A best-practice framework of program indicators for monitoring a comprehensive approach to the tuberculosis epidemic

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SEARCH
PREVENT
TREAT

Contents

Objective 2

Search, Treat, and Prevent 3

How to use this document 4

General recommendations for data collection 5

Search: Active case-finding 7

- Active case-finding cascade and indicators 8
- Data collection strategies 10
- Using the indicators 11
- Additional data collection 16
- Example 17

Treat: Treatment of TB disease 19

- Treatment cascade and indicators 20
- Data collection strategies 22
- Using the indicators 23
- Additional data collection 26
- Example 27

Prevent: Treatment of TB infection 29

- TB prevention cascades combine searching and treating 30
- Prevention cascade and indicators 31
- Data collection 34
- Using the indicators 35
- Additional data 37
- Example 1 38
- Example 2 39

Appendix: Examples of forms for reporting indicators 40

- Active case-finding 40
- Treatment of TB disease 41
- Treatment of TB infection 42

Objective

Many places are moving toward adopting a comprehensive approach to tackling the TB epidemic. As they do so, a need has been identified for indicators that can be used to monitor, evaluate, and improve program performance. The current performance indicators used by TB programs focus almost exclusively on the treatment of patients who passively present to the health system and are treated for TB disease.* In contrast, a comprehensive approach includes actively searching for people who have TB (active case-finding), enhanced support during treatment, and the treatment of TB infection* to prevent future disease. An expanded indicator framework is required for such an approach.

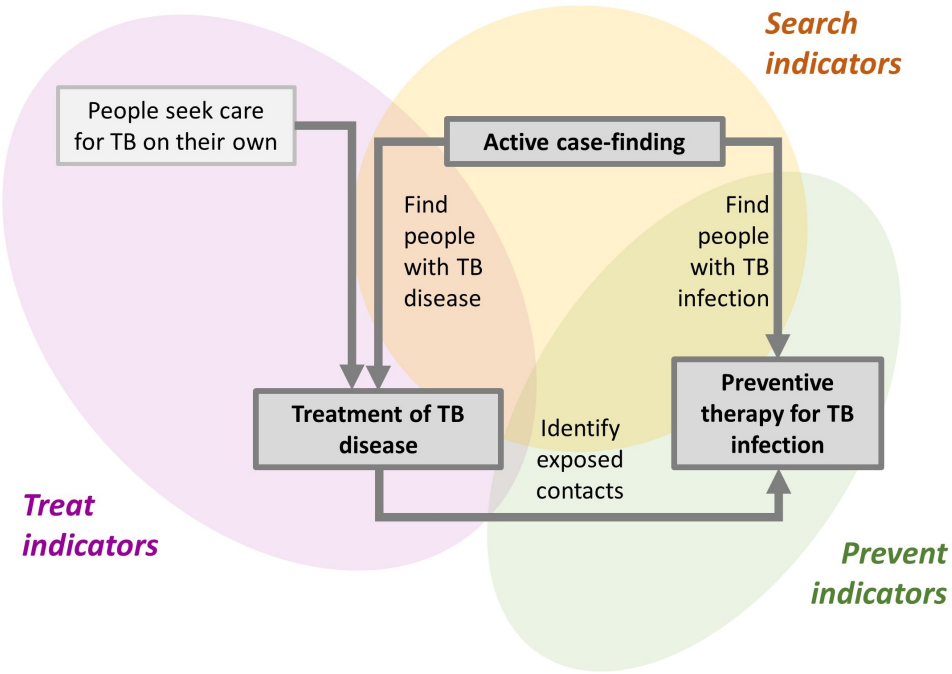
The goal of this document is recommend a best-practice framework of process indicators that can be used to monitor program performance, identify gaps, and measure progress in the implementation of a comprehensive approach to the TB epidemic.

*People with **TB disease** are sick and the TB bacteria in their bodies are actively multiplying. People with **TB infection** do not feel sick, and although they have TB bacteria in their body, the bacteria are not multiplying because the immune system is able to control them. Both TB disease and TB infection should be treated.

Search, Treat, and Prevent

This framework describes three sets of process indicators corresponding to active case-finding, treatment, and prevention. Each is presented as a "cascade" of steps with indicators measuring the proportion of people moving from one step to the next.

Despite being presented separately for ease of implementation, these three cascades — and hence, the three sets of indicators — are in fact interconnected. The "Search" indicators, which monitor activities to actively find people with TB disease (or infection), end when a person starts treatment. The success of this treatment is monitored by the "Treat" indicators. People being treated for TB disease have contacts who should receive preventive therapy to treat TB infection; the process of evaluating these contacts and giving them preventive therapy is monitored by the "Prevent" indicators. The "Prevent" indicators can also be used to monitor efforts to deliver preventive therapy to other high-risk groups who are identified and evaluated through an active case-finding approach.



How to use this document

This document was developed to help individual programs to monitor their own performance. It illustrates at a conceptual level a framework for data collection and analysis that can be used to evaluate gaps in care delivery for all the components of a comprehensive approach to the TB epidemic. Each program will have to develop its own implementation strategy for data collection, monitoring, and evaluation. This document is not meant as an implementation guide; however, case studies and examples of reporting forms are provided to help programs start their own implementation discussions.

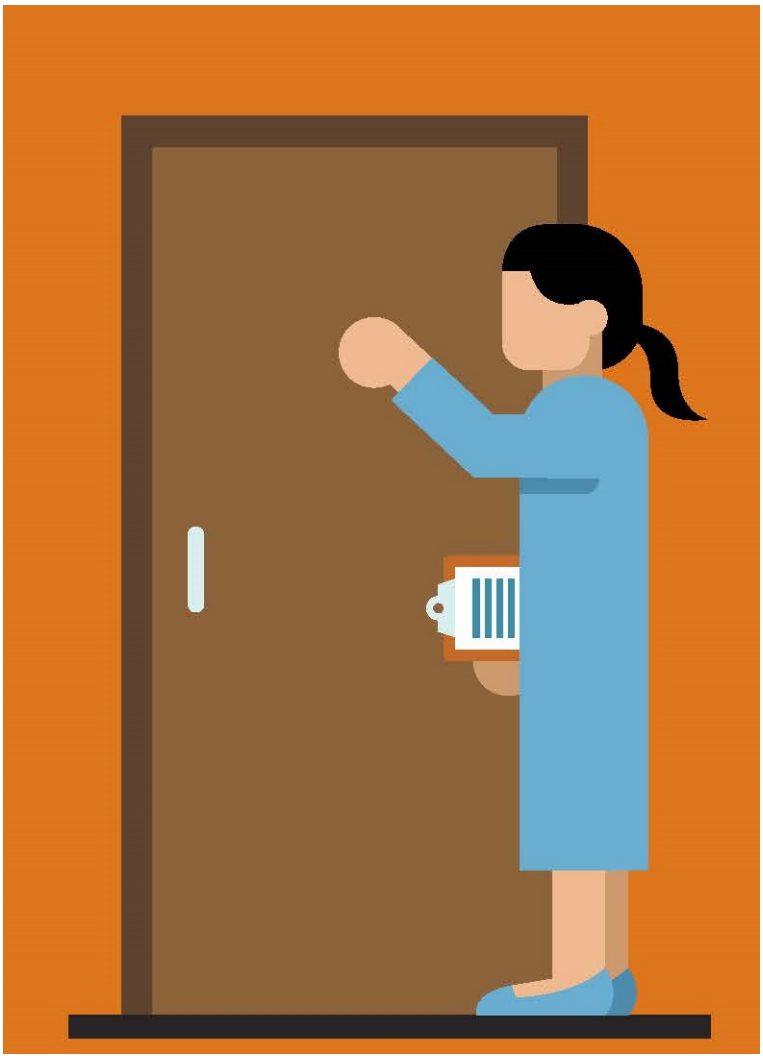
The framework itself was designed for maximal adaptability. There has been no attempt to standardize the specific information to be collected across different settings. Rather, the information that is collected may vary across sites, depending on what activities are being implemented, what data are already being routinely collected, and the local capacity for additional data collection. We recommend that for an individual program, consistent information should be collected over time so that changes in performance can be evaluated.

