a national smear microscopy laboratory manual?
- Are standard operating procedures (including biosafety procedures) distributed and in use by all diagnostic units?
- Have internal and external quality assurance programs been implemented?
- Is there a plan for maintenance of laboratory equipment?

- Has a program for supervision of peripheral and intermediate laboratories been implemented?
- Have all aspects of training in smear microscopy been addressed (both initial training and retraining in the case of substandard performance)?
- Do smear microscopy services adequately "cover" the population?
- Are culture examination and drug susceptibility testing available at the appropriate level?

Internationally accepted indicators have not yet been developed for many aspects of laboratory performance. This is due in part to the difficulty of assessing quality, the overlap in jurisdiction of "laboratory issues" within MOH, and the fact that many aspects of "diagnosis" are beyond the control of the laboratory. For instance, failure to obtain a sufficient number of smears from a TB suspect may relate to the patient's behavior and the ability of the health facility staff to explain the importance of the examination or the timeliness of the logistical system that transports specimens, smears, or smear results between health centers and microscopic centers. Nonetheless, a few standard indicators related to laboratory function are presented in this section.

Within the domain of laboratory services, direct examination of sputum for *M. tuberculosis* remains the key test for diagnosis of pulmonary TB. The Ziehl-Neelsen technique for staining acid-fast bacilli (AFB) has remained the method of choice for TB diagnosis for many decades. The technique is fast, has high specificity in high-prevalence countries, and enables the immediate identification of those patients who are most infectious and usually most ill. Moreover, microscopy is also the cheapest and most simple technique, applicable to the most difficult environments. The technique for examination of AFB by fluorescence microscopy (FM) on the basis of auramine staining can be used as well. FM is widely used in industrialized countries and has been introduced in developing countries in laboratories with workloads of more than 50 slide examinations per day.

Optimal performance in smear microscopy requires good laboratory practices (GLP). GLP involves proper smearing, staining, and reading techniques, and it is contingent on good equipment and reagents and a safe laboratory environment. Smearing, staining, and reading practices can be maintained and improved through training of laboratory technicians, plus regular supervision. For further improvements of the reliability and efficiency of the lab technicians' work, a quality assurance program is required, involving both internal activities (rechecking of slides and proficiency testing) and periodic external reviews.

It is not enough that individual laboratories work well; a comprehensive network is crucial for good TB control. A network links health facilities to microscopic units in such a way that people (or sputum samples or slides, depending on how the network is designed) are moved quickly and conveniently to obtain the diagnosis. In poorly functioning networks, the delay between obtaining a sputum smear and transmitting the smear examination results back to the health facility may lead to the loss of follow-up of suspects who are not aware of their diagnosis.

Clinical Suspicion (Case-Finding Effort)

To diagnose pulmonary TB among symptomatic people presenting themselves to health facilities, clinicians must be mindful of TB as a possible diagnosis, and they must be able to recognize a TB "suspect" (someone with pulmonary symptoms, including prolonged cough). Then they must think to order the appropriate examinations (i.e., sputum smear examination with or without chest radiograph). The volume of TB suspects examined over time and the proportion of suspects who are found to be smear positive provide evidence that health facilities are making an effort in terms of case-finding. Another measure of case-finding effort and appropriate use of sputum smear microscopy to diagnose TB cases is the proportion of diagnostic smears to suspects examined. These two indicators are presented in this section.

Diagnostic Performance

Another aspect of diagnosis is the work-up of smear-negative and extrapulmonary cases. It is relatively easy for health facility staff with a low level of medical training to diagnose smear-positive pulmonary TB cases; however, diagnosis of smear-negative and extrapulmonary TB cases may involve considerable expertise in reading chest radiographs and eliminating alternative diagnoses. One indicator in this section deals with the diagnosis of smear-negative pulmonary TB cases.

Indicators

- Existence of comprehensive laboratory network
- TB microscopy coverage
- TB microscopy units with adequate workloads
- TB microscopy units submitting slides for rechecking
- TB suspects who are smear positive
- Smear-negative cases properly diagnosed
- Detected smear-positive cases registered for treatment (inverse of primary default rate)

Resources

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Laboratory services in tuberculosis control. Part I: organization and management. Geneva, World Health Organization, 1998 (WHO/TB/98.258).

