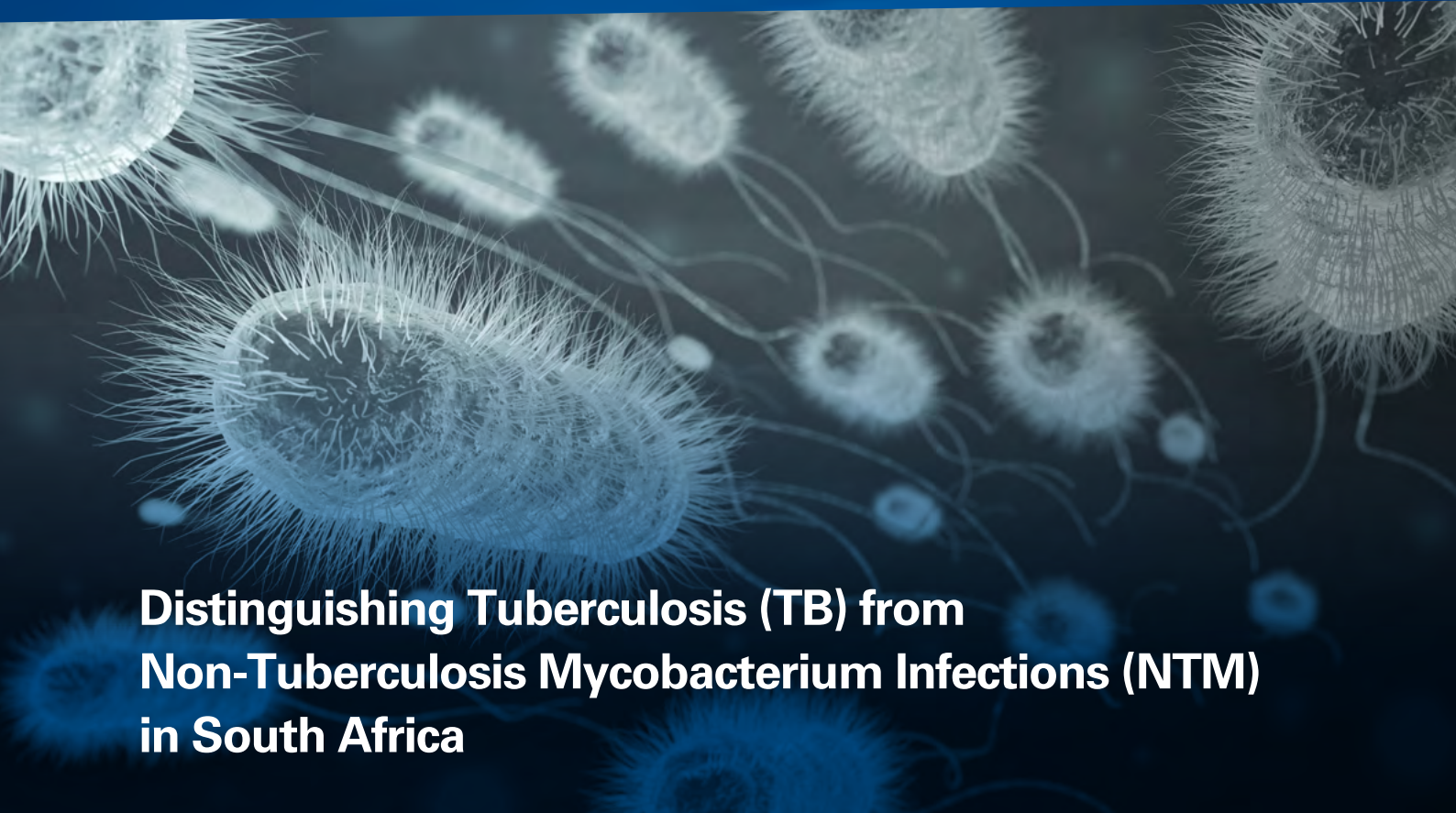


# P O L I C Y   B R I E F

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## Distinguishing Tuberculosis (TB) from Non-Tuberculosis Mycobacterium Infections (NTM) in South Africa

