THE STATE OF TB

IN SOUTH AFRICA

WHAT ABOUT TB MORTALITY?

A report by the TB Accountability Consortium
March 2024

TB Accountability Consortium

ACKNOWLEDGEMENTS

The TB Accountability Consortium was set up in 2021 as a collective that brings together all the stakeholders in the National TB response: policymakers, scientists, activists, researchers and civil society bodies. From the inception of the program, TBAC has set its sights on establishing a platform that reflects on the changing face of health advocacy in the increased visibility of the TB programme. This is through the programmatic, financial and political accountability lens to improve programme outcomes. In this brief space of time, we have been able to form fulfilling partnerships such as those within the SANAC Civil Society Forum and its TB Task Team, TB Proof as well as the Treatment Action Campaign, who have all been instrumental in sharing their inputs.

We would like to dedicate this report to those who have lost their lives or loved ones to TB, and to those who have survived to tell their stories. #SITSHELE

PROJECT TEAM

Project oversight and editorial review: Dr Samantha Maughan

Authors: Ms Celene Coleman
Ms Hanifa Mahlangu

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www.witshealth.co.za

www.rhap.org.za

010 601 7427

158 Jan Smuts Avenue, Rosebank, Johannesburg, 2196

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ACRONYMS AND ABBREVIATIONS

ART	Antiretroviral treatment
DR-TB	Drug-resistant TB
DS-TB	Drug-sensitive TB
HIV	Human Immunodeficiency Virus
LAM	Lipoarabinomannan
RHAP	Rural Health Advocacy Project
SOP	Standard Operating Procedures
TB	Tuberculosis
TBAC	TB Accountability Consortium
TPT	TB Preventive Therapy
TUTT	Targeted universal testing for TB
USAID	United States Agency for International Development
WHO	World Health Organization

CONTENTS

As South Africa fights to save the lives of those with TB, the question we must ask is: Who is dying from TB and why?

1

INTRODUCTION

There have been many innovations to advance tuberculosis (TB) care[1], yet it remains a major cause of death. Across the globe, one person dies from TB every 2 seconds.[2] In 2022, this amounted to about 1.3 million deaths;[2] a marked decrease from 2010 when almost 2 million people died from TB.[3]

In 2021, South Africa, which has a high TB burden, had over 304,000 new TB cases and 56,000 people died of TB.[4] This equates to about 832 people contracting TB and 153 dying every day.[4]

The aim of the current South African National TB Recovery Plan is to reverse losses caused by the COVID-19 pandemic and accelerate progress towards ending TB by 2035.[5] In addition to this, the focus of the new South African national TB guidelines on treatment of TB infection (2023) is on providing TB preventive treatment to all individuals exposed to TB.[6] In spite of these efforts, many South Africans are still dying from TB and the numbers remain a concern. As South Africa fights to save the lives of those with TB, the question we must ask is: Who is dying from TB and why?

This report explores the reasons for South Africa's relatively high TB infection and death rates, and what can be done to change the trajectory of this epidemic. Using peer-reviewed and grey literature, it looks at various factors, including co-morbidities and challenges encountered in implementing the TB care cascade, in order to recommend strategies to strengthen TB programmes in South Africa.

> Worldwide, someone dies from TB **every 2 seconds.**[2]

2

BACKGROUND: WHO IS DYING FROM TB IN SOUTH AFRICA?

In 2021, of the 304,000 people who fell ill with TB, 54% were male, 36% were female and 10% were children.[7] Of these, only 172,194 were notified (i.e. officially reported),[7] which suggests that about 43% of people with TB were not linked to care. This would not only lead to a deterioration of the patient's health, but it also contributes to ongoing transmission of TB.

In 2021, South Africa recorded over 304,000 new TB cases, which resulted in **56,000 deaths**. This equates to about 832 people contracting TB and 153 dying from TB every day.[4]

GENDER

According to data from South Africa's National TB Register, men are more likely to die from TB than women.[8] In 2019 it was estimated that there were 1.7 times more TB deaths among men than among women.[9] It is thought that the discrepancy between TB deaths in men and women is due in part to factors such as men's lower participation in HIV-related services,[9] lower TB testing rates,[9] poorer adherence to TB treatment and higher rates of loss to follow-up than women.[8] A South African study in KwaZulu-Natal's rural uMkhanyakude district found that even though conditions such as HIV, elevated blood pressure and elevated blood glucose were more common in women, men were more likely to have active and lifetime TB.[10] Sociological factors like a higher prevalence of smoking and alcohol use among men, compared to women, play a role in higher TB incidence and TB death rates in men.[9]

COMORBIDITIES

THE INTERCONNECTEDNESS OF DISEASES

The design of chronic disease care in low- and middle-income countries like South Africa, often leads to ineffective care of patients with multiple chronic illnesses (multimorbidity).[11] This is of great concern for patient outcomes because people with multimorbidity are at greater risk of disability and premature mortality, and tend to use more healthcare services and resources.[11] Hence, countries like South Africa need an integrated approach or a multi-disease focus in healthcare services, particularly for those in rural areas for whom access to healthcare is even more challenging.

South Africa has a quadruple burden of disease, which includes infectious diseases, non-communicable diseases, maternal and child mortality, and injuries.[11] The co-existence of high rates of HIV and TB alongside non-communicable diseases such as diabetes, exemplifies this multiple burden of disease, and the challenge of managing it.[11] The interaction of these diseases and their various treatment regimens make managing them complex. A 2021 South African study involving over 17,000 people in KwaZulu-Natal's rural uMkhanyakude district, explored the overlap of communicable (infectious) and non-communicable diseases.[10] The study aimed to assess the prevalence and overlap of four diseases: HIV, TB, high blood pressure and diabetes.[10] It found that 2.3% of the study population had two or more controlled diseases and that 9.5% had two or more diseases, one of which was uncontrolled.[10] While the study showed that HIV had the highest prevalence and the highest rate of optimal control, it also highlighted the poor diagnosis and treatment of TB, and of elevated blood glucose and blood pressure.[10]

These findings emphasise the importance of integrated care for chronic diseases in South Africa, to ensure that these intersecting epidemics are optimally managed and controlled.