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Indicator 4.1

EXISTENCE OF COMPREHENSIVE LABORATORY NETWORK

Definition

The existence of a comprehensive laboratory network, organized according to three levels: peripheral (often called "district"), intermediate (often called "regional"), and central (often called "national"). This is a yes/no indicator.

What It Measures

This indicator measures the capacity of the TB control program to accurately diagnose and monitor TB patients at all levels of the public health service delivery system and perform other higher level laboratory functions, such as mycobacterial drug resistance surveillance.

How to Measure It

This indicator is measured by an assessment of at least one laboratory at each level to determine the existence of the following minimum components of a comprehensive laboratory network:

- Peripheral laboratories are capable of performing sputum smear microscopy.
- Intermediate laboratories are capable of providing supervision, monitoring, training, and quality assurance to peripheral laboratories as well as performing sputum smear microscopy and culture examination.
- Central laboratories are capable of performing sputum smear microscopy, culture examination, and drug susceptibility testing. Also, the central level must be capable of providing training, performing quality assurance and proficiency testing, and conducting drug resistance surveillance among new and previously treated cases.

These three levels must also be connected through the following:

- Referral and communication mechanisms
- An established system of supervision.

Data Sources

- TB laboratory register and forms

Frequency & Function

This indicator should be measured annually until established.

Strengths & Limitations

The existence of a laboratory network is not a guarantee of adequate performance, because low quality may persist at any level.

Indicator 4.2

TB MICROSCOPY COVERAGE

Definition 1

Percentage of all TB microscopy units that cover a population size within the recommended range of 50,000 to 150,000 inhabitants.

$$\frac{\text{Number of TB microscopy units that cover a population of a size within a recommended range}}{\text{Total number of TB microscopy units}} \times 100$$

Definition 2

Average population per TB microscopy unit.

$$\frac{\text{Total population}}{\text{Total number of TB microscopy units}} \times 100{,}000$$

What It Measures

There are two measures of TB microscopy assessing the adequacy of population coverage by TMUs. The population covered by a TMU should neither be too large, since this could result in poor diagnostic quality owing to work overload of laboratory staff, nor too low, since this could result in poor diagnostic quality owing to a lack of routine use of the necessary skills. The recommended population size per microscopy unit is between 50,000 and 150,000. In most settings, this size results in workloads within the recommended rage of 2 to 20 smears per day. The recommended range of population sizes is relatively large because of the variation of geographical settings within a country. For example, a smaller population per unit may be acceptable in rural areas with low population density. On the other hand, in urban areas, with a higher population density, the population per unit may be relatively large. Additionally, the interpretation of this indicator depends greatly on the underlying prevalence of TB.

How to Measure It

1. The number of inhabitants that each microscopy unit serves is needed. This information should be available at the microscopy unit or MOH. If this number falls within the recommended range (50,000 to 150,000), the microscopy unit is counted in the numerator. The total number of microscopy units for which this information is available is the denominator.

2. The numerator is available from the most recent census data. The denominator is available from the NTP.

Data Sources

- Census statistics
- NTP records
- MOH records

Frequency & Function

This indicator should be measured annually for planning purposes.

Strengths & Limitations

Overlap in coverage area between central and peripheral sites may obscure measurement of this indicator. For example, the population coverage for a microscopy unit at a hospital may be reported as relatively large, but the actual population coverage may be lower if additional units at peripheral levels (e.g., health centers) exist. Therefore, it is necessary to be comprehensive in the determination of the actual number of TMUs for a given population. The second calculation to measure TB microscopy coverage is a crude number. It does not consider urban or rural population differences unless the total population and the number of units can be disaggregated into urban and rural groups.

Indicator 4.3

TB MICROSCOPY UNITS WITH ADEQUATE WORKLOADS

Definition

Percentage of all TB microscopy units with an average daily staff workload within a recommended range (2 to 20 slides per day per microscopist).

$$\frac{\text{Number of TMUs with an average daily staff workload within a recommended range}}{\text{Total number of TMUs for which data are available}} \times 100$$

What It Measures

This indicator assesses the appropriateness of workloads for laboratory staff. The number of patients should neither be too large, since this could result in poor diagnostic quality owing to work overload of laboratory staff, nor too low, since this could result in poor diagnostic quality owing to a lack of routine use of the necessary skills. The recommended workload for one laboratory technician to be able to ensure adequate quality is between 2 and 20 slides per day (a day being equal to 8 hours) with a light microscope (minimum of 10 slides per week and maximum of 20 per microscopist per day on average).

