FRAMEWORK OF INDICATORS AND TARGETS FOR LABORATORY STRENGTHENING UNDER THE END TB STRATEGY

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Abbreviations

BMU	basic management unit
DR-TB	drug-resistant TB
DST	drug-susceptibility testing
EQA	external quality assessment
HIV	human immunodeficiency virus
LPA	line probe assay
MDR-TB	multidrug-resistant TB
POC	point of care
RR-TB	rifampicin-resistant TB
TB	tuberculosis
WHO	World Health Organization
WRD	WHO-recommended rapid diagnostic

Introduction

Background

The World Health Organization's (WHO's) End TB Strategy calls for the early diagnosis of tuberculosis (TB) including universal drug-susceptibility testing (DST). A prerequisite for any national TB programme to reach this goal is a quality-assured laboratory network equipped with rapid diagnostics. This *Framework of indicators and targets for laboratory strengthening under the End TB Strategy* serves as a guide for all countries developing plans for laboratory strengthening during 2016–2025. The indicators measure programmes' capacity to detect TB accurately and rapidly using new diagnostics (known as WHO-recommended rapid diagnostics, or WRDs),[1] provide universal DST,[2] and ensure the quality of testing. The 12 core indicators will be monitored globally by WHO as countries progress towards reaching the targets; additional stratified indicators are also included for monitoring at the country level when recording and reporting systems allow. This framework of indicators complements WHO's frameworks of indicators for collaborative TB and HIV activities,[3] for activities targeting latent TB infection (which is being finalized), and the top 10 priority indicators for monitoring the End TB Strategy.[4]

Sources of data required

Calculating indicators related to TB detection and DST coverage requires data on notified TB cases recorded in the basic management unit (BMU) TB register, not from laboratory registers.[5] In countries that have not yet adopted electronic TB registers, the data needed for these indicators may require periodic surveys of BMU TB registers from a nationally representative sample of patients; altering paper-based BMU quarterly reporting forms is not recommended. The data required to calculate the indicators related to the quality of testing will come from quality assurance reports from the laboratory network.

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[1] WRDs employ molecular techniques to detect TB.

[2] In 2016, universal access to DST is defined as providing DST for at least rifampicin for all patients with bacteriologically confirmed TB and providing further DST for at least fluoroquinolones and second-line injectable agents for all TB patients with rifampicin-resistant TB. DST methods include genotypic (molecular) and phenotypic methods.

[3] A guide to monitoring and evaluation for collaborative TB/HIV activities: 2015 revision. Geneva: World Health Organization; 2015 (WHO/HTM/TB/2015.02, WHO/HIV/2015.1; http://www.who.int/tb/publications/monitoring-evaluation-collaborative-tb-hiv/en/, accessed 1 October 2016).

[4] Implementing the End TB Strategy: the essentials. Geneva: World Health Organization; 2015 (WHO/HTM/TB/2015.31; http://www.who.int/tb/publications/2015/The_Essentials_to_End_TB/en/, accessed 1 October 2016).

[5] Definitions and reporting framework for tuberculosis: 2013 revision. Geneva: World Health Organization; 2013 (WHO/HTM/TB/2013.2; http://www.who.int/tb/publications/definitions/en/, accessed 1 October 2016). See Section B.3.2, pp. 13–18.

Calculating country capacity for diagnostic testing

A country's capacity for diagnostic testing was previously monitored using indicators and global targets that described the number of microscopy centres per 100 000 population and the number of culture and DST laboratories per 5 million population. These global targets are no longer used, given advances in diagnostic technologies and the need for country-specific targets that consider epidemiology and issues of patient access (such as urban versus rural populations, and specimen referral systems). A recommended methodology for calculating country-specific targets for the numbers of tests and facilities for each of the main diagnostic technologies – microscopy, WRDs (including the Xpert® MTB/RIF assay [Cepheid, Sunnyvale, CA, United States]), culture and DST – is provided in Annex 1.

Indicators for laboratory strengthening under the End TB Strategy

Objective 1. Increase access to rapid and accurate detection of TB

Indicator 1.	Does the national diagnostic algorithm indicate a WRD[a] is the initial diagnostic test for all people with signs and symptoms of TB?
Indicator 2.	Percentage of notified new and relapse TB cases tested with a WRD as the initial diagnostic test
Indicator 3.	Percentage of notified new and relapse TB cases with bacteriological confirmation[b]
Indicator 4.	Percentage of testing sites using a WRD at which a data connectivity system has been established that transmits results electronically to clinicians and to an information management system
Indicator 5.	Does national policy indicate that TB diagnostic and follow-up tests provided through the national TB programme are free of charge or that fees can be fully reimbursed through health insurance, or both, for all people with signs and symptoms of TB?