General recommendations for data collection

We have recommended data elements that should be feasible to collect as part of a routine program. However, we realize that the infrastructure may not yet be in place to collect all of the recommended data. This should not be a barrier to starting; programs can work toward building more robust monitoring systems as they proceed.

We strongly recommend that all data be collected separately for adults and children because sick children are often managed in different parts of the health system than adults. In addition, programs may choose to stratify data collection for populations of interest in their local context, particularly where disparities are suspected.

There are two possible approaches to collecting data on these cascades: programs can collect data on groups of individuals moving through the cascade (individual-level cohort data), or programs can collect the numbers of people who complete each cascade step during a certain time period (aggregate cross-sectional data). Individual-level cohort data are more robust. To collect individual-level data, it is necessary to have data systems that allow the tracking of individuals over time. Longitudinal registers can accomplish this goal if diagnosis and care delivery occur in a single health facility. Electronic health records can be used even when diagnosis and care are delivered in different health facilities. Records held by patients themselves (e.g. paper treatment cards or mobile apps that do the same thing) are another option. If it is not possible to track individuals through all the steps of a cascade, programs can use aggregate cross-sectional data to fill in the missing steps. If large numbers of patients are assessed, then the indicators calculated using aggregate cross-sectional data can be comparable to what would be found using individual-level data. Finally, for any data elements for which no data sources currently exist, operational research protocols on small cohorts of patients can be used to assess the current situation.



SEARCH

Search: Active case-finding

Around 40% of people with TB are missed by health services annually.[1] Active case-finding is necessary to find these missing cases. Active case-finding refers to activities that bring TB screening and diagnostic services to people who might otherwise not seek them. Active case-finding should be used for populations who are at increased risk of having TB, who are vulnerable, or who have poor access to existing health care services so that they can be diagnosed and treated early. Strategies can and should vary depending on the setting and the population served. This monitoring framework should be applied to each separate active case-finding activity that is performed.

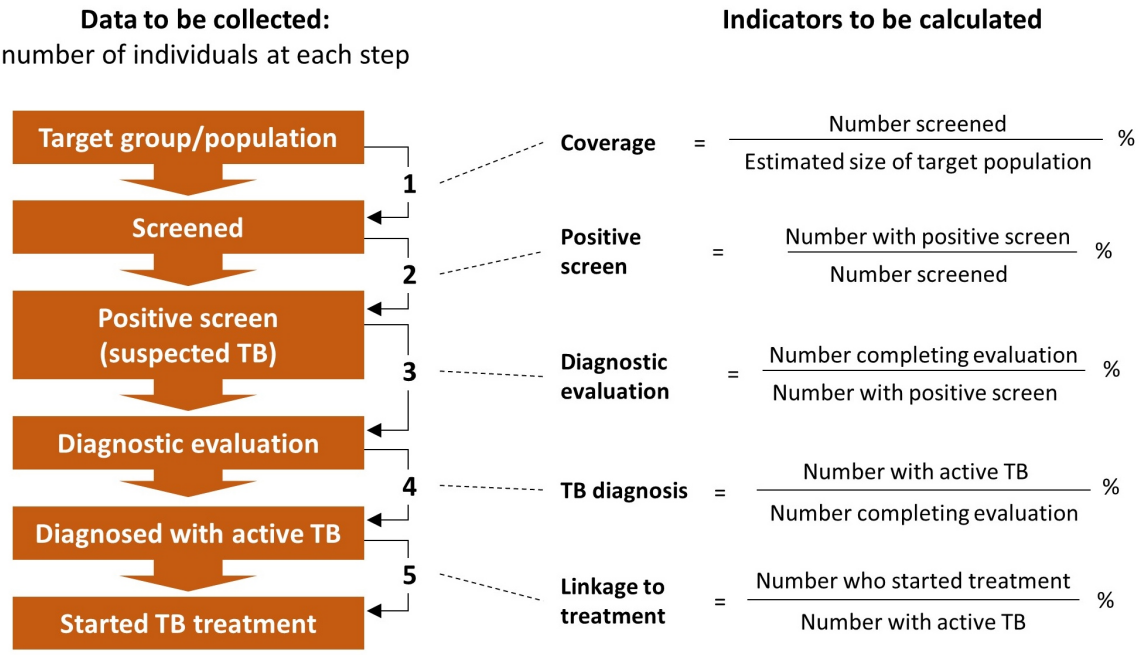
A monitoring framework for active case-finding activities was developed by the Stop TB Partnership and has been used to monitor and evaluate activities funded by the TB REACH initiative.[2] This document summarizes that framework.

[1] World Health Organization. Global tuberculosis report 2016. WHO/HTM/TB/2016.13.
[2] Blok L et al. A pragmatic approach to measuring, monitoring and evaluating interventions for improved tuberculosis case detection. International Health 2014; 6(3):181-8.

Active case-finding cascade and indicators

For any active screening activity, there is a **target group/population**, or a collection of people who will receive the screening, diagnostic, and treatment services. These individuals are **screened**, which means that they undergo a procedure to identify people with a higher likelihood of having active TB disease; people identified by this screening procedure are said to have "**screened positive**." Examples of TB screening procedures are questionnaires about TB-related symptoms and chest x-ray. Any individual who screens positive is considered to have suspected TB**.** These individuals should receive a **diagnostic evaluation**, which is used to confirm active TB disease. Diagnostic evaluations generally include diagnostic tests for active TB disease such as smear microscopy or molecular assays (e.g. Xpert MTB/RIF [Ultra]). Anyone who is **diagnosed with active TB disease** should immediately be **started on appropriate TB treatment**. Individuals in high-risk groups – such as contacts of people with TB and people living with HIV/AIDS – who are not diagnosed with active TB disease should be screened for TB infection and treated accordingly (see chapter "Prevent: Treatment of TB infection").

Recording the number of individuals at each step of the cascade allows for the calculation of key performance indicators that can be used to identify gaps and compare the utility of different active case-finding strategies within target populations.



1. Coverage indicates how well the screening activity has reached the people it was designed to benefit.

2. The percentage of people with a **positive screen** indicates how effective the screening process is at identifying people who might have TB.

3. The percentage of people who complete a **diagnostic evaluation** indicates whether everyone who should have received a diagnostic evaluation in fact does.

4. The percentage of evaluated people with a **TB diagnosis** is a measure of how much TB is being diagnosed in the target population. The inverse of this (the number evaluated divided by the number with active TB) is the **number needed to test**, or **NNT**. The NNT is the number of individuals that must undergo a diagnostic evaluation to identify one person with TB.

5. Linkage to treatment indicates whether everyone diagnosed with TB was started on treatment.

Data collection strategies

Data on the active case-finding cascade should be collected separately for each strategy/approach that is implemented. Data collection for most of the steps of the cascade should be built into the implementation of the activity itself.

For continuous activities, such as screening programs for high-risk groups, indicators can be calculated periodically (e.g. quarterly) to monitor implementation over time. For discrete activities, such as a screening campaign in a particular community, indicators can be calculated for the activity as a whole.

Using the indicators

These indicators can help to identify gaps in implementation and to monitor whether they have been addressed. They can also be used to compare the performance of different active case-finding strategies to make decisions about whether to expand or scale back an activity.