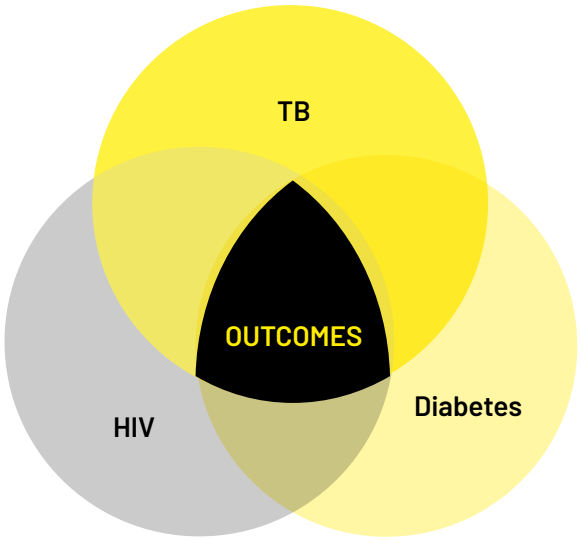


FIGURE 1: The interaction of TB, HIV and diabetes influences TB outcomes for South Africa

RISK FACTORS FOR TB

According to World Health Organization (WHO) 2022 data, many new TB cases are attributable to the following five risk factors:[12]

FIGURE 2: Risk factors for TB

Adapted from World Health Organization. Global tuberculosis report 2023 [Internet]. Henva: World Health Organization; 2023 cited 2024, Jan 15]. Available from https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023

The following section of the report focuses on HIV and diabetes as important co-morbidities and risk factors for TB. Other risk factors, such as gender and sociological factors for TB, and associated mortality rates, will be discussed in later chapters.

> **Globally, of the 630,000 deaths from an HIV/AIDS-related illness in 2022, 30% were due to TB.[15]**

HIV

According to the 2022 Joint United Nations Programme on HIV/AIDS (UNAIDS) World TB Day factsheet, TB remains the leading cause of death in people living with HIV.[13] These individuals are at a much higher risk of progressing to TB illness because of their compromised immune system.[14] Globally, of the 630,000 deaths from an HIV/AIDS-related illness in 2022, 30% were due to TB.[15]

While South Africa showed a general downward trend in HIV-positive TB mortality, with 52 per 100,000 HIV-positive people dying of TB in 2022 compared to 80 per 100,000 in 2015,[16] people with HIV still made up an estimated 57% of TB deaths. These results show that while the implementation of antiretroviral therapy (ART) has assisted in reducing TB mortality in HIV-positive people, HIV is still a major factor in TB deaths in South Africa.

In South Africa, over 8.2 million people are living with HIV, with 5.5 million on ART.[5] With ART, HIV has become a manageable chronic condition[17] and the scale-up of this treatment has ultimately resulted in TB control gains as well, with a reduction in TB incidence and deaths.[5] However, inflammatory processes associated with HIV, even in the presence of ART, may increase the progression from latent to active clinical TB.[15] This may explain why HIV-positive patients who have latent TB are 20 times more likely than HIV-negative patients to develop active disease within five years of initial infection.[18] While ART has been shown to reduce systemic inflammation and immune activation, inflammatory marker levels are nevertheless still much higher in HIV-positive patients compared to those in HIV-negative patients.[15]

Although the South African healthcare system has saved countless lives by successfully implementing ART, it has not as successfully addressed the burden of multimorbidity.[11] Thus, the question remains: Are people with HIV still dying of TB in relatively high numbers because the system has not managed to improve diagnosis and treatment of TB at the same pace as HIV, or is the high percentage of HIV-positive TB deaths a result of the ongoing inflammation caused by HIV, even in the presence of ART?

Perhaps it is a combination of both. Either way, early diagnosis and effective treatment of TB are crucial to preventing deaths in the HIV-positive population.

DIABETES

In 2021, 537 million adults between 20 and 79 years of age, were living with diabetes globally,[19] with an expected rise to 629 million people by 2045.[20] The majority of type 2 diabetes (more than 80%) is found in low- and middle-income countries, and in areas where TB is endemic,[20] which has potentially serious medical and social consequences.

Diabetes increases susceptibility to TB, worsens TB treatment outcomes, and leads to more deaths, treatment failures and recurrent disease, especially when diabetes is poorly controlled.[20] It increases the risk of developing TB up to three times and doubles the risk of TB death during treatment.[20]

The higher death rate amongst patients with both TB and diabetes may be explained by the fact that, in addition to diabetes, TB has an association with increased risk of cardiovascular complications such as heart attack and stroke.[20]

The presence of diabetes is also associated with more severe TB disease, as well as TB drug resistance, slower treatment response and higher toxicity rates.[20] Hence, diabetes worsens the treatment outcomes of TB, which often leads to TB recurrence after treatment, or death.[21]

In South Africa, diabetes is the second general leading cause of death.[22] Modelled data from the District Health Barometer 2018/19 show that South Africa had a diabetes prevalence of 10.6% and a treatment coverage of 35.8%,[23] which implies that many people suffering from the disease are not on treatment.

A study conducted in Khayelitsha in the Western Cape demonstrates why this is of particular concern. Using routinely collected longitudinal data from 440 cases, it was found that the active TB prevalence was four times higher than the national average amongst diabetes patients.[24]

Since diabetes is the second leading cause of death in South Africa[22] and has serious interactions with diseases such as TB, how can diabetes programmes and monitoring be prioritised in South Africa?

KEY MESSAGES

In South Africa, men are more likely to die from TB than women.

An integrated approach is needed to manage people with multiple chronic illnesses.

People with HIV still make up more than half of TB deaths in South Africa.

Diabetes increases the risk of getting and of dying from TB.