Objective 2. Reach universal access to DST[c]

Indicator 6.	Does national policy and the diagnostic algorithm indicate there is universal access to DST?
Indicator 7.	Percentage of notified, bacteriologically confirmed TB cases with DST results for rifampicin
Indicator 8.	Percentage of notified, rifampicin-resistant TB cases with DST results for fluoroquinolones and second-line injectable agents

Objective 3. Strengthen the quality of laboratory services

Indicator 9.	Percentage of diagnostic testing sites that monitor performance indicators and are enrolled in an EQA system for all diagnostic methods performed
Indicator 10.	Percentage of DST sites that have demonstrated proficiency by EQA panel testing for all DST methods performed
Indicator 11.	Percentage of laboratories conducting culture, line probe assay or phenotypic DST, or a combination of these, in which a formal quality management system is being implemented that aims to achieve accreditation according to international standards
Indicator 12.	Is the National Reference Laboratory accredited according to the ISO15189:2012[d,e] standard?

DST: drug-susceptibility testing; EQA: external quality assessment; LPA: line probe assay; WRD: WHO-recommended rapid diagnostic.

[a] WRDs use molecular techniques to detect TB.

[b] A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or a WRD.

[c] In 2016, universal access to DST is defined as providing DST for at least rifampicin for all patients with bacteriologically confirmed TB and providing further DST for at least fluoroquinolones and second-line injectable agents for all TB patients with rifampicin-resistant TB. DST methods include genotypic (molecular) and phenotypic methods.

[d] ISO 15189:2012. Medical laboratories: requirements for quality and competence. Geneva: International Organization for Standardization; 2012 (https://www.iso.org/obp/ui/#iso:std:iso:15189:ed-3:v2:en, accessed 1 October 2016).

[e] Accreditation should comply with the most recent version of the ISO15189 standard.

Detailed description of indicator framework: targets, indicator calculations and remarks

Objective 1. Increase access to rapid and accurate detection of TB

Indicator 1.	**Does the national diagnostic algorithm indicate a WRD is the initial diagnostic test for all people with signs and symptoms of TB?**
Target 2020	Yes, for all countries *Note:* The target should be reached by 2018 for countries with high burdens of TB and HIV, and MDR-TB.
Remarks	• Assumption: By 2017, a new POC rapid diagnostic with sensitivity similar to that of liquid culture will be recommended by WHO as the initial diagnostic test for all people with signs and symptoms of TB.

Indicator 2.	**Percentage of notified new and relapse TB cases tested with a WRD as the initial diagnostic test**
Target 2020	80% of cases
Target 2025	100% of cases
Numerator	Number of notified new and relapse TB cases tested with a WRD as the initial diagnostic test
Denominator	Number of notified new and relapse TB cases
Remarks	• WRD test results may be positive or negative. • Assumption: By 2017, a new POC rapid diagnostic with sensitivity similar to that of liquid culture will be recommended by WHO as the initial diagnostic test for all people with signs and symptoms of TB. • WHO will monitor this indicator in low- and middle-income countries. • Where electronic registers or periodic surveys allow stratification, national-level monitoring of this indicator should be stratified by patient risk group: a target of 100% should be reached by the end of 2018 for people living with HIV and people at risk of DR-TB. • As additional proxy indicators for patients' access to WRD testing, some countries may wish to monitor the percentage of districts or basic management units with WRDs, or the percentage of eligible specimens being referred for testing at sites that have WRDs. • This indicator is also included as one of the top 10 priority indicators for monitoring the implementation of the End TB Strategy.[a]

Indicator 3.	Percentage of notified new and relapse TB cases with bacteriological confirmation[b]
Target 2020	80% of cases (relapse cases: 90%)
Target 2025	90% of cases (relapse cases: 95%)
Numerator	Number of notified new and relapse TB cases with bacteriological confirmation
Denominator	Number of notified new and relapse TB cases
Remarks	• Assumption: By 2017, a new POC rapid diagnostic with sensitivity similar to that of liquid culture will be recommended by WHO as the initial diagnostic test for all people with signs and symptoms of TB. • Where electronic registers or periodic surveys allow stratification, national-level monitoring of this indicator should be stratified by site of disease (pulmonary versus extrapulmonary), by age group (children versus adult), and by HIV status, given the challenges of obtaining bacteriological confirmation using available sputum-based tests among people living with HIV and children, and the challenges of collecting specimens for detecting extrapulmonary TB. • The indicator's targets will be reviewed and refined based on the performance characteristics of technologies that are available and in the pipeline.

Indicator 4.	Percentage of testing sites using a WRD at which a data connectivity system has been established that transmits results electronically to clinicians and to an information management system
Target 2020	100% of sites
Numerator	Number of testing sites using a WRD at which a data connectivity system has been established that transmits results electronically to clinicians and to an information management system
Denominator	Number of testing sites using a WRD
Remarks	• Electronic data connectivity solutions are able to rapidly make test results available to clinicians and information management systems (including a laboratory information management system or an electronic register, or both) via the Internet, mobile data networks or text messaging (SMS).

Indicator 5.	Does national policy indicate that TB diagnostic and follow-up tests provided through the national TB programme are free of charge or that fees can be fully reimbursed through health insurance, or both, for all people with signs and symptoms of TB?
Target 2020	Yes, for all countries *Note:* The target should be reached by 2018 for countries with a high burden of TB.
Remarks	• Monitoring of this indicator may be cross-checked by data captured in patient cost surveys, when data are not subject to significant patient recall bias.

DR-TB: drug-resistant TB; MDR-TB: multidrug-resistant TB; POC: point of care; SMS: short messaging service; WRD: WHO-recommended rapid diagnostic.