Coverage

Active case-finding activities strive to reach all members of a target population, but the extent to which this occurs differs based on the way that the activity is designed and implemented. For example, an activity that involves sending screening teams to visit each home in a neighborhood until everyone is screened may achieve very high coverage. In contrast, parking a mobile screening van in the same neighborhood may achieve lower coverage because this strategy relies on people voluntarily going to the van.

It is important to have some idea of the coverage being achieved in order to assess whether it is likely to make a difference. For instance, an activity that finds many people with TB but only reaches 10% of the target population is unlikely to make an impact at the population-level because the case detection in the 90% of the population who was not screened will not improve. It is also important to estimate coverage to plan for resource allocation if the decision is made to scale up the activity to reach the entire target population.

It can be tricky to calculate coverage when multiple active case-finding attempts are carried out in a single target population or when a continuous activity is sustained within a target population. The reason is that some individuals may be screened more than once, leading to an overestimate of coverage. Attempts to estimate coverage should therefore take into account repeated screenings of the same individuals. This can be done simply by applying a correction factor: for instance, if it is believed that 10% of the target population ends up being screened twice, then the coverage estimate can be reduced by 10%.

Positive screen

There is no target value for the percentage of screened people who should screen positive, indicating that they are increased risk of having TB. This percentage is affected by the amount of TB in the target population and also the screening procedure used. In a population with a lot of TB, the percentage of people screening positive will be higher. In addition, a screening procedure that makes it easier for people to screen positive will also increase this percentage. For instance, asking people if they have had any TB symptom for any amount of time in the last month will induce more people to answer "yes" than asking people if they have been coughing continuously for the past 2 weeks. While a screening procedure that makes it easier for people to screen positive may increase the number of TB cases detected, it also requires more people to complete diagnostic evaluation procedures. Therefore, the screening procedure, the capacity of the system for diagnostic evaluations, and the vulnerability of the target population should all be considered when using the positive screen percentage to inform decisions.

In vulnerable populations where the consequences of undiagnosed TB are serious, then it is a good idea to use a screening procedure that maximizes the percentage of people screening positive to ensure that no cases are missed. Common examples of highly vulnerable populations include people living with HIV and young child contacts of TB patients, in whom the risk of death from undiagnosed TB is high. Active case-finding activities are warranted in these populations even if the positive screen percentage remains low.

Diagnostic evaluation

The percentage of people who are evaluated after screening positive should be very high. The percentage evaluated is a procedural indicator that reflects the implementation of the activity. Measuring it helps to ensure that people are not lost between screening and diagnostic evaluation. If the right people are being identified during screening (i.e. those at higher risk for TB) and a system is put in place to ensure that everyone with a positive screen completes the diagnostic evaluation procedure, then the evaluation rate will be very high. If it is not, then a few reasons should be considered.

First, it is possible that it is too difficult or inconvenient for people to complete the diagnostic evaluation procedure. For any diagnostic test that involves a sputum sample (e.g. sputum smear microscopy or Xpert MTB/RIF [Ultra] assay), ensuring good sample collection may require providing individuals with a private area to produce a sample, coaching people through the process of producing sputum, and devising systems to allow the collection of samples in the morning when sputum production is easier. For evaluations that require chest x-ray, easy and affordable access to x-ray facilities must be ensured. If there is a long line to enter a sputum collection area, x-ray facility, or clinical consultation room, then many people who screen positive may leave the area before completing the diagnostic evaluation procedure. If efforts are not made to overcome logistical barriers, then a poor rate of diagnostic evaluation may be observed.

The logistics of transport and laboratory capacity can also affect the completion of diagnostic evaluations. High rates of sample contamination, testing backlogs, stock-outs of laboratory supplies, and power outages can all affect the ability of the laboratory system to complete the diagnostic testing procedures.

Beyond this, it is important to ensure that the TB program is aware of the test results and that the results are incorporated into patient records.

TB diagnosis

There is no target value for the percentage of evaluated people who should be diagnosed with TB. A very low percentage may mean that the wrong population is being tested. However, a high percentage (>10%) may mean that only the highest-risk individuals or those who are most sick are being evaluated; because it is possible that these individuals would be diagnosed by the healthcare system in a timely fashion anyway, the impact of the active case-finding activity may thus be limited. Therefore, a balance must be struck to evaluate people who are at risk for TB, but to find the non-obvious people with TB who are more likely to be missed by a health system that relies on passive case-finding.

The percentage of evaluated people who are diagnosed with TB is affected by the screening procedure used. A screening procedure that identifies only people at the highest risk for TB (e.g. cough lasting over 2 weeks) may result in a high diagnostic rate but also miss many cases who do not have such strong signs of TB risk. In contrast, a screening procedure that identifies more people for testing (e.g. any TB symptom and/or abnormal chest x-ray) may produce a lower diagnostic rate, but may also succeed in diagnosing more cases.

Among those diagnosed with TB, the percent with bacteriologically confirmed disease should be assessed. If a very high percentage of cases is bacteriologically confirmed, then there is likely underdiagnosis of extrapulmonary and paucibacillary disease; this is especially true for children.

As TB incidence decreases, it should become harder to find cases of TB. Therefore, it is reasonable to expect that over a span of years, if the comprehensive approach to TB succeeds in reducing TB incidence, then percentage of people diagnosed with TB will decrease. This does not mean that active case-finding activities should stop.

Linkage to treatment

All people diagnosed with TB must receive appropriate prompt treatment. Even if the team that is implementing the active case-finding activity does not directly provide treatment, it is critical that linkage to appropriate treatment is provided and monitored as part of the activity. If this indicator is not >90%, then additional activities may be required to bolster linkage.

Appropriate treatment means treatment that is effective against the form of disease that a person has. People with drug-resistant TB need different treatment regimens than people with drug-susceptible TB. In settings where diagnostic evaluation is done via the Xpert MTB/Rif [Ultra] assay, which detects rifampicin resistance at the time of TB diagnosis, linkage to appropriate treatment for people with rifampicin-resistant TB can be evaluated as a separate indicator. People with rifampicin-resistant TB should only be considered to have started appropriate treatment when they receive a second-line regimen. In settings where drug resistance is not diagnosed immediately (e.g. settings that use smear microscopy), it may be more feasible to assess linkage to any treatment as a primary indicator, then conduct periodic chart reviews on cohorts of patients to assess linkage to second-line treatment for people eventually diagnosed with drug-resistant TB.

Limitation of these indicators

While these indicators can help to monitor the performance of active case-finding activities, they cannot indicate whether these activities are increasing the total number of TB cases diagnosed in the population. It is possible that active case-finding activities may diagnose TB in people who would have eventually been diagnosed passively by the health system. While it is still beneficial to diagnose and treat these individuals earlier, a comprehensive approach to the TB epidemic requires also finding the people with TB who would otherwise not make it into healthcare systems on their own.

Additional data collection

For programs with a high capacity for data collection, there are some additional data elements that can be collected to better understand the performance of active case-finding activities.

Timing: The timing of progression between steps can offer insight into the efficiency of procedures and help identify delays. If data are being collected on individuals during the active case-finding activity, the date at which each procedure is completed can be recorded. The difference (in days) between the date at which one procedure is completed and the date the next procedure is completed can be computed for each step. To describe the average performance of the activity, this information can either be expressed as a median and range, or as a percentage of patients with an unacceptably long delay between procedures. For example: "People completed diagnostic evaluations a median of 3 days (range: 0–12 days) after screening positive" or "For 15% of people, it took over 7 days to complete diagnostic evaluations after screening positive."

Reasons for loss from cascade: The reasons why people do not move from one step to the next can also be recorded to inform the optimization of procedures.