### Executive summary

The 2019 Global Tuberculosis Report by the World Health Organization (WHO) identifies tuberculosis (TB) as one of the top 10 causes of death worldwide. Of the 10 million people diagnosed with TB, approximately 1.6 million deaths were attributed to the disease. In some way, this implies that the 2014 WHO End TB Strategy has not been entirely successful, particularly in poorer countries where fewer resources were allocated for its implementation due to competing priorities. Among the causes of the strategy's failure is the misdiagnosis of tuberculosis (TB), which is sometimes attributed to infections caused by non-tuberculosis mycobacterium (NTM). This poses a critical challenge to South Africa's healthcare system. Misdiagnosed cases of TB compromise treatment efficacy, resulting in resistance to medication, escalate healthcare costs due to unnecessary treatments and, perhaps prolong hospital stays, while delaying appropriate care for affected individuals. Such setbacks threaten the objectives of the National Strategic Plan for HIV, TB, and STIs (2017-2022) to reduce the burden of these diseases in South Africa. Furthermore, they hinder the progress of achieving the goals of the WHO End TB Strategy. There is clearly an urgent need for improved diagnostic capabilities, enhanced clinician training, increased public awareness, and updated policy guidelines to effectively address this growing issue. Thus, this brief's key recommendations include the following:

- Strengthening diagnostic frameworks with advanced molecular tools
- Enhancing clinician (scientific) capacity for NTM-TB differentiation
- Implementing NTM-specific surveillance and reporting systems to increase public health compliance and controls
- Revising national TB guidelines to incorporate NTM protocols to improve efficacy of treatment
- Re-evaluating the critical concentration of anti-TB drugs and optimising drug dosages
- Launching targeted public health campaigns to increase awareness, enhance prevention measures, and mitigate TB transmission by addressing sources of contamination and reducing exposure.

## Introduction

While global TB incidents have decreased, the African continent continues to face challenges with sporadic TB infections. As such, even in South Africa, TB infections continue to place a significant burden on the public health system. However, the rise of NTM infections complicates the diagnosis and care process. NTMs, which exhibit symptoms, such as chronic cough, fever, and weight loss, are frequently misdiagnosed as TB as a result of limitations in the current diagnostic practices. This mismanagement leads to ineffective treatments, prolonged patient suffering and a significant strain on South Africa's already burdened healthcare system. Addressing this issue is vital for achieving the nation's health policy goals, including those outlined in the Sustainable Development Goals (SDGs), particularly SDG 3, which focuses on ensuring healthy lives and promoting well-being for all.

Routine diagnostic tools like sputum smear microscopy and GeneXpert lack the ability to differentiate between NTM and mycobacterium tuberculosis (MTB), resulting in:

- misdiagnosis and inappropriate treatment,
- delayed care for NTM patient,
- increased healthcare costs and burden,
- undermining of TB control programmes and national targets.

## Policy context

As a signatory to international conventions, South Africa fully embraced and implemented the 2014 WHO End TB Strategy. With its relatively strong public health infrastructure and capacity, South Africa has made significant strides in TB management through initiatives like the rollout of GeneXpert and the support provided by the National Health Laboratory Service (NHLS). The NTM are opportunistic pathogens responsible for both pulmonary and extrapulmonary infections. These mycobacteria are commonly found and spread in soils and water ecosystems. Against this background, diagnostic limitations for NTM infections are inevitable and jeopardise the efficacy of these advancements. If this gap is not addressed, South Africa risks falling short of its 2030 TB elimination targets under the WHO's End TB Strategy.