[a] Implementing the End TB Strategy: the essentials. Geneva: World Health Organization; 2015 (WHO/HTM/TB/2015.31; http://www.who.int/tb/publications/2015/The_Essentials_to_End_TB/en/, accessed 1 October 2016).

[b] A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or a WRD.

Objective 2. Reach universal access to DST

Indicator 6.	**Does national policy and the diagnostic algorithm indicate there is universal access to DST?**
Target 2020	Yes, for all countries *Note:* The target should be reached by 2018 for countries with a high burden of MDR-TB.
Remarks	• In 2016, universal access to DST is defined as providing DST for at least rifampicin for all patients with bacteriologically confirmed TB and providing further DST for at least fluoroquinolones and second-line injectable agents for all TB patients with RR-TB. • DST methods include genotypic (molecular) and phenotypic methods.

Indicator 7.	**Percentage of notified, bacteriologically confirmed TB cases with DST results for rifampicin**
Target 2020	100% of cases *Note:* The target should be reached by 2018 for countries with a high burden of MDR-TB.
Numerator	Number of notified, bacteriologically confirmed TB cases with DST results for rifampicin
Denominator	Number of notified, bacteriologically confirmed TB cases
Remarks	• Monitoring of this indicator by WHO will be stratified by new versus history of previous treatment: a target of 100% should be reached in all countries by the end of 2018 for people with previous treatment. • Where electronic registers or periodic surveys allow stratification by method of DST testing, the percentage of bacteriologically confirmed TB cases with DST results for rifampicin **using a molecular method as the initial drug-susceptibility test** should be monitored at the national level. By 2020, the initial method should use a molecular (genotypic) technology (which currently includes the Xpert MTB/RIF assay, LPAs or sequencing) for all tested cases (Target 2020: 100% of cases). • In settings with a high frequency of isoniazid resistance, countries may also wish to monitor the percentage of notified, bacteriologically confirmed TB cases with DST results for isoniazid. • This indicator is also included as one of the top 10 priority indicators for monitoring implementation of the End TB Strategy.[a]

Indicator 8.	**Percentage of notified, rifampicin-resistant TB cases with DST results for fluoroquinolones and second-line injectable agents**
Target 2020	100% of cases
Numerator	Number of notified RR-TB cases with DST results for fluoroquinolones and second-line injectable agents
Denominator	Number of notified RR-TB cases
Remarks	• Second-line anti-TB agents to be tested include fluoroquinolones and second-line injectable agents, as specified by national guidance. Anti-TB agents tested are subject to change in line with future WHO recommendations on DST and treatment regimens. DST results include those from molecular methods (for example, LPAs) or liquid culture methods.

DST: drug-susceptibility testing; LPA: line probe assay; MDR-TB: multidrug-resistant TB; RR-TB: rifampicin-resistant TB.

[a] Implementing the End TB Strategy: the essentials. Geneva: World Health Organization; 2015 (WHO/HTM/TB/2015.31; http://www.who.int/tb/publications/2015/The_Essentials_to_End_TB/en/, accessed 1 October 2016).

Objective 3. Strengthen the quality of laboratory services

Indicator 9.	**Percentage of diagnostic testing sites that monitor performance indicators and are enrolled in an EQA system for all diagnostic methods performed[a]**
Target 2020	100% of sites
Numerator	Number of diagnostic testing sites (stratified by type of diagnostic testing) that monitor performance indicators and are enrolled in an EQA system for all diagnostic methods performed, as defined in remarks below
Denominator	Number of testing sites (stratified by type of diagnostic testing)
Remarks	• Monitoring of this indicator should be stratified by the type of diagnostic testing: microscopy, WRD (including the Xpert MTB/RIF assay), LPA, culture or phenotypic DST. • For WRDs, key performance indicators should be monitored at least monthly and remote monitoring should be used via a data connectivity solution. • EQA should include regular supervision visits and panel testing (or slide rechecking, in the case of microscopy), according to the national system.

Indicator 10.	**Percentage of DST sites that have demonstrated proficiency by EQA panel testing for all DST methods performed**
Target 2020	100%
Numerator	Number of DST sites that have demonstrated proficiency by EQA panel testing, as defined in remarks below
Denominator	Number of DST sites
Remarks	• Monitoring of this indicator should be stratified by first-line and second-line DST. • DST includes phenotypic and molecular methods. • Panel testing should be conducted at least annually. • Demonstrated proficiency is defined as a site achieving satisfactory results, per the EQA programme's predetermined criteria, on the most recent panel tested.

Indicator 11.	**Percentage of laboratories conducting culture, LPA or phenotypic DST, or a combination of these, in which a formal quality management system is being implemented that aims to achieve accreditation according to international standards**
Target 2020	50% of laboratories
Target 2025	100% of laboratories
Numerator	Number of laboratories conducting culture, LPA or phenotypic DST, or a combination of these, in which a formal quality management system is being implemented that aims to achieve accreditation according to international standards
Denominator	Number of laboratories conducting culture, LPA or phenotypic DST, or a combination of these
Remarks	• Evidence that laboratories have established a formal quality management system include conducting a baseline assessment of the laboratory's quality management system using a recognized checklist based on ISO 15189:2012, developing an action plan for quality improvements and starting to implement recommendations. The checklist should specify requirements for quality and competency aimed at developing and improving TB laboratory services to raise the quality to ISO standard 15189:2012.[b,c]

Indicator 12.	Is the National Reference Laboratory accredited according to the ISO15189:2012[b,c] standard?
Target 2020	Yes, for all countries with a high TB burden
Target 2025	Yes, for all countries

DST: drug-susceptibility testing; EQA: external quality assessment; LPA: line probe assay; WRD: WHO-recommended rapid diagnostic.

