

# Tuberculosis management

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## Description of condition and intervention

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*, affects most commonly the lungs. The medium of transmission for TB is mainly through droplet route like when people with lung TB cough, sneeze or spit. Global estimates indicate that about 10 million people every year fall ill with tuberculosis (TB); and about 1.5 million people die from TB annually. Thus, TB is by far the most infectious disease impacting mortality. Further, TB is the leading co-morbidity in people with HIV. The treatment for drug-susceptible TB consists of four drugs primarily Rifampicin, Isoniazid, Ethambutol and Pyrazinamide, given into two phases to the patient-the intensive phase (for two months) and continuation phase (for 4 months). Second-line drugs are indicated as treatment regimen for drug-resistant TB and generally given for a time-period ranging from 9 to 24 months.

Drug resistance in TB is an important challenge in management of TB cases, affecting those with this condition significantly economically and socially. Estimates indicate around half a million people get affected by drug resistant TB every year. Only one-third are able to get access to quality treatment for drug resistant TB. This condition could be multi-drug resistant (MDR) TB or extensively drug resistant (XDR) TB. By definition, MDR-TB is caused by *Mycobacterium Tuberculosis* (*M. tuberculosis*) strains that are resistant to at least both rifampicin and isoniazid. While XDR-TB is resistant to any fluoroquinolone drug as well as to at least one of three

second-line injectable drugs (namely capreomycin, kanamycin and amikacin). Source: WHO, DCP3, WHO 2020.

This evidence brief assesses effects and costs of the following interventions in subsequent sections:

*Drug susceptible tuberculosis management*

*Drug resistant tuberculosis management*

## International guidelines

Organization	Indications/recommendations	Applicability in LIC & Lower MIC settings
World Health Organization	<p>WHO consolidated guidelines on tuberculosis: module 1: prevention: tuberculosis preventive treatment</p> <p>WHO consolidated guidelines on tuberculosis Module 2: Screening – Systematic screening for tuberculosis disease</p> <p>WHO consolidated guidelines on tuberculosis Module 3: Diagnosis - Rapid diagnostics for tuberculosis detection</p> <p>WHO consolidated Guidelines on Tuberculosis, Module 4: Treatment - Drug-Resistant Tuberculosis Treatment  <a href="https://www.who.int/health-topics/tuberculosis#tab=tab_1">https://www.who.int/health-topics/tuberculosis#tab=tab_1</a></p>	Yes

## Intervention attributes

### Type of interventions & Delivery platform

Table 1: Type of interventions & delivery platform

Intervention	Type	Delivery platform
<p>Drug-susceptible TB management</p> <p>Pulmonary tuberculosis: Core diagnostics</p> <p>Extrapulmonary TB: Core Diagnostics</p>	Diagnostic	First-level hospital
<p>Drug resistant tuberculosis management</p> <p>Multidrug-resistant (MDR) TB: Core diagnostics</p>		Referral hospital

Extensively drug-resistant (XDR) TB: Core diagnostics		
Drug-susceptible TB management Pulmonary tuberculosis, no HIV: Treatment Pulmonary tuberculosis, with HIV: Treatment Extrapulmonary TB, no HIV: Treatment Extrapulmonary TB, with HIV: Treatment  Drug resistant tuberculosis management Multidrug-resistant (MDR) TB, no HIV: Treatment Multidrug-resistant (MDR) TB, with HIV: Treatment Extensively drug-resistant (XDR) TB, no HIV: Treatment Extensively drug-resistant (XDR) TB, with HIV: Treatment	Curative	Treatment of pulmonary tuberculosis-health centre  Treatment for extra- pulmonary tuberculosis- First- level hospital   Treatment for MDR and XDR TB- Referral hospital

## Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions

that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

## Time dependence

Moderate level of urgency. Treatment outcomes may be affected by some days of delay.

## Population in need of interventions

Table 2: Population in need of interventions

Intervention	Treated population		Affected population		Disease state addressed
	Treated age	Treated fraction	Affected age	Affected fraction	
Drug-susceptible TB management Pulmonary tuberculosis: Core diagnostics Extrapulmonary TB: Core Diagnostics  Drug resistant tuberculosis management Multidrug-resistant (MDR) TB: Core diagnostics  Extensively drug-resistant (XDR) TB: Core diagnostics	0 to 99 years both genders; incidence based	1	No health impact considered for diagnostic intervention		Drug-susceptible tuberculosis and HIV/AIDS - Drug-susceptible tuberculosis HIV/AIDS  Multidrug-resistant tuberculosis without extensive drug resistance and HIV/AIDS multidrug-resistant tuberculosis without extensive drug resistance  Extensively drug-resistant tuberculosis and HIV/AIDS - extensively drug-resistant tuberculosis
Drug susceptible TB treatment for Pulmonary tuberculosis, with no HIV and with HIV	0 to 99 years both genders; incidence based	0.8 (assumed same for both with and without HIV)	0 to 99 years both genders	0.8 Same as treated fraction	Drug-susceptible tuberculosis  HIV/AIDS - Drug-susceptible Tuberculosis

