

SECTION 8

TUBERCULOSIS (TB)

This section provides information about tuberculosis (TB) for people living with HIV.

What is TB and how do you get it? Why does TB matter for people living with HIV? How can TB be prevented? What are the symptoms? Which tests and treatments do people with TB need?



After reading this section, you will have a basic understanding of:

- » What TB is
- » TB and HIV
- » How a person can get TB
- » How to prevent TB
- » What can happen to a person with TB
- » TB symptoms
- » TB testing
- » TB treatment
- » Drug-sensitive TB
- » Drug-resistant TB
- » TB Q and A



WHAT IS TUBERCULOSIS (TB)?

TB is caused by bacteria, called *Mycobacterium tuberculosis*, that usually infects the lungs. It is the world's deadliest infectious disease – but it can be prevented and cured.

In 2018, **HIV was the biggest risk factor for TB** in South Africa; 177,000 people living with HIV became infected with TB, and 42,000 of them died from it.

Globally, nearly a quarter of all people have been infected with TB, but not everyone falls ill from it. Most people have latent **TB Infection (LTBI)**, which means that their immune system is stopping TB from making them ill. People with LTBI do not have symptoms, and they cannot transmit TB.

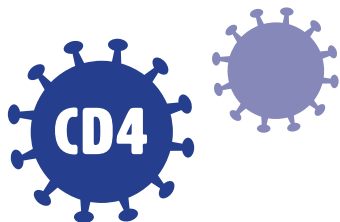
LTBI can develop into active TB, usually within two years. Overall, 5 to 10 per cent of all people with latent TB develop active TB, but rates of active TB are much higher among people living with HIV (See TB and HIV).

People with active TB can transmit it to others if they are not treated. Each year, up to 15 people who are close contacts of someone who has untreated active TB become infected.

Active TB is most common in the lungs, but it can spread from the lungs into the bloodstream, where it can infect any part of the body except the hair and nails. This is called extrapulmonary TB. People living with HIV are more likely to have extrapulmonary TB than HIV-negative people.

EXTRAPULMONARY TB IS MOST COMMON IN:

- » The lymph nodes (a network of infection-fighting glands in the neck, under the chin, the armpits and groin);
- » The pleura, a layer of skin that surrounds the lungs;
- » The bones and joints;
- » The brain and spinal cord.



TB AND HIV

TB is a common and serious co-infection among people living with HIV. Without treatment, HIV and TB worsen each other.

TB is the leading cause of death among people living with HIV, although it can be prevented and cured. **Antiretroviral therapy (ART)**, which is recommended for all people living with HIV, lowers the risk for active TB, as does TB preventive treatment.

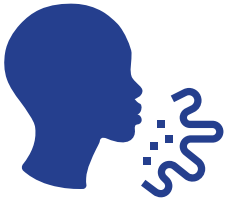
HIV increases the risk for TB, because it weakens the immune system. People living with HIV and LTBI are over 20 times more likely to develop active TB than HIV negative people.

HIV testing is recommended for all people with TB, and TB testing is recommended for all people living with HIV.

TB is more difficult to diagnose in people living with HIV, especially those with a low CD4 cell count (less than 200 cells), as they are more likely to have extrapulmonary TB.

Smear microscopy, a common test for TB bacteria in sputum (mucus from a person's lungs), is less reliable in people living with HIV, because they may be too ill to produce sputum, or because they have lower levels of TB bacteria in their sputum.

Routine TB testing is important for people living with HIV, because active TB, including extrapulmonary TB, can be treated – and cured.



HOW DOES SOMEONE GET TB?

TB is airborne. It spreads from person to person in tiny droplets. These **droplets** go into the air when a person who has TB in their lungs is **coughing, sneezing, spitting, singing or talking.** If another person inhales them, they can become infected with TB.

A person can get TB more than once, even after they were cured by treatment; this is called reinfection. Sometimes, people with TB fall ill soon after finishing treatment; this is called relapse.



HOW CAN TB BE PREVENTED?

Each person can help to prevent TB in their community by:

- » covering their mouth when they are coughing or sneezing;
- » getting tested for TB and taking treatment to prevent them from falling ill with active TB – or to cure active TB; and
- » stopping smoking can help to prevent TB, since smoking increases the risk of, and worsens TB infection.

People living with HIV can **lower their risk of TB** by taking ART and TB preventive treatment. In people living with HIV and LTBI, TB preventive treatment lowers the risk for active TB by 60%.

In South Africa, during 2018, 65% of people living with HIV who entered care were receiving TB preventive treatment.