[a] Guide for providing technical support to TB laboratories in low- and middle-income countries. Geneva: Global Laboratory Initiative, Stop TB Partnership; 2015(http://stoptb.org/wg/gli/assets/documents/guideforprovidingtechnicalsupport_gb_web.pdf, accessed 1 October 2016). See Section 2.3.2h. Quality indicator monitoring.

[b] ISO 15189:2012. Medical laboratories: requirements for quality and competence. Geneva: International Organization for Standardization; 2012 (https://www.iso.org/obp/ui/#iso:std:iso:15189:ed-3:v2:en, accessed 1 October 2016).

[c] Accreditation should comply with the most recent version of the ISO15189 standard.

Annex 1. Recommended methodology for calculating country-specific targets

Recommended methodology for calculating country-specific targets for microscopy, WRDs (including the Xpert MTB/RIF assay), culture and capacity for DST: 2016–2020

Notes:

Assumptions **in red** may be modified by countries based on their actual data or algorithms. The proposed methods do not consider the possible future use of biomarkers for screening for TB.

An Excel worksheet for calculating these targets is available at http://www.who.int/tb/publications/labindicators.

Numbers in the calculations of the examples have been rounded to the nearest thousand.

Microscopy

In line with the objective of increasing patients' access to rapid and accurate WRDs, all countries should aim to phase out microscopy as an initial diagnostic test by no later than 2025. Currently, microscopy is needed in all countries for monitoring TB patients' responses to treatment.

Calculations for planning the numbers of smear examinations and microscopy facilities by 2020 (to be phased in during 2016–2020)

Assumptions

In 2020, **20%** of previously untreated HIV-negative adults with signs and symptoms of TB will receive microscopy as the initial diagnostic test (2 smears per person), and all drug-susceptible TB cases will receive follow-up smears for treatment monitoring (**3** visits [at months 2, 5 and 6], with **2** smears per visit). The smear-positivity rate will remain **10%** (1 smear-positive case for each 10 people with signs and symptoms of TB).

Sum of smear examinations in 2020 = $a + b$

a. Annual number of diagnostic smears in 2020 = **20%** of smear-positive, HIV-negative new adult cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms needed to be tested to find 1 case) x **2** smears per visit.

b. Annual number of follow-up smears for treatment monitoring in 2020 = number of pulmonary TB cases x **3** visits x **2** smears per visit.

Target number of microscopy facilities in 2020

Countries should not invest in establishing additional microscopy facilities. Countries that have positioned a WRD as the initial diagnostic test for all people with signs and symptoms of TB and that have established reliable WRD supply systems and specimen referral systems,

may create referral hubs for microscopy for treatment monitoring. Existing microscopy facilities may be upgraded with light-emitting diode (or LED) microscopy technology to improve their effectiveness and the efficiency of testing.

Xpert MTB/RIF assay (or future analogous replacement technologies)

In line with the objectives of increasing patients' access to rapid and accurate WRDs and reaching universal DST for rifampicin resistance, countries should increase access to the Xpert MTB/RIF assay (or a future analogous replacement technology) as an initial diagnostic test and as a test for rifampicin resistance. Future technologies that separate TB detection from DST would require different calculations, depending on the target patient groups.

Calculations for planning the numbers of Xpert MTB/RIF tests and GeneXpert facilities by 2020 (to be phased in during 2016-2020)

Assumptions

in 2020, the Xpert MTB/RIF assay will be provided as the initial diagnostic test to **100%** of all people living with HIV who have signs and symptoms of TB, **100%** of children with signs and symptoms of TB, **100%** of all people at risk of having DR-TB, **80%** of previously untreated HIV-negative adults with signs and symptoms of TB, and **100%** of new TB cases as a test for drug-susceptibility.

Sum of Xpert MTB/RIF tests in 2020 = $a + b + c + d + e$

The annual number of Xpert MTB/RIF tests in 2020 will include:

a. People living with HIV who have signs and symptoms of TB = annual number of people living with HIV in care x % of people living with HIV in care who are clinically screened x average number of times that clinical screening is performed per person per year (**2** times) x % of persons clinically screened and found to have signs and symptoms of TB (**15%**) x % coverage of Xpert MTB/RIF testing (% of those with signs and symptoms of TB who will have access to Xpert MTB/RIF testing).

b. Children with signs and symptoms of TB = annual number of notified paediatric TB cases x **4** in settings with a high HIV prevalence (in settings with a high HIV prevalence, typically between 25% and 33% of all children with signs and symptoms of TB will be notified as a TB case, often on clinical or radiological evidence; this results in a factor of 3 or 4 needed to calculate the number of children needing to be tested in order to have 1 notified TB case) or x **6** in settings with a low HIV prevalence (in settings with a low HIV prevalence, a lower percentage of all children with signs and symptoms of TB will be diagnosed and notified as having TB; a factor of 6 means that of 6 children with signs and symptoms of TB, 1 will be notified as a TB case).

