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Multidrug-resistant tuberculosis: latest opinions on epidemiology, rapid diagnosis and management

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Purpose of review
This review addresses the escalating global challenge of multidrug-resistant tuberculosis (MDR-TB) in Sub-Saharan Africa, with a focus on its complex comorbidity with HIV/AIDS. Emphasizing the urgency of the issue, the review aims to shed light on the unique healthcare landscape shaped by the convergence of high prevalence rates and intersecting complexities with HIV/AIDS in the region.

Recent findings
A notable increase in MDR-TB cases across Sub-Saharan Africa is attributed to challenges in timely diagnoses, treatment initiation, and patient treatment defaulting. The literature underscores the critical need for proactive measures to address diagnostic and treatment gaps associated with MDR-TB, particularly concerning its comorbidity with HIV/AIDS.

Summary
To effectively manage MDR-TB and its co-morbidity with HIV/AIDS, proactive screening programs are imperative. The review highlights the necessity of active follow-up strategies to ensure treatment adherence and reduce default rates, offering evidence-based insights for improved disease management in the region.

Keywords
comorbidity, epidemiology, HIV/AIDS, MDR-TB, Sub-Saharan Africa

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the *Mycobacterium tuberculosis* (MTB). Until the COVID-19 pandemic, TB was the leading cause of death worldwide from a single infectious agent ranking above HIV/AIDS. It is still among the top 10 causes of death in the world today causing 1.3 million deaths in non-HIV persons and 214 000 deaths among HIV-infected individuals in 2021 [1]. An alarming 7.5 million people were newly diagnosed with TB in 2022 [2], which could be associated with a backlog from previous years due to a halt in healthcare service delivery worldwide from the COVID-19 pandemic. Globally, there has been a decrease in TB mortality from an estimated 1.4 million people in 2021 to an estimated 1.3 million people in 2022 [95% confidence interval (95% CI) 1.18–1.43] [2]. However, this is still a long way from the global targets put forward by the WHO in its 2015 'END TB' strategy. This strategy aims to reduce the absolute number of TB deaths by 95% and the absolute number of new cases by 90% by the year 2035 [3].

The emergence of MTB-resistant strains to TB treatment is the foremost contributing factor in the slow decline of TB incidence and the control of the disease as it leads to multidrug-resistant TB (MDR-TB). MDR-TB has been defined as TB caused by the MTB bacilli that is resistant to at least rifampicin (RIF) and isoniazid (INH), the two first-line medicines used for the treatment of TB [4]. The rise in MDR-TB has long been attributed to treatment defaulting causing difficulties in diagnosis and subsequent treatment. MDR-TB puts an increased burden on the health system in terms of cost, and on the patient due to the longer treatment duration [5]. The estimated world incidence of MDR-TB in 2019 was

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KEY POINTS

- Global challenge: The article underscores the rising global threat of multidrug-resistant tuberculosis (MDR-TB) in Sub-Saharan Africa, calling for urgent interventions.
- Diagnostic gaps: Challenges in timely diagnoses, treatment initiation, and patient defaulting contribute to the surge in MDR-TB cases, emphasizing the need for proactive measures.
- Screening and follow-up: The review advocates for proactive screening and active follow-up strategies to manage MDR-TB and its co-morbidity with HIV/AIDS in Sub-Saharan Africa.
- Healthcare impact: MDR-TB strains healthcare systems, reshaping resource allocation dynamics, and straining existing infrastructure.

465 000 (95% CI 400 000–535 000) with an estimated mortality of about 182 000 (95% CI 113 000–250 000), and according to the WHO 2023 global tuberculosis report, these statistics have been stable [2].

Sub-Saharan Africa has eight of the 30 high MDR/RR-TB burden countries, with six countries (Congo-DRC, Nigeria, Mozambique, South Africa, Zimbabwe, and Zambia) having a high HIV/AIDS and MDR-TB burden [2,6]. As such, sub-Saharan Africa has the highest MDR-TB/HIV co-infections. Despite this, studies have shown that the burden of MDR-TB in sub-Saharan Africa is poorly reported with data being obtained from only 50% of the countries majority of which are from Southern and East African countries [7▪,8]. The objective of this review is to synthesize the most recent MDR-TB epidemiology, diagnostics, and management providing a meticulous examination of the current state of MDR-TB in Sub-Saharan Africa.