Table 1. South African recommendations for TB preventive treatment (2014)

Children living with HIV, all ages	Isoniazid, 8–12 mg/kg (up to a maximum of 300 mg per day) for at least 6 months
Adults living with HIV, including pregnant women	Isoniazid, 4–6 mg/kg (up to a maximum of 300 mg per day) for at least 6 months



World Health
Organization

WORLD HEALTH ORGANIZATION RECOMMENDATIONS FOR TB PREVENTIVE TREATMENT (2020)

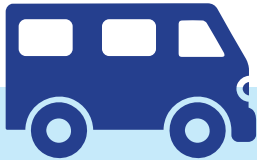
WHO recommends TB
preventive treatment for:

- » Infants (age less than 12 months) living with HIV who have had close contact with a person who has TB and are unlikely to have active TB, or as recommended by national TB guidelines
- » Children (age 12 months or more) living with HIV who are unlikely to have active TB, if they live in settings with high TB rates
- » All children living with HIV who have successfully completed active TB treatment
- » Adults and adolescents living with HIV, including pregnant women, who are unlikely to have active TB.

Table 2. WHO-recommended regimens for TB preventive treatment in all settings, regardless of HIV status*

PREFERRED
6 or 9 months of daily isoniazid
3 months of weekly rifapentine plus isoniazid
3 months of daily isoniazid plus rifampicin
ALTERNATIVE
1 month of daily rifapentine plus isoniazid
4 months of daily rifampicin

*For people living with HIV, avoid drug interactions between rifampicin/ rifapentine and ARVs.



OPEN THE WINDOWS

TB spreads on crowded, poorly ventilated public transport. Opening the windows of taxis, buses and trains lowers the risk.

Healthcare facilities also have a role in TB prevention. Since TB spreads in crowded indoor setting where no fresh air or sunlight can come in, it is important for healthcare facilities to practice infection control in waiting areas, including:

- » Keeping the windows open
- » Avoiding overcrowding and long waiting times
- » Posting information about covering your mouth when you cough or sneeze
- » Giving people who are coughing masks and tissues
- » Separating people who are coughing
- » Asking people if they have TB symptoms



WHAT HAPPENS TO PEOPLE WITH TB?

Untreated TB can be deadly, especially for people living with HIV. It can cause permanent lung damage that worsens over time, making it hard for people to breathe and putting them at risk for other illnesses.

TB SYMPTOMS

The most common symptoms of TB in the lungs are:

- » A cough that lasts for more than two weeks
- » Fever
- » Night sweats
- » Losing weight
- » Not feeling hungry
- » Tiredness

With extrapulmonary TB, the most common symptoms are:

- » Fever
- » Night sweats
- » Losing weight

Other symptoms depend on which part of the body TB has infected.



TB TESTING

All people living with HIV should be tested for TB regularly, and all people with TB should be tested for HIV.

LTBI TESTING

WHO recommends LTBI testing and TB preventive treatment for people of all ages who are living with HIV. LTBI testing is done by a tuberculin skin test or blood test.

ACTIVE TB TESTING

TB can be more difficult to diagnose in people living with HIV, especially if the CD4 cell count is low (less than 200 cells). Smear microscopy, a common test for TB bacteria in sputum (mucus from a person's lungs), is less reliable in people living with HIV, because they may be too ill to produce sputum, or because they have lower levels of TB bacteria in their sputum.

A rapid urine test, called **TB-LAM**, has been recommended by WHO for **improving TB diagnoses in people living with HIV who have a low CD4 cell count** (less than 100 cells) and TB symptoms, or for all people living with HIV who are very ill.

Since 2014, South Africa has recommended **Xpert MTB-RIF as the first test for everyone who has signs and symptoms of TB**. It can diagnose TB and resistance to a powerful first-line TB drug called rifampicin in just two hours.

People who have rifampicin resistant TB need additional tests to see which TB drugs will work for them. (See TB Drug Resistance, page X)

EXTRAPULMONARY TB

People living with HIV are more likely to have extrapulmonary TB.

Different tests are used to diagnose extrapulmonary TB, depending on where it is in the body, including biopsy, (where a small sample of tissue or fluid is removed and examined under a microscope).

TREATING TB AND HIV

ART is recommended for all people living with HIV, at any age or CD4 cell count, and during treatment for all forms of TB. People living with HIV who have not started ART should begin it soon as possible – and within eight weeks of starting TB treatment.

During 2018, 75% of people living with HIV were successfully treated for TB in South Africa.

Taking TB and HIV medicines regularly is the most important thing a person can do to ensure that their treatment will work. Managing treatment for HIV and TB can be difficult; people may need support and counselling to help them with side effects and adherence.