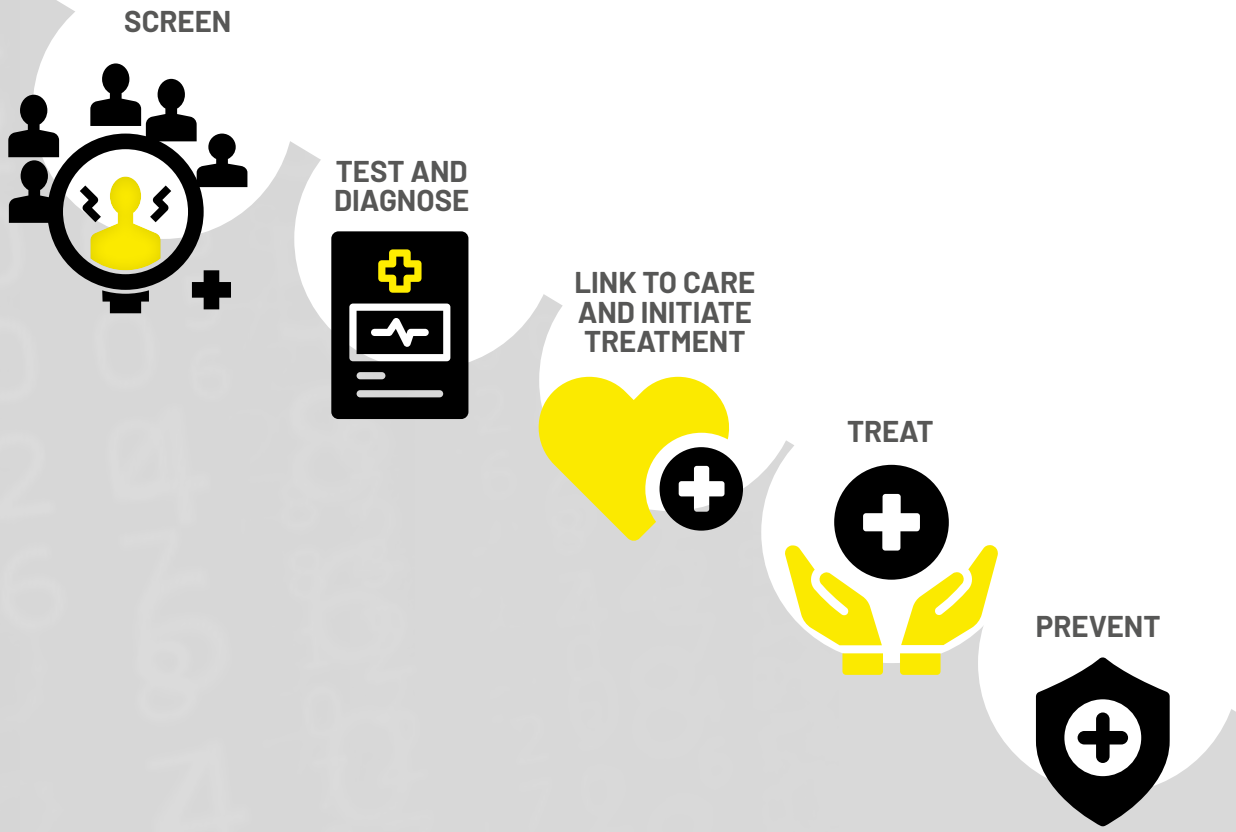
3

THE TB CARE CASCADE

The care cascade "evaluates patient outcomes for a disease across stages of care".[25] Steps in the TB care cascade include finding TB patients, linking them to care and providing them with treatment. In practice, these steps flow into one another, which results in some overlap. In this report, however, the steps are discussed as distinct sections.

The following chapters explore how the different stages in the TB care cascade influence mortality rates by examining the challenges experienced in:

- Screening
- Testing and diagnosis
- Linkage to care and treatment initiation
- Treatment
- Prevention



4

SCREENING

Although TB screening is designed to identify people at risk of TB,[26] many studies have found that symptom screening has a low probability of identifying all potential TB cases.[26–28] This may result in individuals living with undiagnosed TB, which increases their risk of dying from the disease. Every year in South Africa, approximately 150,000 TB cases are missed.[29] Possible reasons for this include missed opportunities to screen for TB, TB cases that are not detected during screening, and poor screening for TB in patients with co-morbidities.

WHAT SHOULD BE HAPPENING: GUIDELINES AND POLICIES

The standard operating procedure (SOP) for TB screening and testing in South Africa includes TB screening of all patients who enter health facilities and of those in targeted community settings.[30] Ideal Clinic policy states that patients should be screened for TB when their vital signs are recorded, through symptom screening: asking about the presence of a cough, fever, weight loss and profuse sweating at night.[31] WHO recommendations for TB screening also include rapid molecular diagnostic tests in people with HIV, and digital chest x-rays.[30]

HOW HEALTHCARE WORKERS AFFECT TB SCREENING

The approach to screening used by healthcare workers influences the screening outcome of a patient, especially when symptom screening is used. A small qualitative study conducted in the Buffalo City Metro district of the Eastern Cape found that healthcare workers often based their decision to screen patients for TB on their cough type and duration, and symptom severity, rather than screening protocol.[32] In addition, the screening questions they used did not always align with South African guidelines.[32] Healthcare workers also noted that a patient's behaviour or attitude might influence whether or not they were screened.[32]

Another mixed methods study in the Amajuba District of KwaZulu-Natal found that the TB screening questions and practices that were used did not always align with Ideal Clinic guidelines and that recording of data on TB screening was incomplete and inaccurate.[31] A qualitative study in King Sabata Dalindyebo sub-district in the Eastern Cape found that although every patient that attended a health facility was meant to be screened for TB, competing disease priorities and daily demands caused TB screening to take a back seat.[33] Healthcare workers in this study reported that TB screening could be overwhelming and their perception was that it was more of a priority to screen for and treat HIV.[33] TB screening challenges of this kind lead to delayed diagnosis of TB, which in turn delays treatment[31] and increases the risk of transmission and death from TB.

TB SCREENING METHODS

The type of screening tool used has an impact on the success of TB screening. A study conducted in the rural Vhembe District in Limpopo concluded that symptom screening is not helpful in identifying TB cases during contact tracing.[34] The study looked at how many of the household contacts of newly diagnosed TB patients also had TB. It found that of the 11 household contacts confirmed to have active TB, 9 (82%) would not have been identified by symptom screening methods because they were asymptomatic.[34] South Africa's first TB prevalence survey showed that 57.7% of TB cases were asymptomatic and would therefore not be picked up with symptom screening.[28] Cases such as these would require screening methods such as digital chest x-rays to identify them.[27,28] The use of sensitive TB screening methods (such as digital chest x-rays) is recommended in other literature as a means to improve the effectiveness of TB screening.[34–36]

In the SOP for TB screening and testing, the National Department of Health has two algorithms for TB screening.[30] For people presenting at health facilities, the algorithm shows that if a person has risk factors for TB such as a previous TB diagnosis, a household TB contact or they are HIV-positive, then a sputum sample should be collected for TB testing regardless of symptoms.[30] In the case of people screened in the community, a patient with no TB symptoms should have a chest x-ray.[30] However, the cost of implementing chest x-rays as a routine screening tool may require further analysis.

In a TB screening study conducted among prison inmates (61,580) in four South African provinces, symptom screening combined with chest x-rays cost $25,560 per 1,000 inmates, compared to a cost of $17,097 for symptom screening only.[37] The use of chest x-rays did, however, help to detect more TB cases.[37] This indicates that if South Africa were to use symptom screening combined with chest x-rays, the number of potential TB cases (including those with subclinical TB) detected during screening would increase, but that, as this study showed, it would be at a considerable additional cost.[37]

A pilot study was conducted in 2021 to evaluate the feasibility of using mobile chest x-rays to screen for TB in South Africa.[38] The study was to be completed in May 2022.[38] However, while an independent assessment of the pilot study was presented at the TB Conference in Durban, no written report was made available to the public at that time.[39] The study aimed to use the outcomes to scale up the use of mobile chest x-rays for screening in other South African provinces but funding for this would have to be requested.[38]

TB SCREENING OF PATIENTS WITH CO-MORBIDITIES

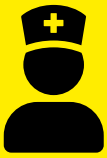
Patients with HIV and diabetes need to be screened because they are at risk of developing TB. Due to the significant interactions of TB, diabetes and HIV, screening simultaneously for all three diseases is strongly recommended, in order to vigorously treat them, and thereby improve TB outcomes in South Africa.[40]

Evidence suggests that TB symptom screening may not be an effective method in those with HIV and diabetes, because a high proportion of these patients are asymptomatic.[24] There is also some overlap between the symptoms of diabetes and TB (for example, weight loss and fatigue). Thus, in people with diabetes, typical TB symptoms do not necessarily help to differentiate TB cases from non-TB cases, which also makes TB symptom screening less effective.[24]

For these reasons, it is recommended that those with HIV be screened using chest x-rays, because a chest x-ray increases the detection of potential TB.[41] The same recommendation may be applicable to those with diabetes as well.