The recommended range for an acceptable workload is relatively large because of differences in population densities (Indicator 4.2). In rural areas with a low population density, a minimum number of laboratories may be required to ensure access to diagnostic facilities, even if the average number of slides examined becomes relatively low. It should nevertheless not be fewer than two slides per day on average. The workload per laboratory staff member should not exceed 20 slides per day with a light microscope. More than one microscopist may use one microscope (the limitation is on staff reading of slides). Fluorescent microscopy should be considered when the workload exceeds 50 slides per day.

How to Measure It

Information on laboratory staff workloads can be obtained from laboratory registers (in units using light microscopes) by counting the number of slides examined per microscopist per day. This information should be used to determine the number of laboratories that have a staff workload within the recommended range. This is the

numerator. The total number of TB microscopy laboratories for which information is available is the denominator.

Data Source

- TB laboratory register

Frequency & Function

This indicator should be measured annually for planning purposes at the facility, district, regional, and central levels.

Strengths & Limitations

The value of this indicator will be low if staff workloads are outside the recommended range, either above or below. The reasons for an unacceptably high workload include an inadequate number of TMUs or laboratory technicians for a given population, or overly suspicious primary health care workers. The reasons for an unacceptably low workload include having too many TB microscopy laboratories or laboratory technicians, or low levels of cases declared suspicious by providers. Additionally, the value must be interpreted in the context of the numerous activities, not all TB related, that a laboratory technician performs on a daily basis.

Indicator 4.4

TB MICROSCOPY UNITS SUBMITTING SLIDES FOR RECHECKING

Definition

Percentage of all TB microscopy units for which slide rechecking results, one component of a quality assurance (QA) system, are available.

$$\frac{\text{Number of TB microscopy units for which slide rechecking results are available during a specified period}}{\text{Total number of units performing TB smear microscopy during the same period}} \times 100$$

What It Measures

This indicator measures the existence of one critical component of a QA system, which is defined as a system designed to continuously improve the reliability, efficiency, and use of TB laboratory services. NTPs should have a QA system that covers all TB laboratories in the country. A low proportion of TMUs with QA results indicates the need for further development of the laboratory QA system.

How to Measure It

The presence of slide rechecking results should be verified at the laboratory. Most laboratories keep records of the slides that were sent for rechecking and the results that were sent back to them from the regional or central levels. The number of laboratories that have slide rechecking results available is the numerator. The total number of TB microscopy units in the respective areas assessed is the denominator.

Data Sources

- Laboratory records containing QA results

Frequency & Function

Since QA is a routine function of the laboratory network, this indicator can be measured quarterly or annually during monitoring visits.

Strengths & Limitations

This indicator is a proxy for measuring the existence of a complete QA system for laboratory control, as described above. Rechecking of slides is a fairly quick and easy measure to demonstrate that some aspect of quality control is being implemented at the laboratories. This indicator does not measure the quality of smear microscopy at the laboratories; it simply measures whether quality checks are being done.

Indicator 4.5

TB SUSPECTS WHO ARE SMEAR POSITIVE

Definition

Percentage of TB suspects who are found to be smear positive.

$$\frac{\text{Number of TB suspects found to be smear positive during a specified period}}{\text{Number of TB suspects identified clinically during the same period}} \times 100$$

This indicator is also known as the suspect positivity rate.

What It Measures

This indicator measures case detection effort among health staff. Increased case detection effort should lead to increased case detection (Indicator 1.1). The target for this indicator should be around 10%: A value higher than 10% may indicate that clinicians are not well aware of TB symptoms and only send those patients at advanced stages of TB for sputum examination. When X-rays are used as a filter to select patients who should have a sputum smear examination, positivity rates are expected to be higher than 10%. A value less than 10% may indicate that the clinicians are referring too many "suspects" for sputum smear examination, and laboratory services can be overburdened with unnecessary negative examinations, which could compromise the quality of their work.

How to Measure It

The numerator and denominator can be obtained from the TB laboratory register or a "cough register" maintained at the treatment facility. This register lists all TB suspects who have been referred for chest X-ray and/or sputum smear examinations. In this case, each facility—and the district as a whole—can calculate the indicator.

In addition, the health facility can monitor the number of suspects identified per patient population (e.g., per outpatient visits), and the district as a whole can monitor the number of suspects identified per population.