ADHERENCE TIPS

It is important to get information and advice to help you adhere to your HIV and TB treatment, such as:

- » The number and size of tablets and how many times a day do you need to take them
- » If they need to be taken with or without food
 - » Taking pills can become part of your daily routine, just like brushing your teeth
 - » An alarm can help remind you to take your TB and HIV treatment.
 - » Ask your family or friends for help with reminders to take your TB and HIV treatment
 - » Plan ahead: if you are going away, take extra pills with you
- » How to store them
 - » Try to keep your pills in the same place
 - » Keep an emergency supply with a friend. But remember to keep them in a cool spot and replace them before they get too old.
- » What the side effects are
 - » Go to your clinic if you have side effects

Ask about getting extra support from a treatment counsellor at your clinic.



The type and length of treatment for TB differs, depending on whether it is drug-sensitive (DS-TB, meaning that it can be successfully treated with isoniazid and rifampicin) or drug-resistant (DR-TB), and which drugs it is resistant to.

Table 3. TB drug side effects

DRUG	USE	COMMON SIDE EFFECTS
Bedaquiline	DR-TB	Nausea, weight loss, joint pain, headache, chest pain, coughing up blood, rash, elevated liver enzymes and amylase levels
Clofazamine	DR-TB	Nausea, stomach pain, vomiting, appetite loss, heartburn, indigestion, constipation, diarrhoea, pain in the chest and throat, skin discoloration, dry or itchy skin
Delamanid	DR-TB	Nausea, vomiting, headache, dizziness, abnormal heartbeat
Ethambutol	DS- TB	Nausea, vomiting, stomach pain, appetite loss, numbness and tingling in the hands and feet
Isoniazid	DS-TB, LTBI	Nausea, vomiting, stomach pain, diarrhoea, tingling or burning in the hands and feet, abnormal liver enzyme levels
Levofloxacin	DR-TB	Nausea, vomiting, stomach pain, heartburn, diarrhoea, constipation, vaginal itching and/or discharge
Linezolid	DR-TB	Nausea, vomiting, stomach pain, diarrhoea, changes in the way food tastes, white patches in the mouth, change in the colour of the teeth or tongue, headache, dizziness, rash, itching, vaginal burning, itching or irritation
Pretomanid	DR- TB	Nausea, vomiting, stomach pain, appetite and weight loss, heartburn, constipation, diarrhoea, headache, rash, dry skin, itching, acne, difficulty falling or staying asleep
Pyrazinamide	DS-TB	Vomiting, appetite loss, fever, skin rash, yellow skin or eyes, painful or swollen joints, dark urine, difficulty urinating, unusual bruising or bleeding
Rifampicin	DS-TB, LBTI	Nausea, vomiting, diarrhoea, gas pain, heartburn, stomach cramps, appetite loss, yellow, temporary changes in the colour of your skin, teeth, saliva, urine, stool, sweat, and tears (to reddish-orange, or brown) n itching, flushing, headache, dizziness, clumsiness, muscle weakness numbness, pain in arms, hands, legs and feet, drowsiness, difficulty concentrating, confusion, behaviour change, vision changes, painful or irregular menstruation
Rifapentine	LTBI	Temporary changes in the colour of your skin, teeth, saliva, urine, stool, sweat, and tears (to yellow, reddish-orange, or brown), dizziness, fainting, and sweating
Terizidone	DR-TB	Nausea, vomiting, rash, severe depression, panic attacks, psychosis, seeing and hearing things that are not there, paranoia, slurred speech, dizziness and convulsions



DRUG-SENSITIVE TB TREATMENT

In South Africa, there is a standard treatment for drug-sensitive TB for people living with HIV: adults, including during pregnancy, adolescents and children over 8 years of age who weigh at least 30 kg.

Infants who do not have TB symptoms should be given isoniazid (10 kg/day) for 6 months. Infants with TB symptoms should be given standard TB treatment.

Table 4. South African standard treatment of new and previously treated TB, including extrapulmonary TB), 2017

Body weight	Intensive phase (Daily for 2 months) rifampicin (150 mg), isoniazid (75 mg), pyrazinamide (400 mg), ethambutol (275 mg)	Continuation phase (Daily for 4 months)
30-37 kg	2 tablets	2 tablets: rifampicin (150 mg) and isoniazid (75 mg)
38-54 kg	3 tablets	3 tablets: rifampicin (150 mg) and isoniazid (75 mg)
55-70 kg	4 tablets	2 tablets: rifampicin (300 mg) and isoniazid (150 mg)
Over 70 kg	5 tablets	



TB DRUG RESISTANCE

Drug resistance happens when TB changes its structure in a way that **stops a drug from working**. TB drug resistance can develop from missing doses, treatment interruptions, drug stockouts and other circumstances.