There needs to be an aggressive investment in both budgeting and effective programming to ensure the efficient application of advanced technology, the retention of existing critical skills, and the advancement of medical research. Such a collective effort would position the healthcare system more effectively to better understand these complex pathogens, improve patient care and enhance overall disease control.

Currently, some of the some key issues and challenges include:

- Clinical overlap: Overlapping symptoms between NTM and TB make differentiation challenging.
- Diagnostic gaps: Diagnostic tools like GeneXpert and microscopy are designed to detect MTB and may fail to identify NTM.
- Inappropriate treatments: Anti-TB drugs are ineffective against NTMs, leading to misguided treatment.
- Systemic burden: Misdiagnoses result in inflated healthcare costs and deteriorating patient healthcare outcomes.

## Research method and approach

This policy brief arises from an in-depth analysis of existing data sources, including strategies, annual progress reports, official medical and scientific publications from relevant entities (such as medical laboratories), as well as respective policies and strategies.

## Results and policy implications



TB is an infectious disease that spreads from person to person, while NTM infections are not contagious and do not transmit between individuals. In simple terms, TB is a pulmonary disease caused by mycobacterium tuberculosis (MTB). It significantly impacts human health, leading to widespread morbidity and mortality. Recent epidemiological studies highlight tuberculosis mycobacteria as the cause of lung infections in humans. NTM-based lung diseases encompass a group of disorders where individuals come into contact with mycobacteria that occur naturally in soil and water. These diseases are typically environmental in origin and do not necessarily result in illness.

Although TB and NTM share several fundamental cellular and molecular processes, the susceptibility of hosts to these infections differs. TB is transmitted through the inhalation of aerosol droplets containing MTB, which are generated by patients with symptomatic TB. In contrast, NTM are primarily disseminated through aerosols originating from the environment, such as contaminated soils and water ecosystems.

## Policy recommendations

There are striking differences in the presentation of TB and NTM infections. NTM diseases present in a disseminated, extrapulmonary form as opposed to a miliary or pulmonary presentation commonly seen in TB. Diagnostic modalities for TB, including molecular diagnosis and drug-susceptibility testing (DST), are more advanced and offer a higher rate of sensitivity and specificity, compared to the tools available for diagnosing NTM infections. In general, drug-sensitive TB is effectively treated using a standard multi-drug regimen that includes well-established first- and second-line antibiotics. In contrast to TB, NTM species exhibit significant heterogeneity in their susceptibility to standard anti-TB drugs. Consequently, the treatment of NTM diseases typically involves the use of macrolides, combined with injectable aminoglycosides. Overall, this implies that at the moment, the treatment of NTM diseases remains largely empirical and not entirely successful.

### 1. Enhance diagnostic capacity:

- Deploy advanced tools, such as Line Probe Assay (LPA) and Next-Generation Sequencing (NGS).
- Expand the use of culture-based diagnostics for suspected NTM cases.

### 2. Clinician training:

- Conduct capacity-building workshops focused on improving differential diagnosis skills.
- Integrate NTM-specific systems and guidelines into TB management protocols.

### 3. Surveillance and reporting:

- Establish a national NTM monitoring system under the National Institute for Non-Communicable Diseases (NICD).
- Standardise the reporting of NTM cases across the provinces.

### 4. Revise TB guidelines:

- Update TB programme guidelines to incorporate protocols specifically designed to manage NTM infections.
- Ensure these updates are aligned with WHO strategies for high-burden settings.

### 5. Public health education and awareness campaigns:

- Raise community awareness about NTM infections and their implications.
- Develop educational materials that highlight the importance of accurately diagnosing NTM infections.

## Conclusion

Given the close similarities in the clinical presentation of TB and NTM infections, implementing serious measures to address the misdiagnosis of NTM as TB is essential for strengthening South Africa's healthcare response and achieving TB elimination goals. By adopting these recommendations, the country can ensure effective patient care, reduce systemic burdens, and maintain momentum toward meeting global health targets.

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