People already on TB treatment: People who are receiving TB treatment are excluded from active case-finding initiatives as a first step in the screening process. Recording the number of people who are already on TB treatment when they are screened and comparing this to the number of new cases diagnosed can be helpful for assessing the additional benefit of the active case-finding activity.

Drug resistance: In places using the Xpert MTB/Rif [Ultra] assay, then rifampicin-resistant TB can be recorded as its own diagnosis category. This allows for separate monitoring of whether people diagnosed with rifampicin-resistant disease are linked to appropriate second-line treatment for drug-resistant TB.

TB infection: It is worth noting that while active case-finding has most frequently been used to find people with active TB disease, the same approach can be used to diagnose people with TB infection as well. If an activity aims at finding both people with TB disease and people with TB infection, then the number of people diagnosed with TB infection (with TB disease ruled out) and the number of those people who receive preventive therapy to treat their TB infection should be collected.

Example

As part of an active case-finding initiative,[3] symptom screeners were deployed in the community to identify and test people with a cough lasting at least 2 weeks. Two strategies were used to encourage diagnostic evaluations. In Strategy 1, individuals were referred to a testing center for sputum smear microscopy testing. In Strategy 2, individuals were asked to give sputum samples in the community, which the screeners then took to the testing centers; anyone with a positive sputum smear was contacted to start treatment. After three months of implementation, the program team reviewed project data, which are shown in the table below. (Note that the size of the target population and the number of people screened are not presented here, so coverage and the percentage with a positive screen are not discussed.)

Cascade step	Number of people		Indicator	Value of indicator	
	Strategy 1	Strategy 2		Strategy 1	Strategy 2
Positive symptom screen	524	1,836			
Completed diagnostic evaluation	0	1,030	Proportion completing evaluation	0%	56%
Diagnosed with TB	0	206	Proportion diagnosed with TB	N/A	20%
Started treatment	0	204	Linkage to treatment	N/A	99%

It became clear that individuals who were referred to testing centers did not actually arrive for testing (0% completing evaluation using Strategy 1), likely due to acute access barriers. On the other hand, sputum collection in the community (Strategy 2) resulted in 56% of people with symptoms being tested. A high percentage of those tested were diagnosed with TB (20%) and there was excellent linkage to treatment (99%). Based on these project data, Strategy 1 was abandoned in favor of Strategy 2 for all symptomatic individuals. Community-based sputum collection procedures were improved so that in subsequent quarters, the percentage of people completing evaluation rose to a stable 85%.

[3] Data from TB REACH. The location and details of the initiative are not presented because data were unpublished at the time this document was prepared.

TREAT

Treat: Treatment of TB disease

TB programs currently focus most of their efforts on treatment. Programs typically collect data on the numbers of patients who initiate treatment and the number who successfully complete treatment. However, these two steps comprise only a portion of the entire pathway that a person with TB must travel on the road to being cured. Failing to account for the gaps in care delivery that occur throughout the pathway can lead to a lack of impact despite high treatment completion rates.

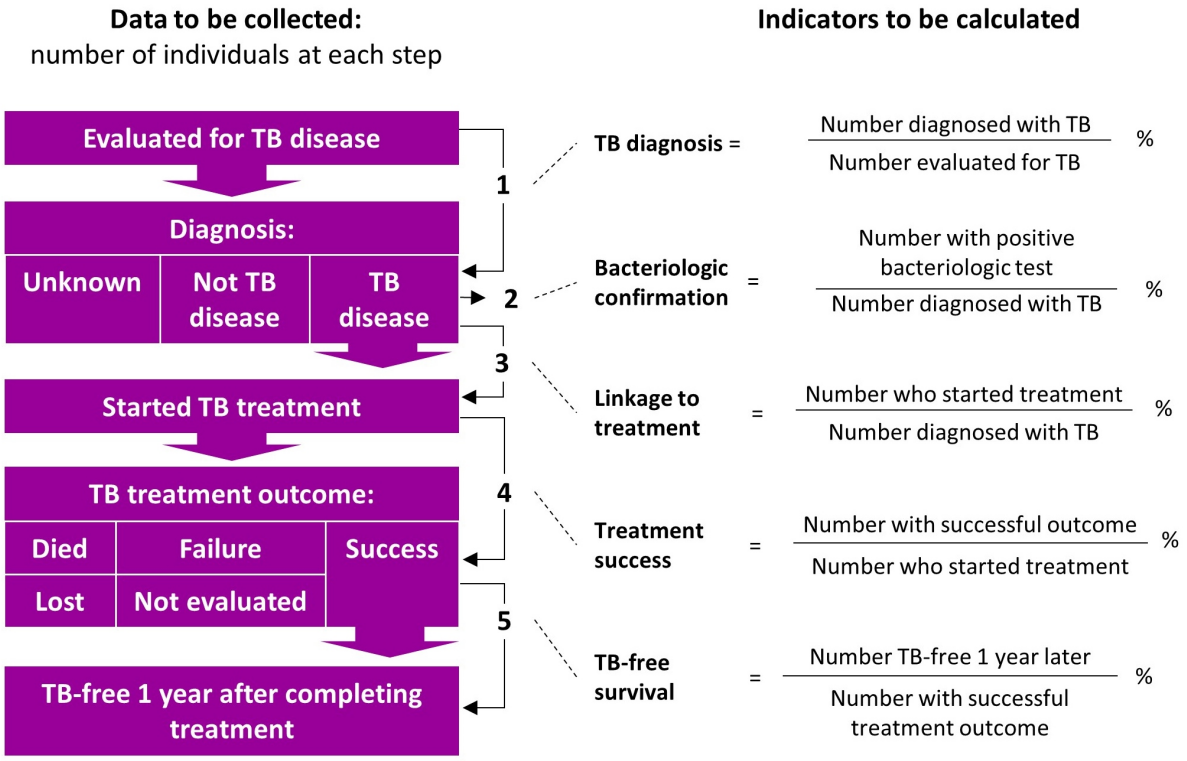
This monitoring framework lays out a comprehensive treatment cascade that allows programs to identify gaps in care delivery that occur from the point where a person with TB enters the healthcare system to the point where he or she is cured. The cascade is based on seminal work evaluating the Indian public sector care cascade.[4]

The treatment cascade has several processes in common with the active case-finding cascade (see chapter "Search: Active case-finding"), including evaluation, diagnosis, and starting treatment. However, the treatment cascade is meant to assess what happens to people who seek care for TB on their own, in addition to those who are treated after having been diagnosed as part of active case-finding activities. Even if a program has not yet started to do active case-finding, the treatment cascade should be applied to assess existing health services.

[4] Subbaraman R. et al. The tuberculosis cascade of care in India's public sector: a systematic review and meta-analysis. PLoS Medicine 2016; 13(10):e1002149.

Treatment cascade and indicators

The treatment cascade begins when a person is **evaluated for TB disease**. This evaluation may include several different procedures, such as laboratory tests, clinical evaluation, and chest x-ray. The evaluation process may be very fast (e.g. if a person immediately has a positive laboratory test result), or may last a couple of weeks (e.g. if the person initially has a negative sputum test and is sent home with 2 weeks of antibiotics to rule out pneumonia). At the end of this process, a person should get a **diagnosis**: either they have TB disease or they do not have TB disease. Those diagnosed with TB disease should immediately **start appropriate TB treatment**. A standard set of **TB treatment outcome** definitions is currently used by TB programs.[5] According to these definitions, both patients with documented bacteriologic cure and patients who completed treatment without evidence of failure but without documentation of cure are considered to have experienced **treatment success**. However, the true gold standard for determining if someone has been cured of TB is whether they experience **TB-free survival**; that is, they continue to live free from TB after completing treatment.



[5] World Health Organization. Definitions and reporting framework for tuberculosis – 2013 revision. WHO/HTM/TB/2013.2

1. The percentage of evaluated people who receive a **TB diagnosis** helps to measure the diagnostic capacity that is required to detect a certain number of cases.