c. People at risk of having DR-TB = people with signs and symptoms of TB who have a history of successful treatment (**4** x relapses) + other people who have a history of treatment (previously treated cases – relapses) + contacts of RR-TB cases (**4** x number of RR-TB cases). In settings with a high frequency of MDR-TB, all people with signs and symptoms of TB and their contacts should be tested using the Xpert MTB/RIF assay as the initial diagnostic test.

d. Previously untreated HIV-negative adults with signs and symptoms of TB = **80%** of smear-positive new TB cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms of TB who need to be tested to find 1 case) x % of TB

patients that are HIV-negative x % of TB patients who are adults.

e. TB cases for DST purposes = **100%** x [new TB cases – (cases in groups *a* + *b* + *d* above, receiving the Xpert MTB/RIF assay as the initial diagnostic test)].

Target number of GeneXpert facilities in 2020

Those who are planning the required capacity for Xpert MTB/RIF testing and the procurement of additional GeneXpert machines must first consider existing machine throughput and the need for planned interventions to increase utilization, including improving clinicians' awareness, adopting broader diagnostic algorithms that cover more patient groups, and strengthening referral systems. The number of GeneXpert machines required to run a targeted number of tests should be calculated on a module basis, under the assumption that each module is expected to perform an average of **3** tests per working day (**12** tests per 4-module GeneXpert machine) x **240** working days per year. If working hours preclude a throughput of 720 tests/module per year (3 tests per module/day), then a throughput based on actual data should be used, and the target number of modules should be increased. Ideally, the number and placement of facilities should be calculated from the bottom-up: the number of cases per facility or per district would be used in the above algorithm to allow for a realistic expectation of coverage. GeneXpert machines may comprise 1, 2, 4, 16 or more modules, depending on the throughput needed in a facility. The continued maintenance of machines, including the use of extended warranties, is needed to reach the targeted throughput.

Culture and DST

Calculations for planning the numbers of culture and DST examinations and culture and DST facilities by 2020 (to be phased in during 2016-2020)

Assumptions

By 2020, WRDs with sensitivity similar to that of liquid culture, including for people living with HIV, should replace the need for culture as a diagnostic test. Culture will continue to be needed for culture-based DST and for monthly monitoring of treatment for patients with RR-TB. Rapid genotypic DST methods (including LPA) and phenotypic culture-based DST methods should be used based on the anti-TB agents used in national treatment algorithms.

Sum of culture and DST examinations should equal (*a* + *b*) x 1.1 to account for the additional 10% of examinations needed for quality control, control testing and repeat testing

The annual number of culture/DST examinations in 2020 will include:

a. Number of DST examinations at time of diagnosis = number of WRD-detected RR-TB cases.

b. Number of cultures for treatment monitoring of RR-TB cases = number of RR-TB cases enrolled on treatment x **18** (monthly culture for duration of treatment; to be adjusted if shorter regimens are used) x **1** culture per month.

Target number of culture and DST facilities in 2020

The required number of facilities for culture and DST should be calculated based on the average facility throughput by country and by the types of tests performed (an average facility may perform **10 000** examinations per year).

Example 1. Country in Africa with a high MDR-TB frequency and high HIV frequency

TB epidemiology: 2015

TYPE OF TB	NO. OF CASES
Pulmonary, bacteriologically confirmed	
New cases	24 500
Relapse cases	1 500
Pulmonary, clinically diagnosed	
New cases	23 500
Relapse cases	2 000
Extrapulmonary	
New cases	6 000
Relapse cases	500
Previously treated cases, excluding relapses	500
Total cases notified	58 500
No. (%) of TB cases among children	3 750 (6.5%)
% HIV-positive TB patients	52%
% HIV-negative TB patients	48%
HIV-positive people clinically screened for TB	550 000
Estimated % of TB cases with MDR-TB	
New cases	4.0%
Previously treated cases	15%
Laboratory-confirmed RR-TB including MDR-TB cases (estimated RR-TB including MDR-TB, among notified TB cases)	500 (2 500)

MDR-TB: multidrug-resistant TB; RR-TB: rifampicin-resistant TB.

Number of smear examinations: 2020

a. Annual number of diagnostic smears = **20%** of smear-positive, HIV-negative new adult cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms who need to be tested to find 1 case) x **2** smears per visit = **20%** x 24 500 bacteriologically confirmed new cases x 48% (% of patients who are HIV-negative) x 93.5% (6.5% of patients are children) x 10 x 2 smears per visit = 44 000 smear examinations.

b. Annual number of follow-up smears in 2020 = number of pulmonary TB cases x **3** visits x **2** smears per visit = 52 000 x 3 visits x 2 smears per visit = 310 000 smear examinations.

Sum: 354 000 smear examinations in 2020.