		Pulmonary TB			
Drug susceptible TB treatment for extrapulmonary tuberculosis, with no HIV and with HIV	0 to 99 years both genders; incidence based	0.2 (assumed same for both with and without HIV Pulmonary TB)	0 to 99 years both genders	0.2 Same as treated fraction	Drug-susceptible tuberculosis  HIV/AIDS - Drug-susceptible Tuberculosis
Treatment for drug-resistant tuberculosis-  multidrug-resistant tuberculosis without extensive drug resistance	0 to 99 years both genders; incidence based	1	0 to 99 years of those with the condition	1  1	Multidrug-resistant tuberculosis without extensive drug resistance  HIV/AIDS multidrug-resistant tuberculosis without extensive drug resistance
extensively drug-resistant tuberculosis		1		1	HIV/AIDS - extensively drug-resistant tuberculosis
Surgery for management of MDR/ XDR-TB treatment failure		0.02		0.02	

## Intervention effect and safety

Table 3: Effect and safety of interventions for treatment of tuberculosis

Effect of intervention		Certainty of evidence
Mortality		
First-line treatment for pulmonary tuberculosis	The four-drug treatment regimen of first-line drugs (isoniazid, rifampin, pyrazinamide, and ethambutol) achieves cure rates of more than 95% in trial conditions and more than 90% in treatment under the oversight of tuberculosis-control programs. These drugs are given for a minimum of 6 months in two phases: 2 months of all four drugs in the intensive phase and 4 months of isoniazid and rifampin in the	Review

First-line treatment for extrapulmonary tuberculosis	continuation stage (Zumla et al 2013 & Combs et al 1990).	
Second-line treatment for multi-drug resistant tuberculosis without extra drug resistance	Assumed same as above	Meta-analysis
Second-line treatment for extra-drug resistant tuberculosis	A meta-analysis by Bastos, Lan and Menzies 2017 reported a pooled estimate of treatment success of 0.61 from included cohort studies for treatment of multi-drug resistant tuberculosis.	Meta-analysis
	A meta-analysis by Bastos, Lan and Menzies 2017 reported a pooled estimate of treatment success of 0.31 from included cohort studies for treatment of extra-drug resistant tuberculosis.	(See appendix)

## Model assumptions

Table 4: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Intervention		
<b>Cost parameters</b>		
Treated population and fraction	See Table 2	Epidemiological data from Global Burden of Disease Study 2019
<b>Effect parameters</b>		

Affected population	See Table 2	
Affected fraction	See Table 2	
Comparison	No intervention	
Mortality reduction (RRR) First-line treatment for pulmonary tuberculosis	0.9	Same efficacy assumed for HIV/AIDS drug susceptible tuberculosis
First-line treatment for extrapulmonary tuberculosis	0.9 (assumed same as above)	
Second-line treatment for multi-drug resistant tuberculosis without extra drug resistance	0.61 Bastos, Lan and Menzies 2017	Same efficacy assumed for HIV/AIDS multidrug-resistant tuberculosis without extensive drug resistance
Second-line treatment for extra-drug resistant tuberculosis	0.31 Bastos, Lan and Menzies 2017	Same efficacy assumed for HIV/AIDS - extensively drug-resistant tuberculosis

## Intervention cost

The cost for chest X-Ray and sputum test AFB is estimated to be 39.43 and 38.12 USD per unit in 2010 in Brazil (Azadi et al 2014). The total cost of first-line treatment is estimated to be 455.5 USD in 2011 in South Africa (cost of retirement as a proxy). Out of the total cost of treatment, the cost of Anti TB drugs and diagnostics and monitoring is estimated at 188.84 and 183.77 USD consecutively (Pooran, Pieterse, Davids, Theron, Dheda 2013).

The cost of Referral of cases of treatment failure for drug susceptibility testing; enrollment of those with MDR-TB for treatment per WHO guidelines (either short or long regimen) is estimated at 8444.57 USD per episode in 2011 in South Africa (Pooran, Pieterse, Davids, Theron, Dheda 2013). The cost of specialized TB services, including management of MDR- and XDR-TB treatment failure and surgery for TB, is estimated to be 5549.36 USD in 2011 in South Africa (Using the cost of surgery as a proxy.)

## References

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## Appendix

### Literature Review for effectiveness & safety

This literature search is an example of Level 1 search for intervention inputs taken from DCP3 or generated in an ad hoc manner (e.g., quick google search found one study of cervical cancer screening cost-effectiveness that was used to create an effectiveness parameter for that intervention).

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, metaanalysis, systematic review, clinical practice guidelines).

An overview of all TB interventions in FairChoices: DCP Analytics Tool, interventions assessed in this evidence brief are marked in bold.

Active TB case finding in HIV+ individuals and other high-risk groups, linkage to care
TB contact tracing, linkage to care
TB preventive therapy (Isoniazide) for high-risk people (e.g., PLHIV)
<b>Drug-susceptible TB management</b>
<b>Pulmonary TB</b>
<b>Pulmonary TB, no HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>Pulmonary TB, HIV</b>

<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>Extrapulmonary TB</b>
<b>Extrapulmonary TB, no HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>Extrapulmonary TB, HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>Drug-resistant TB management</b>
<b>Multidrug-resistant (MDR) TB</b>
<b>MDR TB, no HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>MDR TB, HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>Extensively drug-resistant (XDR) TB</b>
<b>XDR TB, no HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>XDR TB, HIV</b>
<b>Core diagnostics</b>
<b>First-line treatment</b>
<b>Surgery for management of MDR/ XDR-TB treatment failure</b>