SEARCH METHODS

PubMed database and Google Scholar search engine were searched to retrieve articles published in the last five years on MDR-TB in sub-Saharan Africa using search terms: 'Drug-resistant tuberculosis' OR 'MDR' OR 'XDR' OR 'MDTB' OR 'Rifampicin Resistance' OR 'RR-TB)) AND ('sub-Saharan Africa' OR 'Africa'). Only primary quantitative studies were selected from the search output. The title of the study, year of study, study setting, study design, MDR-TB confirmed number of cases, MDR-TB/HIV co-infection proportion, and the outcome explored were characteristics retrieved from the studies (Table 1) [9–13,14▪▪,15–21,22▪▪,23,24▪▪,25–29,30▪,31▪,32–36,37▪▪,38–48,49▪▪,50▪].

EPIDEMIOLOGY OF MULTIDRUG-RESISTANT TUBERCULOSIS IN SUB-SAHARAN AFRICA

Sub-Saharan Africa shoulders a considerable burden of multidrug-resistant tuberculosis (MDR-TB), standing as a focal point for addressing this global health challenge [51–55]. Out of the 30 countries identified with the highest MDR-TB burden, eight are concentrated in Sub-Saharan Africa. The intersection of high MDR-TB prevalence with elevated rates of HIV/AIDS in six of these countries creates a complex healthcare landscape, presenting unique challenges for disease management. Compounding the complexity, the existing literature highlights a pervasive deficiency in comprehensive reporting on MDR-TB, particularly in certain regions.

The WHO Global Tuberculosis Report 2022 reveals consistent proportions among new TB patients, ranging from 3.6 to 3.9%, and among previously treated TB patients, ranging from 18 to 20% (Table 2) [56]. The global trend of incident cases demonstrates a gradual decline, from 517 000 in 2015 to 450 000 in 2021, while the African regional trends show a similar decreasing pattern, declining from 90 000 to 77 000 over the same period [57].

Social and economic factors such as stigma, discrimination, and poverty are some of the factors identified as drivers for MDR-TB in these countries. Studies have reported the highest prevalence of MDR-TB among disadvantaged communities with little to no education, poor housing, and low income [58–60]. Poverty therefore increases the risk of MDR-TB. Patients with MDR-TB have reportedly self-isolated because of rejection from family and community members, or fear of infecting others, which has directly affected their health-seeking behaviours [61].

HIGH-BURDEN COUNTRIES

Eight countries in Sub-Saharan Africa are classified as high-burden for MDR-TB (Fig. 1). These nations bear a substantial proportion of the global MDR-TB burden, confronting significant challenges in disease management and control. These include Angola, Democratic Republic of Congo, Mozambique, Nigeria, South Africa, Somalia, Zambia, and Zimbabwe [56,62].

The geographical and demographic diversity within this list emphasizes the widespread impact of MDR-TB across the region, necessitating targeted and region-specific interventions to address the multifaceted challenges associated with the disease. South and East sub-Saharan African countries are affected by the challenges compared to other regions (Fig. 1).

Table 1. Characteristics of MDR-TB primary studies conducted in sub-Saharan Africa as of 2020