Number of Xpert MTB/RIF tests (or analogous replacement technology): 2020

a. People living with HIV who have signs and symptoms of TB = annual number of people living with HIV in care x % of people living with HIV who are clinically screened x average number of times that clinical screening is performed per year (**2** times) x % of persons screened and found to have signs and symptoms of TB x % coverage of Xpert MTB/RIF testing = 550 000 x **2** x **15%** x **100%** = 165 000.

b. Children with signs and symptoms of TB = notified paediatric TB cases x **4** in settings with a high HIV prevalence = 3 750 cases x **4** = 15 000.

c. People at risk of having DR-TB = people with signs and symptoms of TB who have a history of successful treatment (**4** x 4 000) + other people who have a history of treatment (previously treated cases – relapses = 500) + RR-TB contacts (500 in 2015, which is expected to increase to 2 500 in 2020 = 4 x 2 500) = 16 000 + 500 + 10 000 = 26 500.

d. **80%** of previously untreated HIV-negative adults with signs and symptoms of TB = **80%** of smear-positive new TB cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms who need to be tested to find 1 case) x % of HIV-negative TB patients x % of patients who are adults = **80%** x 24 500 x 10 x 48% x 93.5% = 88 000.

e. TB cases for DST purposes = new TB cases (54 000) – number of new TB cases that will have Xpert MTB/RIF testing as the initial diagnostic test (people living with HIV + children + 80% HIV-negative adult new cases) = (54 000 x 52%) + (54 000 x 6.5%) + (54 000 x 48% x 80% x 93.5%) = 54 000 – 51 000 = 3 000 x **100%** = 3 000.

Sum: 298 000 Xpert MTB/RIF tests in 2020.

Number of facilities with GeneXpert machines: 2020

So, 298 000 tests/**720** tests/module per year = 414 modules in 2020, which is divided among GeneXpert machines comprising various numbers of modules (for example, 1,2,4, or 16 modules). One or more GeneXpert machines may be placed at a facility, depending on specimen referral networks.

Number of culture examinations and drug-susceptibility tests: 2020

For DST, the number of RR-TB cases = 500 in 2015, which is expected to increase to 2 500 in 2020 = 2 500.

For culture for treatment monitoring of RR-TB cases: number of RR-TB cases enrolled on treatment x **18** (monthly culture for 18 months, with 1 tube per test) x **1** culture per month = 2 500 x 18 = 45 000.

An additional 10% of examinations is needed for quality control and repeat testing = 45 000 cultures x 1.1 and 2 500 drug-susceptibility tests x 1.1.

Sum: 50 000 cultures and 3 000 drug-susceptibility tests = 53 000 examinations in 2020.

Number of culture and DST facilities: 2020

For 53 000 examinations/**10 000** examinations per year = 5 culture and DST facilities.

Example 2. Country in Africa with a low MDR-TB frequency and high HIV frequency

TB epidemiology: 2015

TYPE OF TB	NO. OF CASES
Pulmonary, bacteriologically confirmed	
New cases	24 500
Relapse cases	800
Pulmonary, clinically diagnosed	
New cases	23 500
Relapse cases	1 000
Extrapulmonary	
New cases	6 000
Relapse cases	500
Previously treated cases, excluding relapses	500
Total cases notified	56 800
No. (%) of TB cases among children	3 700 (6.5%)
% HIV-positive TB patients	52%
% HIV-negative TB patients	48%
HIV-positive people clinically screened for TB	550 000
Estimated % of TB cases with MDR-TB	
New cases	1.0%
Previously treated cases	10%
Laboratory-confirmed RR-TB including MDR-TB cases (estimated RR-TB including MDR-TB, among notified TB cases)	200 (600)

MDR-TB: multidrug-resistant TB; RR-TB: rifampicin-resistant TB.

Number of smear examinations: 2020

a. Annual number of diagnostic smears = **20%** of smear-positive, HIV-negative new adult cases (or bacteriologically confirmed as a proxy) x **10** (number of people with signs and symptoms who need to be tested to find 1 case) x **2** smears per visit = **20%** x 24 500 bacteriologically confirmed cases x 48% (% of patients who are HIV-negative) x 93.5% (6.5% of patients are children) x 10 x 2 smears per visit = 44 000 smear examinations.

b. Annual number of follow-up smears in 2020 = number of pulmonary TB cases x **3** visits x **2** smears per visit = 50 300 x 3 visits x 2 smears per visit = 302 000 smear examinations.

Sum: 346 000 smear examinations in 2020.

Number of Xpert MTB/RIF tests (or analogous replacement technology): 2020

a. People living with HIV who have signs and symptoms of TB = annual number of people living with HIV in care x % of people living with HIV who are clinically screened x average number of times that clinical screening is performed per year (**2** times) x % of persons screened and found to have signs and symptoms of TB x % coverage of Xpert MTB/RIF testing = 550 000 x **2** x **15%** x **100%** = 165 000.

b. Children with signs and symptoms of TB = notified paediatric TB cases x **4** in settings with a high HIV prevalence = 3 700 cases x **4** = 15 000.

c. People at risk of having DR-TB = people with signs and symptoms of TB who have a history of successful treatment (**4** x 2 300) + other people who have a history of treatment (previously treated cases – relapses = 500) + RR-TB contacts (200 in 2015, which is expected to increase to 600 in 2020 = **4** x 600)= 9 200 + 500 + 2 400 = 12 000.

d. **80%** of previously untreated HIV-negative adults with signs and symptoms of TB = **80%** of smear-positive new TB cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms who need to be tested to find 1 case) x % of HIV-negative TB patients x % of patients who are adults = **80%** x 24 500 x 10 x 48% x 93.5% = 88 000.

e. TB cases for DST purposes = new TB cases (54 000) – number of new TB cases that will have Xpert MTB/RIF testing as the initial diagnostic test (people living with HIV + children + 80% HIV-negative adult new cases) = (54 000 x 52%) + (54 000 x 6.5%) + (54 000 x 48% x 80% x 93.5%) = 54 000 – 51 000 = 3 000 x **100%** = 3 000.