The questions that remain are whether South Africa has the financial resources to roll out digital chest x-rays for large scale TB screening and whether more investment should go into screening, considering the serious implications of missing potential TB cases.

KEY MESSAGES



Healthcare workers and how they implement TB screening, has an impact on its effectiveness.

Symptom screening is not effective for identifying asymptomatic or subclinical TB.

Digital chest x-rays used in TB screening can help identify asymptomatic individuals but are costly to implement.

Screening for TB, HIV and diabetes should happen simultaneously.

Symptom screening is less effective in people living with HIV and diabetes.

5

TESTING AND DIAGNOSIS

TB TESTING, DIAGNOSIS AND LINKAGE TO CARE

In his presentation at the TB Indaba in June 2023, Professor Norbert Ndjeka, the Chief Director of TB Control and Management at the South African National Department of Health, indicated that it is finding people with TB and linking them to treatment which has the greatest impact on TB incidence and mortality.[42] In keeping with this, a South African study using 2013 data cohorts found that of the losses in the TB care cascade, 5% occur at the stage of access to testing, 13% at the point of diagnosis and 12% at treatment initiation.[43] Therefore, just under a third of patients are lost to the TB care cascade in the stage of testing and linking to care. South African data from 2022 show that 99% of people with TB are accessing tests, 91% are being diagnosed and yet only 75% are notified (officially reported) on treatment.[42] While this may indicate an improvement from 2013, the initial loss to follow-up (people diagnosed with TB but not initiated on treatment[44]) remains high. It should be noted that it is not only diagnosis, but also the point in disease progression at which TB diagnosis occurs that is critical.

The WHO's End TB Strategy highlights that early TB diagnosis is essential to reduce the burden of TB.[45] Early detection of TB reduces transmission and may reduce TB morbidity and mortality as well.[46]

FINDING PEOPLE WITH TB

There are numerous challenges to be overcome in the process of finding people with TB and linking them to care:

- How can patients be diagnosed as early as possible in their disease progression?
- What is the most effective way to find and diagnose those with asymptomatic TB?
- How can health professionals get an adequate sample of sputum from the patient? Could other specimen types (e.g., urine) be more effective in testing for TB?
- How can the health system ensure that those who test positive for TB are linked to care?

EARLY DIAGNOSIS AND MISSED CASES

Ideally, TB diagnosis should happen as early as possible in the disease progression.[47] Undiagnosed cases continue to spread TB in their families and communities and because they are not initiated on treatment, they are susceptible to progressing to severe forms of the disease, placing them at increased risk of disability and death.[48]

In some cases, TB diagnosis occurs during an autopsy which means there were missed opportunities for investigations that may have prevented their death. For example, in a study conducted at Tygerberg Forensic Pathology Services in Cape Town, 6.2% of people (48/770) were identified with TB post-mortem (after death), of which 91.7% had never been previously diagnosed.[49] In the 15 cases for which patient pathway analysis was possible, there was documented evidence of primary healthcare attendance or hospital admissions 6 months before they died, which means that there were missed opportunities for diagnosis.[49]

The realisation that a notable proportion of people are being diagnosed with TB after death, leads to the question: Why are they being missed earlier in their disease progression?

AT WHAT POINT IN THE TB DISEASE CONTINUUM ARE PEOPLE BEING TESTED?

Are people being diagnosed when they are still asymptomatic, through active case-finding, or at primary healthcare level in clinics when they present with symptoms? The concern is that many are diagnosed only when the severity of their disease warrants hospital admission or, as the above study indicates, not at all. Publicly available testing statistics do not specify the number of tests done as part of active case-finding, the level of healthcare at which the testing takes place or, the severity of TB disease at the time of diagnosis. It is thus possible that we do not have an accurate picture of whether or not South Africa's testing strategies are effective because we do not know at what point in the disease progression diagnosis occurs.

ACTIVE CASE-FINDING AND TUTT

Active case-finding in the community is one way to increase early TB diagnosis; another is to actively test at the level of primary healthcare facilities.

A study conducted in the rural Vhembe and Waterberg districts of Limpopo compared two active case-finding strategies. One strategy involved facility-based case finding at primary healthcare clinics and the other involved tracing the contacts of newly diagnosed TB patients.[36] In both cases, symptom screening was performed prior to an Xpert MTB/RIF molecular test conducted on the sputum of those with symptoms.[36] Researchers found that the more resource-intensive contact-tracing approach did not increase TB treatment initiation, compared to the facility-based approach in rural areas.[36] However, according to a study in Gauteng, KwaZulu-Natal and Western Cape, more than half of the patients (55%) attending primary care clinics whose sputum tested positive for TB, did not have TB symptoms when screened.[46] The high proportion of people with asymptomatic TB is one of the main reasons for introducing Targeted Universal Testing for TB (TUTT).

According to guidelines, TUTT should be offered at hospitals, primary care facilities and at community level,[48] and focusses on testing the following high-risk groups, regardless of TB symptoms: HIV-positive patients (whether newly diagnosed or as part of their annual follow-up for those on ART), those treated for TB within the past two years, and those who have been in close contact with a TB patient in the past year.[30] The results of a 2019 study suggest that TUTT assists in reducing undiagnosed TB in high prevalence settings.[50] This study, which was conducted in three South African provinces (including both rural and urban areas), found that TUTT diagnosed 14% more patients compared to the symptom-directed TB testing, and showed a 17% relative increase in TB patients diagnosed per month compared to the previous year.[50]

EFFECTIVE USE OF TESTING RESOURCES

COST-EFFECTIVENESS

It has also been found that TUTT of TB contacts attending clinics may be a more cost-effective alternative to community and home-based screening for TB,[46] which is in keeping with the results from the Vhembe and Waterberg districts.