Data Sources

- TB laboratory register or cough registers

Frequency & Function

The indicator should be calculated on a quarterly and annual basis.

Strengths & Limitations

Although this is an indicator of effort among health facility staff at the point where the patient presents through passive case-finding, referral patterns in the community will affect the results. For instance, in a community where private practitioners are skilled at recognizing TB (perhaps with the use of X-ray examination), but refer the patient to public health facilities for sputum examination and possible treatment, the proportion suspects with TB will be high. Similarly, the care-seeking behavior in the community may affect the results. For instance, if care is typically deferred for as long as possible, then many patients qualifying as "suspects" may have a history of cough in excess of 3 weeks, raising the likelihood that TB is the cause of the cough.

A low proportion of suspects may have been classified as smear positive because of poor laboratory function (poor sensitivity in preparing and reading slides from those who are truly smear positive). Although this indicator is useful at an operational level, there are some difficulties in looking at aggregated results at a higher level.

Indicator 4.6

SMEAR-NEGATIVE CASES PROPERLY DIAGNOSED

Definition

Percentage of all adult smear-negative pulmonary TB cases diagnosed with three smears and chest radiograph according to NTP-recommended diagnostic algorithm.

$$\frac{\text{Number of adult smear-negative pulmonary TB cases diagnosed with at least three negative smears and chest radiograph according to NTP-recommended algorithm during a specified time period}}{\text{Total number of adult pulmonary smear-negative cases diagnosed during the same period}} \times 100$$

What It Measures

The indicator assesses the adequacy of diagnosis for smear-negative cases. If diagnostic algorithms are not strictly followed, too many smear-negative TB cases are treated, which results in an unnecessary burden on the NTP and the general health system. A low value points to the need for intensified training and supervision of staff in order to encourage use of the recommended algorithm for diagnosing smear-negative TB.

How to Measure It

Measurement of this indicator requires a review of patient treatment cards for adult smear-negative cases registered during the specified time period with a checklist of components for the NTP-recommended algorithm. The numerator is the number of adult smear-negative cases with evidence of three smears and chest radiograph according to the NTP-recommended algorithm for diagnosing smear-negative TB. The denominator is the total number of adult smear-negative cases registered during the period, according to the laboratory register.

Data Sources

- NTP diagnostic algorithm for smear-negative TB
- TB laboratory register
- TB treatment cards

Frequency & Function

This indicator should be measured annually at the facility level during monitoring visits.

Strengths & Limitations

The determination of this indicator is dependent on the accuracy of information obtained by adhering to the NTP-recommended algorithm for diagnosing smear-negative TB. This indicator is complementary to Indicator 2.4. If the percentage of adult smear-positive cases is less than 50%, then this indicator will help to explain whether the smear-negative cases have been correctly diagnosed.

Indicator 4.7

DETECTED SMEAR-POSITIVE CASES REGISTERED FOR TREATMENT (INVERSE OF PRIMARY DEFAULT RATE)

Definition

Percentage of all detected smear-positive pulmonary TB cases that have initiated treatment.

$$\frac{\text{Number of new smear-positive pulmonary TB cases that have initiated treatment during a specified time period}}{\text{Total number of new smear-positive cases detected during the same period}} \times 100$$

What It Measures

This indicator measures whether or not patients identified by the laboratory as having smear-positive pulmonary TB actually initiate treatment. This indicator is important because it is a proxy for determining 1) whether information flows from the laboratories to treatment facilities, 2) whether a mechanism exists for tracing and informing patients if they do not return to the facility to receive their results, and 3) whether there are adequate resources (e.g., drugs, trained staff) to start treatment. A high proportion of diagnosed patients who are not started on treatment indicates organizational problems, resulting in a risk of death to the diagnosed patient and further transmission to the general population.

How to Measure It

The numerator is the total number of new smear-positive pulmonary TB cases in the TB register during a specified period that have initiated treatment. The number of all smear-positive cases diagnosed (from the laboratory register) in the same period is the denominator. Diagnosed cases properly referred for treatment in another district should not be included in the denominator.

Data Sources

- TB laboratory register
- TB register

Frequency & Function

The indicator should be reported quarterly and annually for facilities, for basic management units (district), and as a summary statistic for regions and the national level.

Strengths & Limitations

Patients lacking documentation of treatment initiation may have started treatment in another district or in a private facility, and the facility that originally diagnosed the patient may not have received or recorded information regarding the referral or transfer.