2. Among those diagnosed with TB, the percentage with **bacteriologically confirmed disease** should be assessed. Depending on the laboratory tests that are routinely performed, a certain percentage of cases is expected to be bacteriologically confirmed if all cases are being diagnosed. If a very high percentage of cases is bacteriologically confirmed, then there is likely underdiagnosis of extrapulmonary and paucibacillary disease; this is especially true for children.

3. Linkage to treatment indicates whether everyone diagnosed with TB was started on treatment. The percentage who do not start treatment has been referred to as the **pre-treatment loss to follow-up** or **initial loss to follow-up** rate. (The term **early default** was also previously used, but should not be used because of the patient-blaming nature of the term "default").

4. Treatment success is an indicator for the quality of the treatment program.

5. TB-free survival is an indicator for the quality of the treatment program since patients will only survive without relapse if they receive appropriate treatment. As the vast majority of relapse disease occurs within 1 year, determining that a former patient is still TB-free 1 year after treatment completion is a robust sign that the patient was cured.

Data collection strategies

Of the three cascades described in this document, the treatment cascade for TB disease is likely to have the most information available within existing data collection systems. Information on patients who start treatment and their treatment outcomes is routinely collected by TB programs. Information on TB evaluations and diagnoses may be present in laboratories or presumptive TB registers, even if it is not currently reported to the TB program. In settings where diagnosis and treatment can occur in the private sector and outside the TB program, it is important to build partnerships to be able to collect information on people served by the private sector.

Using the indicators

These indicators can help to identify gaps in implementation and figure out whether they have been addressed. They can also be used to track trends over time and determine the effects of changes in diagnostic or treatment policies.

TB diagnosis

The percentage of evaluated people who are diagnosed with TB can be informative in several ways. It can be used to estimate the diagnostic testing capacity that would be required to increase TB diagnoses to a certain target. It can also be used to assess the effect of changes in the diagnostic system. For example, if a place switches from using smear microscopy alone to using both microscopy and chest x-ray, then the ratio of TB diagnoses to TB evaluations would be expected to increase. If it does not, then the quality of implementation of the new diagnostic technique may be assessed.

In addition to assessing the percentage of people who are diagnosed with TB, it may also be useful to assess the percentage of people whose diagnosis is unknown (that is, they are never diagnosed with TB but never clearly determined not to have TB). This percentage is an indicator of potential losses from the healthcare system before TB evaluation is complete. Many countries have diagnostic algorithms specifying that a person with a negative smear microscopy or Xpert result should undergo additional evaluations. However, many people do not complete these additional evaluations, which often require additional visits to health facilities. While most of these individuals do not have TB, some do; failing to complete the diagnostic algorithm can cause missed opportunities for early diagnosis and treatment. For children and people with HIV, the consequences of such delayed diagnosis can be severe.

Bacteriologic confirmation

Depending on the laboratory tests that are routinely performed for bacteriologic confirmation, a certain percentage of cases is expected to be bacteriologically confirmed if all cases are being diagnosed. Bacteriologic confirmation is most common for pulmonary TB in adults. Extrapulmonary TB is often not bacteriologically confirmed, particularly in settings that lack the infrastructure to routinely collect non-sputum specimens such as lymph node aspirates. Early-stage disease and disease in children, which generally involve few TB bacteria (i.e. paucibacillary disease), are also often not bacteriologically confirmed because of the difficulty of collecting a sample with enough bacteria to detect. Therefore, if extrapulmonary disease, early disease, and childhood disease are being adequately diagnosed, then many cases will not be bacteriologically confirmed. If the percentage of cases that is bacteriologically confirmed is very high, then underdiagnosis is likely occurring; this is especially true for children.

Linkage to treatment

All people diagnosed with TB must receive appropriate prompt treatment, so the target for this indicator is 100%. The percentage who do not start treatment has been referred to as the **pre-treatment loss to follow-up** or **early default** rate. In some settings, the number of people in this category is as large as the number who start treatment but do not complete it. If large numbers of people are lost to follow-up before starting treatment, then interventions to improve linkage to treatment should be implemented. These may include improving the recording of contact information at the time of the diagnostic evaluation, and using call centers or community health workers to notify patients of diagnostic results rather than relying on patients to return to health facilities.

Appropriate treatment means treatment that is effective against the form of disease that a person has. People with drug-resistant TB need different treatment regimens than people with drug-susceptible TB. People with rifampicin-resistant TB should only be considered to have started appropriate treatment when they receive a second-line regimen.

Treatment success

Treatment success rate is a conventional indicator for the quality of the treatment program, and the target is 100%. This percentage is calculated out of the total number who start treatment, without excluding those in the "not evaluated" category, many of whom are patients who leave the program's jurisdiction. Thus, to achieve a high treatment success rate, a treatment program must not only ensure successful treatment for those who remain in its care, but also take responsibility for ensuring that those who leave its jurisdiction are successfully linked to care to complete treatment. Strengthening linkages in communication and information transfer among health facilities and administrative jurisdictions is important for enabling programs to ensure continuity of care for patients.

Regular assessment of why patients are not treated successfully is important for closing gaps in this indicator. A large proportion of deaths may signal the need for earlier diagnosis or better coordination with HIV services to provide antiretroviral therapy for people with HIV. In contrast, a large proportion of patients lost to follow-up may signal the need for investment in strategies to reach patients in their communities, such as community health workers or call centers. A large proportion of treatment failures may signal the need for earlier drug susceptibility testing, more frequent microbiologic monitoring, or greater investment in adherence support.

TB-free survival

TB-free survival is another indicator for the quality of the treatment program, and the target is 100%. It is possible for treatment success rates to be misleadingly high if follow-up bacteriologic testing to assess cure is not well implemented. Because the vast majority of relapse disease occurs within 1 year after treatment, determining that a former patient is still TB-free 1 year after treatment completion is a robust sign that the patient was cured.

It is possible for a patient to be cured and then fall sick again within 1 year because of a new TB infection. This indicator cannot distinguish between these two causes of disease. However, because the majority of recurrent disease within the first year after treatment is likely to be caused by relapse, the recurrence-free survival rate is still a useful indicator. Furthermore, since achieving 100% recurrence-free survival requires both a 100% cure rate among treated patients and no reinfections, then this can be considered the true long-term indicator for a controlled TB epidemic.

Additional data collection

For programs with a high capacity for data collection or the ability to collect additional data through operational research, there are some additional data elements that can be collected to better understand gaps in the treatment cascade.

Timing: The timing of progression between steps can offer insight into the efficiency of procedures and help identify delays. If the dates of individual procedures are known, then the difference (in days) between the date at which one procedure is completed and the date the next procedure is completed can be computed for each step. To describe treatment delays, this information can either be expressed as a median and range, or as a percentage of patients with an unacceptably long delay between procedures. For example: "People started treatment a median of 1 day (range: 0–45 days) after being diagnosed with TB" or "For 10% of people, it took over 7 days to start treatment after being diagnosed with TB."

Drug susceptibility testing: To ensure appropriate treatment, especially in settings with a lot of drug-resistant TB, it is important for people to get timely drug susceptibility testing. If the number of people who receive drug susceptibility is recorded, then it is possible to evaluate the percentage of diagnosed TB cases that received drug susceptibility testing. If individual-level data are being collected, this information can also be incorporated into the definition of whether a person received appropriate treatment.

TB infection: Testing for TB infection can be incorporated into the evaluation algorithm for high-risk groups such as people living with HIV. Results of testing for infection and provision of preventive therapy can be assessed using the prevention cascade (see chapter "Prevent: Treatment of TB infection").