POINT-OF-CARE TESTING

The Xpert MTB/RIF test for TB is a molecular test that can provide rapid diagnosis of TB and drug resistance.[51] One of the advantages of Xpert technology is that it can provide point-of-care testing with results in about two hours.[51] In South Africa, however, it is still performed in a laboratory setting.[51] This is because a 2011 cost analysis showed that it was substantially less expensive to place the Xpert technology in existing smear microscopy laboratories than at point-of-care (in primary care clinics), and that the benefit to patient outcomes of point-of-care placement would have to be "equally substantial to justify the additional cost".[52] After a recent examination of more than a decade of GeneXpert testing technology for TB in South Africa (2011 to 2023), researchers concluded that true point-of-care testing should be explored to improve linkage to care.[51]

TB CARE CASCADE: TESTING AND DIAGNOSIS

A study in Gauteng, KwaZulu-Natal and Western Cape showed that more than half of patients (55%) attending primary care clinics whose sputum tested positive for TB, did not have TB symptoms when screened.[46]

SPECIMEN TYPE

The same study also showed that while sputum is the most common type of specimen used to diagnose pulmonary TB, it has high rates of unsuccessful tests.[51] This has led researchers to conclude that not only should the quality of collected specimens be improved but that other specimen types should also be introduced for TB testing (e.g., stool in diagnosis of children, and urine).[51] Sputum samples may also be difficult to obtain in certain populations, such as children, HIV-coinfected patients[53] or in those with no symptoms. There is thus a need for TB tests that use alternative specimen types.[53]

Urine lateral flow lipoarabinomannan (LF-LAM) assay is a point-of-care test that takes 25 minutes to yield a result, and detects a bacterial product of TB in the urine.[45] However, due to its sensitivity, LF-LAM is currently only recommended for diagnosis of TB in HIV-coinfected patients.[45] A study conducted in East London, South Africa, found that urine specimens used in the Xpert MTB/RIF Ultra (Ultra) testing platform diagnosed 68% of those with TB, compared to 45% in the urine LAM test and 34% in a sputum Ultra test.[54] While this demonstrates the diagnostic potential of urine Ultra tests, it was conducted on a specific patient group: those admitted to hospital with advanced HIV and TB symptoms.[54] Further research could determine its usefulness in other groups.

A new test called RISK6 has been evaluated for detecting subclinical pulmonary TB from a blood sample and has the potential to be developed into a rapid point-of-care test.[55] It can also be used for screening for TB and monitoring of TB treatment success.[55]

THE BEST TESTING TECHNOLOGY

The question to be answered is which testing technology will work best in the South African context taking into consideration cost-effectiveness, the need for point-of-care testing, especially at primary care level, and the sizeable patient populations from whom sputum may not be easy to obtain?

KEY MESSAGES

Finding people with TB and getting them into TB care has the greatest impact on the number of new TB cases and on TB deaths.

Early TB diagnosis is critical.

Targeted Universal Testing for TB (TUTT) is part of the active case-finding strategy in South Africa and increases the number of TB cases that are diagnosed.

Alternative specimen types to sputum should be explored to diagnose TB more easily and effectively.

TB CARE CASCADE: TESTING AND DIAGNOSIS

6

LINKAGE TO CARE AND TREATMENT INITIATION

Once a patient tests positive for TB they can be started on treatment.[56] This is a crucial step in the TB care cascade, as delays in treatment initiation increase transmission of TB to others[57] and substantially contribute to TB deaths and the severity of TB disease.[58] However, the treatment initiation step in the TB care cascade is a cause for concern. Only 75% of people with TB in South Africa were notified on treatment in 2022,[42] which infers that a quarter of people with TB are not being linked to care.

A study in Dr Kenneth Kaunda District in North West province, looked at people who had died in a hospital complex between 2008 and 2018.[59] The study found that in those with HIV, 54.7% (4,464/8,160) died of TB or with TB as an underlying disease (compared to 5.0% in HIV negative patients),[59] and 33.8% (2,761) of these patients were not on TB treatment when they died.[59] The implication is that a high percentage of people with TB are not being linked to care and thus never gain access to treatment.

This leads to the question: What are the reasons for this initial/pre-treatment loss to follow-up of TB patients in South Africa?

THE ROLE OF HEALTHCARE WORKERS

In an exploratory study conducted in the Western Cape, patients diagnosed with TB revealed that their delay in linking to care was due to a lack of communication by healthcare workers with regard to: their TB diagnosis, the steps to be taken next and the consequences of not taking those steps.[57] Some received SMS (short message service) notifications to attend primary care clinics but did not understand why, because their diagnosis had not been discussed with them.[57] Another reason given for not attending primary care clinics was that they had no referral information from the hospital to give to the staff at the clinic and thus did not feel empowered to go there.[57]

A study conducted in Johannesburg looked at the effectiveness of ward-based outreach teams (WBOTs) and SMSs in improving the initiation of TB treatment.[60] They found that compared to the control group, the use of SMS reminders shortened the time to treatment initiation after diagnosis.[60] However, if taken in conjunction with the qualitative results from the Western Cape study, it is important that healthcare workers relay to patients that an SMS will be sent with their TB test results and further instructions. Another study showed that factors such as the negative attitudes of healthcare workers, and patients being unsure of their appointment dates also contributed to poor linkage to care.[44]

TESTING PROCEDURES

Literature has shown that the actual testing procedures can be a barrier to accessing treatment.[44] In the absence of point-of-care testing,[51] it is incumbent on patients to come back for results and treatment initiation. A 2017 study conducted in three primary care clinics in the Western Cape showed that only 44% of people returned within the stipulated two days for their TB results, and only 68% returned within the two-month study period.[58] Thus, just under a third of patients did not initiate treatment and around a quarter of patients had delayed treatment initiation. Travel time and income-related costs were significant predictors of whether or not patients returned for results, as was the belief that they would have a positive TB result.[58] The latter would likely impact those who are asymptomatic and tested under the TUTT guidelines, because as results from a qualitative study found, a lack of symptoms or feeling well led participants to disbelieve or ignore their diagnosis, and thus, delay seeking care.[57]

DRUG-RESISTANT TB

Another study in the rural OR Tambo District of the Eastern Cape assessed the effectiveness of the decentralised drug-resistant TB (DR-TB) model of care by looking at how long it takes for DR-TB treatment to be initiated.[61] The results revealed that 36.3% of patients initiated treatment within five days, and of these, 13.4% were initiated on the same day as diagnosis.[61] There was also an improvement in the median time to treatment initiation from 2018 (8 days) to 2021 (5.5 days).[61] While researchers concluded that time to treatment initiation improved with decentralisation of care, for a quarter (25.4%) of patients, time to treatment initiation was longer than two weeks.[61] Their recommendations to improve this include having rapid point-of-care testing technology at the decentralised facilities and catering for patients on weekends.[61]

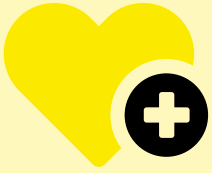
IMPROVING LINKAGE TO CARE

It appears that possible interventions to improve linkage to care centre around solvable changes in testing procedures and the inclusion of comprehensive patient-centred TB counselling services. The question is thus: What steps can the South African health system take now to streamline TB testing procedures and improve patient-centred counselling and care for TB patients?

KEY MESSAGES

Detailed communication by healthcare workers with patients who are testing for TB is essential to ensure that patients receive their TB diagnosis, and know what to do thereafter in order to get started on treatment.

Point-of-care testing and diagnosis may improve linkage to care and treatment initiation in South Africa.