Sum: 283 000 Xpert MTB/RIF tests in 2020.

Number of facilities with GeneXpert machines: 2020

So, 283 000 tests/**720** tests/module per year) = 393 modules in 2020, which is divided among GeneXpert machines comprising various numbers of modules (for example, 1,2,4 or 16 modules). One or more GeneXpert machines may be placed at a facility, depending on specimen referral networks.

Number of culture examinations and drug-susceptibility tests: 2020

For DST, the number of RR-TB cases = 200 in 2015, which is expected increase to 600 in 2020 = 600.

For culture for treatment monitoring of RR-TB cases: number of RR-TB cases enrolled on treatment x **18** (monthly culture for 18 months, with 1 tube per test) x **1** culture per month = 600 x 18 = 10 800.

An additional 10% of examinations is needed for quality control and repeat testing = 10 800 cultures x 1.1 and 600 drug-susceptibility tests x 1.1.

Sum: 12 000 cultures and 660 drug-susceptibility tests = 13 000 examinations.

Number of culture and DST facilities: 2020

For 13 000 examinations/**10 000** examinations per year = 1–2 culture and DST facilities.

Example 3. Country in Eastern Europe with a very high MDR-TB frequency and low HIV frequency

TB epidemiology: 2015

TYPE OF TB	NO. OF CASES
Pulmonary, bacteriologically confirmed	
New cases	4 000
Relapse cases	1 800
Pulmonary, clinically diagnosed	
New cases	6 200
Relapse cases	1 000
Extrapulmonary	
New cases	4 500
Relapse cases	300
Previously treated cases, excluding relapses	4 500
Total cases notified	22 300
No. (%) of TB cases among children	2 200 (10%)
% HIV-positive TB patients	5%
% HIV-negative TB patients or status unknown	95%
HIV-positive people clinically screened for TB	1 000
Estimated % of TB cases with MDR-TB	
New cases	20%
Previously treated cases	60%
Laboratory-confirmed RR-TB including MDR-TB cases (estimated RR-TB including MDR-TB, among notified TB cases)	3 000 (4 000)

MDR-TB: multidrug-resistant TB; RR-TB: rifampicin-resistant TB.

Number of smear examinations: 2020

a. Annual number of diagnostic smear examinations = 0. Given the high frequency of MDR-TB, all people with signs and symptoms of TB should be tested with the Xpert MTB/RIF assay (or analogous replacement technology) as the initial diagnostic test.

b. Annual number of follow-up smears in 2020 = number of pulmonary TB cases x **3** visits x **2** smears per visit = 17 500 x 3 visits x 2 smears per visit = 105 000 smear examinations.

Sum: 105 000 smear examinations in 2020.

Number of Xpert MTB/RIF tests (or analogous replacement technology): 2020

a. People living with HIV who have signs and symptoms of TB = annual number of people living with HIV in care x % of people living with HIV who are clinically screened x average number of times that clinical screening is performed per year (**2** times) x % of persons screened and found to have signs and symptoms of TB x % coverage of Xpert MTB/RIF testing = 1 000 x **2** x **15%** x **100%** = 300.

b. Children with signs and symptoms of TB: see point c. All people with signs and symptoms of TB should be tested with the Xpert MTB/RIF assay.

c. People at risk of having DR-TB: Given the high frequency of MDR-TB, all people with signs and symptoms of TB and their contacts should be tested with the Xpert MTB/RIF assay (or analogous replacement technology) as the initial diagnostic test.

   The annual number of people with signs and symptoms of TB = **10** x number of bacteriologically confirmed cases = 10 x 5 800 = 58 000.

   Contacts of RR-TB cases = **4** x 4 000 = 16 000.

   Total = 74 000.

d. **80%** of HIV-negative people with signs and symptoms of TB: see point c. All people (regardless of HIV status) with signs and symptoms of TB should be tested with the Xpert MTB/RIF assay.

e. TB cases for DST purposes: see point c. All TB cases will have been tested with the Xpert MTB/RIF assay as the initial diagnostic test.

Sum: 74 000 Xpert MTB/RIF tests in 2020.

Number of facilities with GeneXpert machines: 2020

So, 74 000 tests/**720** tests/module per year = 103 modules in 2020, which is divided among GeneXpert machines comprising various numbers of modules (for example, 1,2,4 or 16 modules). One or more GeneXpert machines may be placed at a facility, depending on specimen referral networks.