Adherence: Patients often have trouble completing TB treatment because of the long duration and number of pills. Programs therefore generally seek to monitor adherence (i.e. the extent to which patients are able to take their medications) so that patients who are having trouble with adherence can be provided with additional support. Programs that use electronic adherence monitoring or conventional directly observed therapy can collect data on daily pill consumption. Percentages of patients meeting locally-defined definitions of good adherence can be assessed to determine whether programs need to invest more in treatment support.

Example

An attempt was made to characterize the treatment cascade in the public sector in India to identify existing gaps in care. The numbers of people evaluated by smear microscopy, the numbers of patients starting treatment, and their outcomes were all known through routinely collected data. Data from research studies carried out in India were used to estimate the total number diagnosed and their bacteriologic confirmation, as well as the number of people who survived without relapse for one year after treatment completion. The results for 2013 are shown in the table below.

Cascade step	Number of people[6]	Indicator	Value of indicator
Evaluated for TB (sputum smear microscopy)	8,122,000		
Diagnosed with TB (total)	1,630,000	TB diagnosis	20%
Bacteriologically confirmed	953,300	Bacteriologic confirmation	58%
Bacteriologically unconfirmed	676,700		
Started treatment	1,418,000	Linkage to treatment	87%
Successful treatment outcome	1,222,000	Treatment success	86%
TB-free 1 year after treatment completion	1,049,000	TB-free survival	86%

This exercise produced some important findings. First, failing to link people diagnosed with TB to treatment was as big a problem as failing to successfully treat people who started treatment (87% linkage to treatment versus 86% treatment success). Second, while relatively high percentages of people (>85%) completed each step of the cascade, progressive losses at each step meant that by the end, only 64% of people who were diagnosed with TB achieved TB-free survival.

In the past few years, India's tuberculosis program has worked to build systems capable of collecting the data needed to monitor care delivery throughout the treatment cascade. Efforts that will increase the country's ability to routinely evaluate the cascade include: ensuring widespread use of an electronic notification system, improving engagement with the private sector to collect data on diagnosis and treatment that occurs there, emphasizing the notification of cases at the time of diagnosis, and performing follow-up assessments 6 months and 1 year after treatment completion.[7]

[6] These numbers are rounded estimates presented for illustrative purposes only. Exact figures for sputum smear evaluations can be found in: TB India 2014 RNTCP Annual Status Report. New Delhi, India: Central TB Division, 2014. Exact figures for other values can be found in: Subbaraman R. et al. The tuberculosis cascade of care in India's public sector: a systematic review and meta-analysis. PLoS Medicine 2016; 13(10):e1002149.

[7] RNTCP. National strategic plan for tuberculosis elimination 2017-2025. New Delhi, India: Central TB Division, 2017.

PREVENT

Prevent: Treatment of TB infection

People with TB infection have TB bacteria in their body, but the bacteria are not multiplying because the immune system is able to control them. Because people with TB infection do not feel sick and are not contagious, treating TB infection has traditionally not been prioritized by health systems. However, not offering treatment to these individuals leaves them at risk for future disease; this risk can be quite high in vulnerable populations such as young children and people living with HIV. In addition, mathematical modeling as well as the experiences of settings that have brought TB under control suggest that treatment of TB infection to prevent disease is critical to curbing the TB epidemic.[8]

The terminology around treating TB infection has changed over time. The terms "chemoprophylaxis," "preventive therapy," "latent TB infection (LTBI) treatment," and "TB infection treatment" have all been used to refer to the strategy of giving medications to prevent the development of TB disease. This document uses the term "preventive therapy" to avoid confusion with treatment of TB disease.

Various methods of risk stratification can be used to identify the people at highest risk for developing TB so that they can be given preventive therapy. For instance, many countries have policies recommending preventive therapy for groups of people known to be at high risk for developing TB, such as children who live with TB patients and people living with HIV/AIDS. However, implementation has not been prioritized in settings with high TB burdens.

[8] Rangaka et al. Controlling the seedbeds of tuberculosis: diagnosis and treatment of tuberculosis infection. Lancet 2015; 386(10010):2344.

TB prevention cascades combine searching and treating

To improve implementation of preventive therapy, it is important to view the prevention of TB as a cascade of care, just as TB treatment is. This framework builds on two key publications that have framed the cascade for TB prevention in children living with TB patients[9] and other risk groups.[10]

Since people at high risk of developing TB must be first identified and then treated with preventive therapy, the TB prevention cascade is in fact a combination of the active case-finding cascade and the treatment cascade that have been described in previous chapters. The reason for framing TB prevention as a separate cascade with its own indicators is to emphasize the linkage between finding people at risk and treating them.

[9] Szkwarko et al. Child contact management in high tuberculosis burden countries: a mixed-methods systematic review. PLoS One 2017; 12(8):e0182185.

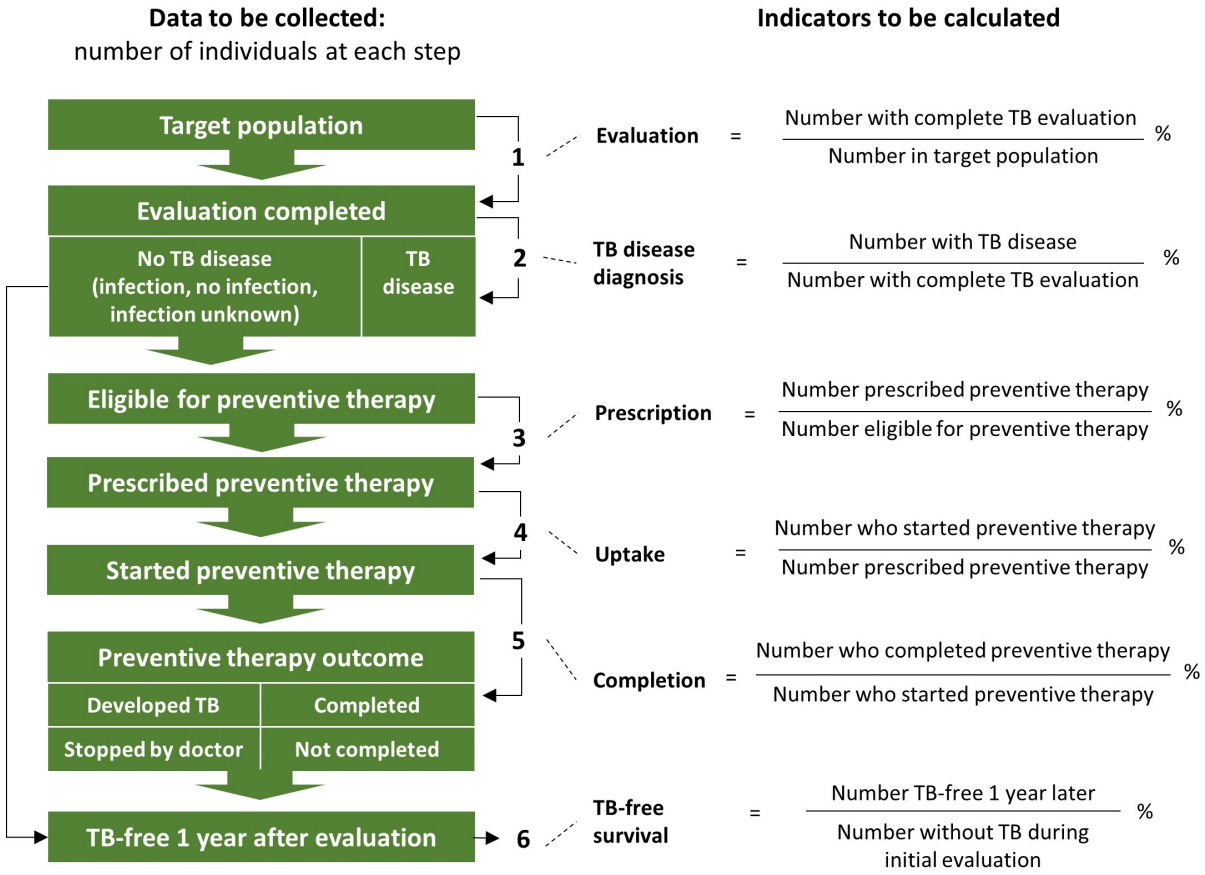
[10] Alsdurf et al. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. Lancet Infect Dis 2016; 16(11):1269-1278.