7
TREATMENT

TB TREATMENT SUCCESS RATE

Treatment success rate is a helpful indicator for evaluating the efficiency of TB programmes.[62] Ensuring that TB patients who have been initiated on treatment, continue to take this treatment, has historically been the focus of TB control programmes in South Africa.[44] It remains an important indicator because assessing treatment outcomes is essential to the End TB Strategy, which has set a target of 90% for treatment success rate.[62]

South Africa currently falls short of meeting this target. According to the mobile application for the WHO TB Report (WHO TB App), South Africa had a 79% treatment success rate for new and relapsed cases in 2021.[63] Furthermore, it has plateaued around this level since 2019.[63] For HIV-positive TB cases, the treatment success rate is also at 79%.[63] However, when looking at relapsed TB cases in isolation or at drug-resistant cases, treatment success drops to 60% and 62% respectively.[63]

These results highlight the need to urgently look for and address the factors responsible for the shortfall. To do this, it is important to distinguish between successful and unsuccessful TB treatment outcomes. Successful treatment outcomes include cure (a negative bacteriological result at the end of treatment) and treatment completion (where there is no bacteriological result at the end of treatment).[62] Unsuccessful TB treatment outcomes include death, defaulting treatment, being transferred out, treatment failure, and loss to follow-up.[62] Interruption in treatment for any reason can increase the risk of both drug resistance and adverse TB outcomes.[62]

This section will focus on answering the question: Why are people who are started on TB treatment still dying of the disease?

PATIENT FACTORS

GENDER

Of the 360,000 South Africans who contracted TB in 2019, 53% were adult men, 36% were adult women and 11% were children under 18.[56] In a study conducted in a rural Eastern Cape hospital, women were more likely to have successful TB treatment outcomes than men.[62] Findings like this may be because women access the health system more often, for reproductive healthcare (such as maternal and contraceptive health services).[64]

A qualitative study in the Buffalo City Metro Health District of the Eastern Cape sought to explain the obstacles that impact men's TB treatment adherence.[65] Male study participants described their difficulty in maintaining their jobs while sick or seeking TB care and treatment.[65] Some had even lost their jobs because the TB illness prevented them from performing their duties or because of the perceived risk to other employees.[65] The impact of unemployment on financial resources, combined with the increased need for food on TB treatment, affected adherence. TB treatment increases hunger and many could not afford food while unemployed.[65] Offering TB services at the workplace may present an opportunity to reach men who have TB and improve their treatment success rates.

Of the 360,000 South Africans who contracted TB in 2019, 53% were adult men, 36% were adult women and 11% were children under 18.[56]

SOCIOLOGICAL FACTORS

A study in the rural KwaZulu-Natal towns of Eshowe and Mbongolwane found that 367 of 368 participants with prior episodes of TB had received treatment.[66] Of this cohort, 12 stopped their treatment for one of the following reasons: they felt better; the financial burden of treatment was too great; they lacked support; a healthcare worker recommended that they stop; or, they saw no improvement in their health.[66]

A qualitative study conducted in Ghana also found that sociological factors such as lack of social support, food insecurity, income insecurity, poor knowledge of TB and its treatment, and long travel distances to treatment centres, impact TB treatment adherence.[67] These findings suggest that to ensure better treatment success rates, it is key to address welfare issues by using existing institutions to identify economically vulnerable people and provide them with financial support throughout their treatment.[67]

HEALTH SYSTEM FACTORS

Many patients who are discharged from hospital on TB treatment experience poor continuity of care resulting in failure to continue their TB treatment at other levels of care.[68] According to a retrospective observational study published in 2018, of 788 TB patients in a Western Cape hospital, only 74% received TB bacteriological tests, 48% received TB medication while in hospital and 36% arrived at primary care clinics to continue with their TB treatment after they had been discharged.[68] The study also found that 24% (191/788) had successful treatment outcomes and 21% died.[68] These findings demonstrate the lack of integration of hospital TB data systems and primary healthcare information systems[68] and the impact this can have on continuity of care. They may also support the findings of other studies, which found that patients were not adequately informed of the next steps they needed to take in their treatment journey.[57]

The Ghana study also suggested that comprehensive counselling of TB patients, including anticipated side effects and consequences of poor treatment adherence, might facilitate a better understanding of TB disease, and that communities should also receive education on TB.[67] Medication dispensing hubs that are closer to the communities may also reduce the transport costs of reaching distant clinics and would in turn reduce interruption or discontinuation of treatment.[67]

South Africa has instituted a similar system – the Centralised Chronic Medicines Dispensing and Distribution (CCMDD) service – whereby patients can collect their medication for HIV and other chronic illnesses from pick-up points closer to home.[69] Although findings from an evaluation funded by the Department of Health suggest that the CCMDD has decongested facilities and improved health outcomes,[69] research to better understand patients' experiences of the service may help to optimise its delivery. For example, one patient interviewed for a news article noted that CCMDD is also affected by medication stockouts, medication errors and technical difficulties, for example, the patient did not receive the SMS they needed to access their medication smart locker.[69]

IMPROVING TB TREATMENT SUCCESS RATES

These findings lead to the question: How can the health system provide more patient-centered TB services with both initial and ongoing support for patients during treatment?

EFFECT OF COMORBIDITIES ON TREATMENT SUCCESS

TB AND HIV INTERDEPENDENCY

HIV co-infection may have an impact on TB treatment success. A rural Eastern Cape study of treatment outcomes for DR-TB patients in hospital found that HIV–TB coinfection made treatment more difficult and resulted in unfavourable treatment outcomes.[62] Reasons for poor TB treatment outcomes in HIV co-infected TB patients included drug interactions, inadequate disease information, having a high pill burden and poor absorption of TB medication.[62]

TB AND DIABETES INTERDEPENDENCY

The notable interaction between diabetes and TB is outlined earlier in this report. Diabetes may increase the severity of TB disease and, as studies have demonstrated, it may also have a negative effect on TB treatment outcomes, including doubling the risk of death during TB treatment.[20] Many of the issues noted in the treatment of patients with HIV–TB coinfection are also relevant to

diabetes–TB comorbidity. These include drug interactions, increased risk of side effects and drug toxicity, and polypharmacy.[20] The presence of diabetes may also necessitate longer duration and higher doses of TB treatment.[20]

INTEGRATION OF SERVICES

The integration of services and integration of health data systems are two key health system variables underlying TB mortality in South Africa.[70] How can the health system better integrate service delivery and data systems to improve TB treatment outcomes?

KEY MESSAGES

South Africa has yet to reach the WHO TB treatment success target of 90%.

Women are more likely than men to have successful TB treatment outcomes, in South Africa.

There is a need to integrate services for treatment of people with multiple chronic illnesses such as TB, HIV and diabetes.