Some people are infected with a form of TB that is already resistant to one or more drugs, even though they have never taken TB treatment. Sometimes people who have taken TB treatment in the past – even for a short time – will develop drug resistance.

DRUG-RESISTANT FORMS OF TB

There are different forms of drug-resistant TB:

- » **Rifampicin-resistant TB (RR-TB):** a form of TB that is resistant to the drug rifampicin, and possibly other first-line TB drugs. It can be treated the same way as **MDR-TB**.
- » **Rifampicin-susceptible, isoniazid-resistant TB (Hr-TB):** a form of TB that is resistant to isoniazid.
- » **Multi-drug resistant TB (MDR-TB):** a form of TB that is resistant to at least rifampicin and isoniazid.
- » **Extensively drug resistant TB (XDR-TB):** a form of TB that is resistant to rifampicin, isoniazid, fluoroquinolone drugs and at least one injectable TB drug.

Drug-resistant forms of TB are harder to treat than drug-sensitive TB, but treatment for drug-resistant TB is improving.

In 2018, **85% of people with drug-sensitive TB were successfully treated**, versus 56% of people with RR/MDR-TB and 39% of people with XDR-TB.

Newer TB drugs with fewer side effects have also increased cure rates among people with drug-resistant forms of TB and are now included in treatment guidelines (see Appendix).



Q AND A

1. WHAT IS TB?

TB, the world's deadliest infectious disease, is caused by bacteria called *Mycobacterium tuberculosis*.

2. HOW DOES A PERSON GET TB?

TB spreads from person to person in tiny droplets that go into the air when a person who has TB in their lungs is coughing, sneezing, spitting, singing or talking. If another person inhales them, they can become infected with TB.

3. WHAT IS LTBI?

Most people have latent TB infection (LTBI), which means that their immune system is stopping TB from making them ill. People with LTBI do not have symptoms, and they cannot transmit TB.

LTBI can develop into active TB. Overall, 5 to 10 percent of all people with latent TB develop active TB, but people living with HIV are 20 times more likely to develop active TB.

4. WHY DOES TB MATTER TO PEOPLE LIVING WITH HIV?

TB is the leading killer of people living with HIV although it can be prevented and treated.

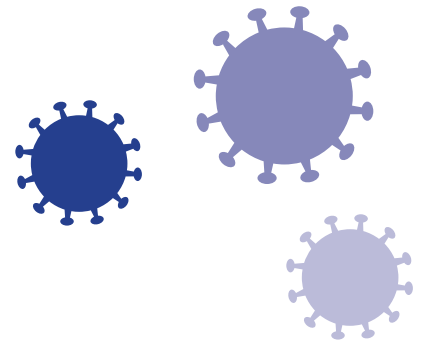
5. HOW CAN TB BE PREVENTED?

Avoiding crowded places with no air circulation and opening the windows in clinic waiting rooms and on public transportation can lower the risk of TB

TB preventive treatment can stop LTBI from developing into active TB, and TB treatment prevents active TB from spreading.

6. WHAT CAN HAPPEN TO A PERSON WITH TB?

Untreated TB can be deadly, especially for people living with HIV. It can cause permanent lung damage that worsens over time, making it hard for people to breathe and putting them at risk for other illnesses.



7. WHAT ARE TB SYMPTOMS?

The most common symptoms of TB in the lungs are:

- » A cough that lasts for more than two weeks
- » Fever
- » Night sweats
- » Losing weight
- » Not feeling hungry
- » Tiredness

The most common symptoms of TB in other parts of the body are:

- » Fever
- » Night sweats
- » Losing weight

8. HOW IS TB TREATED?

TB is treated with a combination of drugs for 6 to 20 months. The length and type of treatment depends on what kind of TB a person has.

9. WHAT IS DRUG-SENSITIVE TB?

Drug-sensitive TB is usually cured by six months of treatment with a combination of drugs.

10. WHAT IS DRUG-RESISTANT TB?

Some forms of TB need to be treated for a longer time, and with certain medicines because it has become resistant to one or more of the drugs used to treat it. Drug-resistant TB takes longer to cure than drug-sensitive TB.