Prevention cascade and indicators

The first part of the prevention cascade involves identifying people in **target populations** at high risk for developing TB, who should be given preventive therapy. Examples of common target populations for preventive therapy include contacts of TB patients, people living with HIV, and healthcare workers. For ease of interpretation, this monitoring framework should be applied to each separate target population. In addition, in places where age is a factor for determining who is eligible for preventive therapy, the monitoring framework should be applied to each relevant age group.

Members of high-risk target populations first undergo **evaluation for TB disease**, and anyone diagnosed with TB disease is started on appropriate TB treatment. Those without TB disease may or may not be tested for TB infection, depending on local guidelines. If testing is performed, individuals can be classified as either infected or not infected; if testing is not performed, then infection status will be unknown.

TB guidelines typically use a combination of age, infection status, and/or other health conditions (e.g. HIV, TB history) to determine whether individuals are **eligible for preventive therapy**. Those who are eligible should receive a **prescription for preventive therapy** and then **start preventive therapy**. For those who start preventive therapy, four outcomes are possible: (1) the person completes preventive therapy (**completed**); (2) the person develops TB while on preventive therapy (**developed TB**), in which case preventive therapy should be stopped and TB treatment initiated; (3) the doctor requests that the person stop taking preventive therapy before completion for a medical reason such as side effects (**stopped by doctor**), or (4) the person stops taking preventive therapy before completion for some other reason, including death (**not completed**). **TB-free survival within 1 year**, or remaining TB-free 1 year after the initial screening, is a measure of successful use of preventive therapy.


Data to be collected:
number of individuals at each step
Indicators to be calculated
Target population
1
Evaluation completed
No TB disease (infection, no infection, infection unknown)
TB disease
2
Eligible for preventive therapy
3
Prescribed preventive therapy
4
Started preventive therapy
5
Preventive therapy outcome
Developed TB
Completed
Stopped by doctor
Not completed
TB-free 1 year after evaluation
6
Evaluation = Number with complete TB evaluation / Number in target population %
TB disease diagnosis = Number with TB disease / Number with complete TB evaluation %
Prescription = Number prescribed preventive therapy / Number eligible for preventive therapy %
Uptake = Number who started preventive therapy / Number prescribed preventive therapy %
Completion = Number who completed preventive therapy / Number who started preventive therapy %
TB-free survival = Number TB-free 1 year later / Number without TB during initial evaluation %

1. The percentage of the target population that completes **evaluation** is an indicator for how well the prevention program has reached the people it is designed to reach.

2. The percentage of people diagnosed with **TB disease** is a measure of the risk for TB in the target population and the success of the prevention program at finding these people.

3. The percentage of eligible people who are **prescribed preventive therapy** is an indicator for how well the health system is implementing preventive therapy guidelines.

4. The **uptake of preventive therapy** is an indicator for both the acceptability of preventive therapy among contacts and the quality of the counseling given by healthcare providers to explain the reason for preventive therapy.

5. **Preventive therapy completion** is an indicator for the quality of the preventive therapy program. Although it would be ideal for everyone to complete treatment, occasional stopping of treatment by the doctor for medical reasons is expected.

6. **TB-free survival** is an indicator for the quality of the preventive therapy program. As the highest risk for TB occurs in the first year after infection, ensuring that people remain TB-free after 1 year is a robust sign that the prevention program is successful.

Data collection

Data collection on contact management occurs, but is not currently standardized. Some settings use contact registers, which are kept at health facilities to record key aspects of the management of each contact listed. Others use data collection forms for contact management that that are kept in the medical charts of TB patients. However, even in places where these instruments are being used for clinical care, systems may not yet exist to report summary data on contact management to the local or national TB program. As monitoring systems are developed and improved, operational research protocols on small cohorts can be used to assess the current situation.

Other than contacts of TB patients, the group most commonly recommended to receive preventive therapy is people living with HIV. Many HIV programs already have systems in place to record information on the use of preventive therapy (e.g. isoniazid preventive therapy registers). Data collection systems for other groups of high-risk individuals, such as healthcare workers, people with diabetes, and people living in congregate settings may have to be developed.

Using the indicators

Evaluation

In high-risk target populations, 100% of individuals should be evaluated for TB disease and for determining eligibility for preventive therapy. In contrast with population-based active case-finding efforts (see chapter "Search: Active case-finding") it is often possible to enumerate target populations for TB prevention. For example, contacts of TB patients can be identified and enumerated by interviewing patients or visiting their homes; people living with HIV are enumerated in registers in HIV care facilities.

If a substantial number percentage of the target population is not evaluated, effort should be made to understand and address the reasons for the gap. There are two common reasons for not completing evaluation: one is that people do not reach the health facilities to be evaluated, and the other is that they do reach the health facilities, but the evaluation process is not completed. The latter often happens if chest x-rays or follow-up visits are required.

Diagnosis of TB disease

Among people who complete TB evaluation, the results of the evaluation should be categorized at a minimum as "TB disease" or "no TB disease." The percentage of people diagnosed with TB depends on both the risk profile of the people being evaluated and the evaluation algorithms being used. A very high yield of TB diagnoses may suggest that only the highest-risk people in the target population are being evaluated. For instance, this can happen in situations where contact investigations focus only on bringing contacts who are already feeling sick into the clinic. On the other hand, a very low yield of TB diagnoses may suggest that clinical diagnoses of TB disease, especially among young children and people living with HIV, are being missed.

For contacts of TB patients, a diagnosis of not having TB disease is equivalent to TB exposure since all contacts are by definition exposed. For some high-risk individuals, TB exposure is sufficient indication for preventive therapy.

In places where testing for TB infection (i.e. tuberculin skin test or interferon gamma release assay) determines eligibility for preventive therapy, evaluation results for contacts *without* TB should be recorded as "infected," "not infected," and "infection unknown." This will make it easy to determine the number of people who are eligible for preventive therapy. If a large percentage of people who should receive testing for TB infection have unknown infection status, then it is likely that incomplete testing is leading to missed opportunities for preventive therapy.

Prescription

100% of people eligible for preventive therapy should be prescribed preventive therapy. Reasons for not receiving a prescription include lack of provider awareness, low acceptability among providers caused by fear or side effects or other negative consequences, low prioritization of preventive therapy by the healthcare system, and drug shortages. If prescription rates are not high, then training of providers or resolution of drug supply issues may be necessary.

Uptake

Ideally, 100% of people who are prescribed preventive therapy would accept it. If a large percentage of individuals are not starting preventive therapy, the reasons for this gap should be investigated. While it is easy to blame patients for not starting preventive therapy, in many situations, patients' healthcare decisions are largely guided by what doctors tell them. People may not start preventive therapy because doctors have not explained the reason for taking medication when one is not sick, or because doctors have focused more on describing the side effects than the benefits of preventive therapy.

Preventive therapy completion

Ideally 100% of people who start preventive therapy would finish it, although occasional stopping of treatment by the doctor for medical reasons is expected. Because there is currently no test for whether TB infection has been successfully treated, the completion of preventive therapy is used as an indicator of treatment success. Completion rates for preventive therapy are currently low in many settings. Strategies for improving completion include using shorter preventive therapy regimens and offering adherence support. For household contacts, it can be an efficient use of resources to provide adherence support for both the TB patient and their contacts receiving preventive therapy at the same time.