SOCIOLOGICAL FACTORS
that affect TB treatment outcomes in South Africa

- Financial cost of accessing care
- Geographical barriers to health facility access
- Social and treatment support systems
- Risks to employment
- Food security
- Poor knowledge of TB

HEALTH SYSTEM FACTORS
that affect TB treatment outcomes in South Africa

- Lack of integrated data systems
- Functioning of community medication collection strategies
- Inadequate patient counselling on TB and TB treatment

8

PREVENTION

TB PREVENTION STRATEGIES

Suboptimal use of TB prevention strategies has been identified as a health system variable that contributes to TB mortality in South Africa.[70] These TB prevention strategies include a wide range of interventions such as:

- Adequate coverage of bacille Calmette-Guérin (BCG) immunisation at birth
- Effective contact tracing and screening/testing of these contacts
- Infection prevention and control measures in health facilities
- Adequate provision and uptake of TB preventive therapy (TPT)
- Prevention and treatment of HIV (given the TB-associated morbidity and mortality in HIV).[70]

TB PREVENTIVE THERAPY

Tuberculosis preventive therapy (TPT) is a critical public health intervention that protects individuals and communities from TB.[71] TPT is a course of TB medication given to people who are infected with the TB bacteria but do not have active TB disease, or to those who have been exposed to TB and are at high risk of developing TB disease.[71] The treatment is intended to eliminate the TB bacteria from the patient's body before it has the chance to cause illness or damage organs, and thus, can substantially reduce the risk of progressing to active TB.[71] TPT is offered to individuals of all ages who may be at risk of developing TB disease, including those exposed to people with active TB, those who have HIV or other conditions that weaken their immunity.[71]

According to the WHO South African country profile, 306,598 newly enrolled HIV patients and 17,012 children under the age of five who were household contacts of people with bacteriologically confirmed TB, were on TB preventive treatment in 2021.[7] However, there was no data for household contacts over the age of five years.[7]

A pragmatic review, using multiple data collection methods, was conducted between May 2019 and January 2020, to assess the effectiveness of TPT implementation in South Africa.[72] Although TPT has the potential to save many lives, the study found that implementation of the programme remains suboptimal in South Africa.[72] Reasons for this included healthcare worker reservations linked to scepticism about the effectiveness of TPT and fears that patients would develop resistance to Isoniazid (one of the TB medicines used in TPT).[72] Due to limited time, healthcare workers also tended to prioritise TB and HIV treatment over prevention.[72] Logistical issues included ineffective contact tracing, resource shortages (necessitating the dispensing of adult TPT to children in some cases), lack of standardised data capturing and reporting procedures, and insufficient patient education.[72]

IMPROVING IMPLEMENTATION OF TB PREVENTATIVE STRATEGIES

In light of the above, how can the health system provide more in-depth healthcare worker training, as well as patient and community education on TB prevention strategies, including TPT?

KEY MESSAGES

TB prevention strategies include immunisation, contact tracing, measures to prevent the spread of TB in health facilities, TB preventive therapy (TPT) and treating HIV.

TPT involves giving TB medication to prevent people who have the TB bacteria in their bodies from developing active TB disease.

TPT implementation in South Africa has faced some challenges and remains suboptimal.

9

HEALTH SYSTEM FACTORS IN TB MORTALITY

In early 2020, the Optimising TB Treatment Outcome task team of the TB Think Tank held a convening of TB stakeholders that included academics, clinicians, advocates, members of non-profit organisations and TB programme officials. Drawing on this wide variety of expertise, a systems thinking approach was used to identify possible health system factors that underlie high TB mortality rates in South Africa and develop a causal loop diagram.[73] This section focuses on leadership and governance in TB programmes, and accessibility of TB services.[73]

GOVERNANCE AND LEADERSHIP

In the 2023 edition of the State of TB in South Africa report, entitled *Closing Governance Gaps to Improve Care*,[74] the issue of governance of TB programmes in South Africa was examined in depth. However, the role of governance and leadership in TB mortality was not explicitly discussed. In their causal loop diagram, one of the loops described by Osman et al. was that of "Leadership and management for outcomes".[73] This loop demonstrated that poor leadership and governance increase the burden of bureaucracy (the considerable number of administrative procedures associated with TB management).[73] This in turn has a negative impact on effective implementation of available TB guidelines, which results in decreased accessibility of services, poor integration of services, and ultimately, worse outcomes (e.g., increased TB mortality).[73] To remedy this, Osman et al. recommend transitioning from a model of transactional leadership to one of participatory leadership.[73] Because this style of leadership is collaborative and can draw on diverse perspectives and strengths, it can help to reduce the burden of bureaucracy and improve access to, and integration of, services. Participatory leadership should ideally also include principles of servant leadership which focuses on the needs of others and thus enables a patient-centred TB service.[73]

It should be noted, however, that factors in existing governance structures may hinder participatory styles of leadership. A study on district health councils in five Gauteng districts looked at whether they had been established, and how effectively they were functioning.[75] The study revealed that political tensions and difficult interpersonal relationships had a negative impact not only on the effectiveness of the councils but also on whether they were established at all.[75] Councils that had been established obtained low scores for accountability to the community.[75] Some study participants (members of existing governance structures) felt it was better for the councils to decide what communities require in terms of health service delivery, without input from the community itself.[75] While this view could be influenced by the lack of clarity on how to engage with communities and what information to share, as well as by a lack of awareness of these governance structures within the community,[75] it nevertheless has a negative effect on community participation in health governance.

Although the abovementioned governance issues are not specific to TB, the District Health System is the vehicle for successful delivery of primary healthcare services,[75] and primary healthcare services are essential to early diagnosis of TB, linkage to care and continuity of TB treatment. The link between quality of governance and health outcomes,[75] is thus evident in the pathway of TB mortality.

ACCESSIBILITY OF TB SERVICES

Accessibility of TB services is evaluated in terms of availability, affordability and acceptability. In their analysis, Osman et al. describe availability as the physical access patients have to services in terms of geographical location, operating hours and which services are available.[73] Affordability is equated with financial access and includes the transport costs to the service and the loss of income experienced by the patient while accessing the service.[73] The impact of affordability is outlined in the section on TB testing, diagnosis and linkage to care, where it is shown that the cost of income lost is a significant predictor of patients returning for their TB test results.[58] Acceptability looks at aspects such as the attitude of healthcare workers, waiting times, and patients' experiences and expectations of the services.[73]

The accessibility of services is influenced by the quality of leadership, availability of resources and the capacity of the health workforce, and is part of the "System Capacity" loop.[73] Rural households were listed among those population groups that tend to have suboptimal access to TB services.[73]

STRENGTHENING THE HEALTH SYSTEM

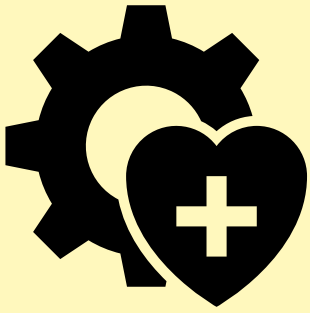
This section leaves us with the following questions:

- What can be done to overcome barriers to a more participatory model of leadership within health governance structures?
- What next steps can the health system take to increase accessibility of TB services to communities and thereby empower patients?

KEY MESSAGES

Participatory leadership in TB programmes is essential to improving TB outcomes, including reducing TB deaths.