Number of culture examinations and drug-susceptibility tests: 2020

For DST, the number of RR-TB cases = 4 000 (estimated as of 2020).

For culture for treatment monitoring of RR-TB cases: number of RR-TB cases enrolled on treatment x **18** (monthly culture for 18 months, with 1 tube per test) x **1** culture per month = 4 000 x 18 = 72 000.

An additional 10% of examinations is needed for quality control and repeat testing = 72 000 cultures x 1.1 and 4 000 drug-susceptibility tests x 1.1.

Sum: 79 200 cultures + 4 400 drug-susceptibility tests = 84 000 examinations in 2020.

Number of culture and DST facilities: 2020

For 84 000 examinations/**10 000** examinations per year = 8 culture and DST facilities.

Example 4. Country in Asia with a low MDR-TB frequency and low HIV frequency

TB epidemiology: 2015

TYPE OF TB	NO. OF CASES
Pulmonary, bacteriologically confirmed	
New cases	24 500
Relapse cases	800
Pulmonary, clinically diagnosed	
New cases	23 500
Relapse cases	1 000
Extrapulmonary	
New cases	6 000
Relapse cases	500
Previously treated cases, excluding relapses	500
Total cases notified	56 800
No. (%) of TB cases among children	3 700 (6.5%)
% HIV-positive TB patients	5.0%
% HIV-negative TB patients	95%
HIV-positive people clinically screened for TB	45 000
Estimated % of TB cases with MDR-TB	
New cases	1%
Previously treated cases	10%
Laboratory-confirmed RR-TB including MDR-TB cases (estimated RR-TB including MDR-TB, among notified TB cases)	200 (600)

MDR-TB: multidrug-resistant TB; RR-TB: rifampicin-resistant TB.

Number of smear examinations: 2020

a. Annual number of diagnostic smears = **20%** of smear-positive, HIV-negative new adult cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms who need to be tested to find 1 case) x **2** smears per visit = **20%** x 24 500 bacteriologically confirmed cases x 95% (% of patients who are HIV-negative) x 93.5% (6.5% of patients are children) x 10 x 2 smears per visit = 87 000 smear examinations.

b. Annual number of follow-up smears in 2020 = number of pulmonary TB cases x **3** visits x **2** smears per visit = 50 300 x 3 visits x 2 smears per visit = 302 000 smear examinations.

Sum: 389 000 smear examinations in 2020.

Number of Xpert MTB/RIF tests (or analogous replacement technology): 2020

a. People living with HIV who have signs and symptoms of TB = annual number of people living with HIV in care x % of people living with HIV who are clinically screened x average number of times that clinical screening is performed per year (**2** times) x % of persons screened and found to have signs and symptoms of TB x % coverage of Xpert MTB/RIF testing = 45 000 x **2** x **15%** x **100%** = 14 000.

b. Children with signs and symptoms of TB = notified paediatric TB cases x **6** in settings with a low HIV prevalence = 3 700 cases x **6** = 22 000.

c. People at risk of having DR-TB = people with signs and symptoms of TB who have a history of successful treatment (**4** x 2 300) + other people who have a history of treatment (previously treated cases – relapses = 500) + RR-TB contacts (200 in 2015, which is expected to increase to 600 in 2020 = **4** x 600) = 9 200 + 500 + 2 400 = 12 000.

d. **80%** of previously untreated HIV-negative adults with signs and symptoms of TB = **80%** of smear-positive new TB cases (or bacteriologically confirmed cases as a proxy) x **10** (number of people with signs and symptoms who need to be tested to find 1 case) x % of HIV-negative TB patients x % of patients who are adults = **80%** x 24 500 x 10 x 95% x 93.5% = 174 000.

e. TB cases for DST purposes = new TB cases (54 000) – number of new TB cases that will have Xpert MTB/RIF testing as the initial diagnostic test (people living with HIV + children + 80% HIV-negative adult new cases) = (54 000 x 5%) + (54 000 x 6.5%) + (54 000 x 95% x 80% x 93.5%) = 54 000 – 37 000 = 17 000 x **100%** = 17 000.

Sum: 239 000 Xpert MTB/RIF tests in 2020.

Number of facilities with GeneXpert machines: 2020

So, 239 000 tests/**720** tests/module per year = 332 modules in 2020, which is divided among GeneXpert machines comprising various numbers of modules (for example, 1,2,4 or 16 modules). One or more GeneXpert machines may be placed at a facility, depending on specimen referral networks.

Number of culture examinations and drug-susceptibility tests: 2020

For DST, the number of RR-TB cases = 200 in 2015, which is expected increase to 600 in 2020 = 600.

For culture for treatment monitoring of RR-TB cases: number of RR-TB cases enrolled on treatment x **18** (monthly culture for 18 months, with 1 tube per test) x **1** culture per month = 600 x 18 = 10 800.

An additional 10% of examinations is needed for quality control and repeat testing = 10 800 cultures x 1.1 and 600 drug-susceptibility tests x 1.1.

Sum: 12 000 cultures and 700 drug-susceptibility tests = 13 000 examinations.

Number of culture and DST facilities: 2020

For 13 000 examinations/**10 000** examinations per year = 1–2 culture and DST facilities.

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THE END TB STRATEGY