TB-free survival

If a prevention program is successful, then 100% of people in high-risk populations would remain free from TB. The indicator of TB-free survival is measured using a denominator of all the evaluated people who did not have TB at the time of the evaluation, not only those who eventually received preventive therapy. If all of these people remain TB-free for 1 year after their initial evaluation, then the preventive therapy program is likely treating the right people and treating them effectively. On the other hand, the development of TB cases in these populations suggests that either more people should be given preventive therapy, or that preventive therapy needs to be delivered more effectively.

Additional data

Contact investigations performed: For monitoring the management of contacts, it is useful to know the percentage of TB patients for whom a contact investigation has been performed. If a large percentage of patients are not having contact investigations performed, then the program is not going to reach these patients' high-risk contacts to offer preventive therapy.

Timing: The timing of progression between steps can offer insight into the efficiency of procedures and help identify delays. If the dates of individual procedures are known, then the difference (in days) between the date at which one procedure is completed and the date the next procedure is completed can be computed for each step. To describe treatment delays, this information can either be expressed as a median and range, or as a percentage of patients with an unacceptably long delay between procedures. For example: "People who started preventive therapy did so a median of 5 days (range: 0–50 days) after beginning the evaluation process" or "For 30% of people, it took over 7 days to start preventive therapy after beginning the evaluation process."

Reasons for loss from cascade: The reasons why people do not move from one step to the next can be recorded to inform the optimization of procedures.

TB infection: In settings that routinely use tests for TB infection as part of the evaluation of high-risk populations, the percentage of tested individuals who test positive for TB infection can be measured as an indicator of exposure risk in the population. However, this percentage is only meaningful if testing coverage is high; if only the highest-risk people are tested for infection, then the percentage who are infected will not be representative of the target population.

Example 1

A hospital in Malawi started a contact investigation program as a way to find more TB cases and increase the use of preventive therapy in young children.[11] This program involved making a visit to the household of each patient with smear-positive TB, collecting sputum from anyone who was coughing, and giving referral slips for chest x-ray to all children under 6 years old. According to Malawi's TB guidelines at the time (1999 edition), all children under 6 years old who live in the households of TB patients were required to receive a chest x-ray as part of the decision to start either TB treatment or preventive therapy. The results for 3 months of implementation is shown in the table below; data are shown for children under 6 years old. (Note that completion of preventive therapy was not reported in this publication).

Cascade step	Number of people	Indicator	Value of indicator
Target population (contacts <6 years old identified during household visit)	113		
Evaluation completed	44	Evaluation	40%
Diagnosed with TB disease	4	TB disease diagnosis	9%
Diagnosed with TB exposure	40		
Eligible for preventive therapy	40		
Prescribed preventive therapy	25	Prescription	63%
Started preventive therapy	25	Uptake	100%

These results showed that substantial numbers of children were being lost from the cascade prior to starting preventive therapy, with only 40% completing evaluation and 63% of eligible children receiving a prescription for preventive therapy. Exploring the reasons for these losses highlighted the resource-related barriers that families faced in accessing preventive therapy. The most common reason for not completing evaluation was that parents could not afford transport to the hospital to have the required x-ray. Similarly, the reason for the low percentage of eligible children prescribed preventive therapy was that the clinical appointment during which preventive therapy would have been prescribed was made for the day after the x-ray procedure; families who did not have the resources to spend the night in town returned to their villages without receiving preventive therapy for the children.

The current Malawi TB guidelines (2012 edition) eliminate the requirement for all children to receive a chest x-ray before starting preventive therapy. Young children who are well and active at the time of evaluation can immediately start preventive therapy, reducing barriers to accessing this important treatment.

[11] Zachariah R et al. Passive versus active tuberculosis case finding and isoniazid preventive therapy among household contacts in a rural district of Malawi. International Journal of Tuberculosis 2001; 7(11):1033-1039.

Example 2

The cascade of care for TB prevention among HIV-positive female sex workers being treated at a clinic in Kenya was assessed by abstracting data from the clinic's medical records.[12] Women with a prior history of TB were excluded from the analysis since they were not eligible for preventive therapy under the Kenyan TB guidelines at the time. Evaluation was a multi-step process including symptom screen, chest x-ray, and counseling for preventive therapy. Data from women attending the clinic over a 9-year period are shown in the table below.

Cascade step	Number of people	Indicator	Value of indicator
Target population (HIV-positive female sex workers in care with no prior TB history in care at the clinic)	642		
Evaluation completed	402	Evaluation	63%
Diagnosed with TB disease	19	TB disease diagnosis	5%
Eligible for preventive therapy	383		
Prescribed preventive therapy	357	Prescription	93%
Started preventive therapy	351	Uptake	98%
Preventive therapy outcomes			
Completed preventive therapy	249	Completion	71%
Developed TB	1		<1%
Doctor stopped preventive therapy	19		5%
Not completed	73		21%
Unknown	9		3%

The step in which most women were lost from the cascade was evaluation (63% completed evaluation). The most common reasons for not completing evaluation were not starting the evaluation process in the first place and not completing the chest x-ray. Prescription and uptake were very high (93% and 98%). The majority (71%) of women who started preventive therapy completed it.

These findings underscore the need to streamline the evaluation process to ensure that more people access preventive therapy.

[12] LaCourse S et al. Evaluation of the isoniazid preventive therapy care cascade among HIV-positive female sex workers in Mombasa, Kenya. Journal of Acquired Immune Deficiency Syndromes 2017; 76(1):74-81.

Appendix: Examples of forms for reporting indicators

Active case-finding

	Data element	Number	Indicator (calculation)	Value
A	Estimated size of target population			
B	Screened		Coverage (B/A)	%
C	Suspected TB (positive screen)		Positive screen (C/B)	%
D	Completed diagnostic evaluation for TB		Diagnostic evaluation (D/C)	%
E	Diagnosed with TB disease		TB diagnosis (E/D)	%
F	Started TB treatment		Linkage to treatment (F/E)	%

Treatment of TB disease

	Data element		Number	Indicator (calculation)	Value
A	**Evaluated for TB disease**				
	Diagnosis			TB diagnosis ([B+C]/A)	%
	B	TB disease: bacteriologically confirmed		Bacteriologic confirmation (B/[B+C])	%
	C	TB disease: not bacteriologically confirmed			
	D	Not TB disease			
	E	Unknown			
F	**Started TB treatment**			Linkage to treatment (F/[B+C])	%
	TB treatment outcome				
	G	Cured		Treatment success ([G+H]/F)	%
	H	Completed treatment			
	I	Treatment failure			
	J	Died			
	K	Lost to follow-up			
	L	Not evaluated			
M	**TB-free 1 year after treatment**			TB-free survival (M/[G+H])	%

Treatment of TB infection

	Data element		Number	Indicator (calculation)	Value
A	**Target population**				
B	**TB evaluation completed**			Evaluation (B/A)	%
	C	TB disease		TB disease (C/B)	%
	D	No TB disease, with TB infection			
	E	No TB disease, no TB infection			
	F	No TB disease, TB infection unknown			
G	**Eligible for preventive therapy**				
H	**Prescribed preventive therapy**			Prescription (H/G)	%
I	**Started preventive therapy**			Uptake (I/H)	%
	Preventive therapy outcome				
	J	Completed		Completion(J/I)	%
	K	Developed TB			
	L	Doctor stopped			
	M	Not completed			
	N	Unknown			
O	**TB-free 1 year after evaluation**			TB-free survival (O/[D+E+F])	%