Having accessible TB services is another essential element in reducing TB mortality.



10

RECOMMENDATIONS AND CONCLUSION

GENDER

1. **Adapt TB services in order to reach more men.** This would involve creating male-friendly TB services that consider the challenges that prevent men from accessing TB care. An example of this would be taking TB services to the workplace which would help to reduce stigma and also minimise loss of income in accessing TB services. Other factors to take into account for this group are: how to increase HIV diagnosis among men and how to address risk factors such as smoking.

COMORBIDITIES

2. **Integrate services** to address the interconnectedness of diseases like TB, HIV and diabetes.
    a. Integrated services, from combined screening to one-stop treatment access and monitoring, should extend across the TB care cascade.
    b. Integration of services will decrease the cost to patients of accessing services and allow the health system to manage three of South Africa's biggest contributors to mortality more comprehensively.

SCREENING

3. **Engage health professionals to address their concerns and questions and educate** them on the TB screening guidelines. This will help to increase ownership of screening by health professionals and ensure that guidelines are fully explained and correctly implemented with regard to:
    a. Symptom screening
    b. Screening for risk factors of TB (linked to TUTT)
    c. The use of digital chest x-rays for screening and what to do when this service is not available.

4. **Conduct a cost analysis** to assess the feasibility of implementing screening using digital chest x-rays at scale.
    a. If a cost analysis has been done, results should be made available to the public.
    b. If chest x-ray screening is not financially feasible it should perhaps be removed from the guidelines to prevent confusion and incorrect use of resources. Alternative measures to be used when the chest x-ray screening service is not available should also be included in the guidelines.

TESTING AND DIAGNOSIS

5. **Specify the stage in the disease progression** at which patients are diagnosed in TB testing data that is collected (e.g., early through active case-finding vs. when the disease is severe, at the point of hospitalisation). This will help to improve accuracy when assessing the effectiveness of TB testing in South Africa.

6. **Roll out point-of-care rapid-testing technology** so that patients can receive their results and be initiated on treatment in the same visit. This will simplify the testing process and help to improve diagnosis and treatment initiation. It will also decrease the cost to patients of transport and time away from work.

7. **Continue to explore the use of other specimen types** (e.g., urine and blood) in TB testing to make it easier to diagnose patients from whom it may be difficult to obtain a sputum sample e.g., asymptomatic patients. Ongoing research is needed in this regard.

LINKAGE TO CARE AND TREATMENT INITIATION

8. **Institute patient-centred TB counselling** that outlines the process of testing, receiving results and follow-up appointments to initiate treatment so that patients feel confident about the steps they must follow and why. Counselling should also include information on the disease itself and the medication used to treat it (e.g., side effects).

TREATMENT

9. As part of patient-centred TB services, **ensure that sociological factors are addressed**, such as:

    a. Income protection or supplementation while on treatment
    b. Linked to the above point, to ensure food security while on treatment to improve treatment success rates.
    c. Provide psychological and educational support at a primary care level throughout treatment.

10. **Integrate data systems** to ensure that patients can be traced throughout their TB treatment journey and all levels of care in the health system. This will improve continuity of care and help to decrease loss to follow-up.

11. **Conduct research on patients' perspectives of CCMDD** to improve and strengthen service delivery via these platforms.

12. **Provide education for healthcare workers** (especially at primary care level) on the complex management of multimorbidity, including the interaction between the actual diseases, as well as the drug interactions of the medications used to treat them.

PREVENTION

13. **Provide in-depth training for healthcare workers on TPT** to address their concerns regarding resistance to TB medication and to ensure correct implementation of TPT guidelines.

14. **Provide education for patients and communities** to ensure demand creation. This can be done through health facilities, local media platforms and community health workers.

HEALTH SYSTEM FACTORS

15. **Ensure that health governance structures are using a participatory model of leadership** in which communities are actively involved in governance functions and decision-making.

    a. Develop guidelines and training for structures such as district health councils on how to increase participation of communities in health governance and the importance thereof.

16. **Increase accessibility of TB services** by:

    a. Taking services to the people (e.g., TB screening and testing at social gatherings, sports events or the workplace). This is especially important to increase access to rural communities and men.

    b. Extend clinic operating hours to include after hours and weekends, to make services easier to access and to decrease loss of income of patients who access TB services.

CONCLUSION

There are many factors that affect TB mortality in South Africa and it can seem like a daunting task for the health system. However, by asking some pertinent questions, we may be able to find solutions that are acceptable, feasible to implement, and have a big impact on reducing TB deaths.

GLOSSARY

Asymptomatic TB/Subclinical TB: People with asymptomatic or subclinical TB are infected with the TB bacteria but have not yet developed any symptoms of the disease.[28] They can, however, spread the disease to others.[28]

Care cascade: A model created to evaluate patient retention and care across the different stages of disease care needed to achieve successful treatment outcomes.[76]

Co-morbidities: Having two or more diseases at the same time.[77]

Isoniazid: A TB medication that is used to treat TB that can also be used to prevent the development of active TB disease in people who only have TB infection.[78]

Latent TB infection: When an individual is infected with TB bacteria but has no TB symptoms, does not feel sick, and cannot spread TB bacteria to others[79] because the TB bacteria are not yet active.[80] Latent TB can develop into active TB if the bacteria start to grow and cause disease.[80]

LF-LAM (lateral flow urine lipoarabinomannan) assay: A test that detects part of the TB bacteria found in the urine, sputum and blood.[81] LF-LAM is used mostly to detect TB in people living with HIV and can be used as a point-of-care test.[82]

Linkage to care: This is defined differently in different contexts. For TB, it can be defined as being registered as a TB patient and started on TB treatment at a health facility after being diagnosed with TB.[57]

Loss to follow-up: When a patient has been on treatment for at least four weeks, and then discontinues treatment for more than eight consecutive weeks (two months).[83]

Multimorbidity: Patients with multiple chronic illnesses.[11]

Point-of-care testing: When a clinical laboratory test is performed at or close to the site where the patient receives care.[84]

Pulmonary TB: Refers to the infection of mycobacterium tuberculosis (the bacteria that causes TB) in the lungs.[85]

Sputum: Phlegm coughed up from deep inside the lungs.[78]

TB disease/Active TB: The active multiplication (growth) of TB bacteria in the body.[79] An individual with TB disease can spread the TB bacteria and cause infection in others (i.e., it can be spread to other people).[79,86] Also known as active TB.[80]

TB infection: When an individual has been exposed to the TB bacteria but their immune system can contain the infection, so they do not get ill and cannot transmit the infection to others.[86]

Transmission: Transfer of disease from one individual to another.[87]

Xpert MTB/RIF Assay: A test that can detect specific parts of the TB bacteria's DNA[88] and can also detect whether the TB bacteria is resistant to the TB drug Rifampicin.[89] It is a rapid test that can yield results two hours from a patient's sputum sample.[90] It can be used as a point-of-care test.[89]

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