APPENDIX

Table 5. South African interim clinical guidance for implementation of injectable free-regimens for rifampicin-resistant tuberculosis in adults, adolescents and children, 2018*

SHORT REGIMEN	
For adults, adolescents and children with RR/MDR-TB including people living with HIV, pregnant women, extrapulmonary TB, with no prior use (for over a month) of second-line TB treatment	
Intensive phase - 4 to 6 months, according to treatment response	Continuation phase: 5 months
Adults and adolescents linezolid (for 2 months), bedaquiline (for 6 months), high-dose isoniazid (for up to 6 months) levofloxacin, clofazimine, pyrazinamide and ethambutol	Continue levofloxacin, clofazimine, pyrazinamide and ethambutol
Children ages 6-12 years , or weighing 15-30 kg, use delamanid instead of bedaquiline (for 6 months)	
Children under age six or weighing less than 15kg, use linezolid (for 2 months), <i>P</i> -aminosalicylic acid, high-dose isoniazid (for up to 6 months) levofloxacin, clofazimine, pyrazinamide and ethambutol	
LONG REGIMEN	
For adults, adolescents and children with RR/MDR-TB, including people who have had more than one month of treatment with second-line TB drugs, people with pre-XDR- and XDR-TB (and their close contacts), people with other forms of drug resistance, people with complicated extrapulmonary TB and people with extensive TB disease in their lungs	
Intensive phase – 6 to 8 months, according to treatment response	Continuation phase: 12 months
linezolid, bedaquiline, levofloxacin, clofazimine, terizidone	

*Choice of drugs and length of treatment is based on drug resistance testing

TABLE 6. WHO recommendations for treating drug-resistant TB, 2020 (including for people living with HIV, with consideration of drug interactions between TB treatment and ARVs)

ISONIAZID-RESISTANT TB	RIFAMPICIN- and MULTI-DRUG RESISTANT TB	EXTENSIVELY DRUG-RESISTANT TB
<p>Rifampicin, ethambutol, pyrazinamide levofloxacin</p> <p>6 months</p>	<p>Shorter regimen (9-12 months) for people who do not have resistance to fluoroquinolones or other drugs used in this regimen, and have not taken any of these medicines for more than a month, do not have severe extrapulmonary TB or extensive TB disease, are not pregnant, and are older than six years of age</p> <p>Longer regimen (18-20 months): at least 4 drugs, comprised of 3 Group A drugs (levofloxacin or moxifloxacin, bedaquiline and linezolid) and 1 Group B drug (clofazimine, cycloserine or terizidone) – if only 1 or 2 Group A drugs are used, include both Group B drugs; if it is not possible to make a regimen from Group A and Group B drugs, add Group C drugs (ethambutol, delamanid, pyrazinamide, imipenem-cilastatin or meropenem, amikacin or streptomycin, ethionamide or prothionamide, P-aminosalicylic acid) to complete it.</p>	<p>Bedaquiline, pretomanid and linezolid can be used in the context of operational research (for people who have never been treated with bedaquiline and linezolid, or were given these drugs for less than 2 weeks)</p> <p>6–9 months</p>

RESOURCES

Cited July 2020

- Clinical Guidelines & Standard Operating Procedure for the Implementation of the Short & Long DR-TB regimens for Adults, Adolescents and Children November 2018 https://www.westerncape.gov.za/assets/departments/health/tuberculosis_-_dr-tb_clinical_guidelines_2018.pdf
- Interim Clinical Guidance for the Implementation of Injectable-Free Regimens for Rifampicin-Resistant Tuberculosis in Adults, Adolescents and Children 2018 http://www.tbonline.info/media/uploads/documents/dr_tb_clinical_guidelines_for_rsa_september_2018.pdf
- South African National TB Guidelines – Adults March 2017
- http://www.mic.uct.ac.za/sites/default/files/image_tool/images/51/TB%20Adult.pdf
- National Tuberculosis Management Guidelines 2014. Health Department, Republic of South Africa
- http://www.tbonline.info/media/uploads/documents/ntcp_adult_tb-guidelines-27.5.2014.pdf
- WHO. Global Tuberculosis Report. 2019. <https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf?ua=1>
- WHO Guidelines on Tuberculosis Infection Prevention and Control – 2019 Update
- <https://apps.who.int/iris/bitstream/handle/10665/311259/9789241550512-eng.pdf>
- WHO. Operational Handbook on Tuberculosis: Module 1: Prevention: Tuberculosis Preventive Treatment
- <https://apps.who.int/iris/bitstream/handle/10665/331525/9789240002906-eng.pdf>
- WHO. Operational Handbook on Tuberculosis. Module 4: Treatment
- Drug-Resistant Tuberculosis Treatment 2020
- <https://www.who.int/publications/item/9789240006997>