Ref.	Title	Study setting	MDR-TB/HIV co-infection proportion	Design	Confirmed MDR-TB cases	Outcome explored
Mutayoba *et al.* [9]	The second national antituberculosis drug resistance survey in Tanzania, 2017–2018	Tanzania	Data not provided	Cross-sectional survey	1408 (new cases) and 149 (previously treated cases)	Prevalence of anti-TB drug resistance, risk factors and burden of MDR-TB
Bakuła *et al.* [10]	Molecular snapshot of drug-resistant Mycobacterium tuberculosis strains from the Plateau State, Nigeria	Plateau State, Nigeria	Data not provided	Molecular epidemiology study	67	Genetic structure of drug-resistant M. tuberculosis population
Wakjira *et al.* [11]	Treatment outcomes of patients with MDR-TB and its determinants at referral hospitals in Ethiopia	Referral hospitals in Ethiopia	Data not provided	Cross-sectional study	136	Determinants of treatment outcomes in MDR-TB patients
Ghebrekristos *et al.* [12]	Xpert MTB/RIF Ultra on contaminated liquid cultures for tuberculosis and rifampicin-resistance detection: a diagnostic accuracy evaluation	Cape Town, South Africa	Data not provided	Diagnostic accuracy evaluation	Data not provided	Sensitivity and specificity of Ultra on contaminated cultures
Oostvogels *et al.* [13]	Transmission, distribution, and drug resistance-conferring mutations of extensively drug-resistant tuberculosis in the Western Cape Province, South Africa	Western Cape Province, South Africa	Data not provided	Whole-genome sequencing study	461	Geographical distribution, transmission clusters, and drug resistance mutations in XDR-TB strains
Pettit *et al.* [14▪▪]	Rifapentine With and Without Moxifloxacin for Pulmonary Tuberculosis in People with HIV (S31/A5349)	International, 13 countries in sub-Saharan Africa, Asia, and the Americas	8%	Randomized open-label phase 3 noninferiority trial	194	TB disease-free survival, adverse events on treatment
Claassens *et al.* [15]	Whole-Genome Sequencing for Resistance Prediction and Transmission Analysis of Mycobacterium tuberculosis Complex Strains from Namibia	Namibia	Not specified	Not specified	136	Phylogenetic classification, resistance prediction, cluster analysis
Said *et al.* [16]	Determining the risk-factors for molecular clustering of drug-resistant tuberculosis in South Africa	South Africa	Not specified	Not specified	Not specified	Risk factors for clustering, demographic, clinical, and epidemiologic characteristics
Gunar Günther *et al.* [17]	Bedaquiline Resistance after Effective Treatment of Multidrug-Resistant Tuberculosis, Namibia	Namibia	N/A	Case report	N/A	Development of resistance to bedaquiline despite optimal treatment for MDR-TB
Muluwork Getahun *et al.* [18]	Minimum inhibitory concentrations of rifampin and isoniazid among multidrug and isoniazid-resistant Mycobacterium tuberculosis in Ethiopia	Ethiopia	Not explicitly mentioned	MIC testing on Mtb isolates	48 MDR/RR TB cases	Quantification of drug resistance for antituberculosis drugs
Getnet Worku *et al.* [19]	Drug sensitivity of clinical isolates of Mycobacterium tuberculosis and its association with bacterial genotype in the Somali region, Eastern Ethiopia	Somali region, Ethiopia	Not explicitly mentioned	Drug sensitivity testing on *M. tuberculosis* isolates	302 M. tuberculosis isolates	Drug sensitivity of *M. tuberculosis* and its association with bacterial genotype
Achilles Katamba *et al.* [20]	Evaluation of Xpert MTB/XDR test for susceptibility testing of Mycobacterium tuberculosis to first and second-line drugs in Uganda	Uganda	Not explicitly mentioned	Cross-sectional study comparing Xpert MTB/XDR test with reference methods	100 samples	Diagnostic accuracy of Xpert MTB/XDR test for drug susceptibility testing

Table 1 (*Continued*)

Ref.	Title	Study setting	MDR-TB/HIV co-infection proportion	Design	Confirmed MDR-TB cases	Outcome explored
Jupiter Marina Kabahita *et al.* [21]	First report of whole-genome analysis of an extensively drug-resistant Mycobacterium tuberculosis clinical isolate with bedaquiline, linezolid and clofazimine resistance from Uganda	Uganda	Not explicitly mentioned	Whole-genome analysis of a clinical isolate	Two isolates	Identification of extensively drug-resistant M. tuberculosis clinical isolates with specific resistances
Ndjeka *et al.* [22▪▪]	Treatment outcomes 24 months after initiating short, all-oral bedaquiline-containing or injectable-containing rifampicin-resistant tuberculosis treatment regimens in South Africa: a retrospective cohort study	South Africa	Not specified	Retrospective cohort study	1387 (688 bedaquiline group, 699 injectable group)	Treatment success, survival, disease-free survival, loss to follow-up, mortality during and posttreatment
Lindy Dickson *et al.* [23]	Organisation of care for people receiving drug-resistant tuberculosis treatment in South Africa: a mixed methods study	South Africa	Not specified	Mixed methods study	191	Geospatial movement patterns, reasons for patient movement, implications of organisational models
Sacha Roxanne Le Roux *et al.* [24▪▪]	The role of emergent champions in policy implementation for decentralised drug-resistant tuberculosis care in South Africa	South Africa	Not specified	Qualitative study	47	Role, strategies, and organisational context of emergent policy champions
Ntwali Placide Nsengiyumva *et al.* [25]	Scaling up target regimens for tuberculosis preventive treatment in Brazil and South Africa: An analysis of costs and cost-effectiveness	Brazil and South Africa	Not specified	Cost-effectiveness analysis	Not specified	TB cases, deaths, DALYs, costs associated with TB
Helen Cox *et al.* [26]	Whole-Genome Sequencing Has the Potential to Improve Treatment for Rifampicin-Resistant Tuberculosis in High-Burden Settings: a Retrospective Cohort Study	Khayelitsha, Cape Town, South Africa	Not specified	Retrospective cohort study	1274 MDR/RR-TB patient treatment episodes (2008–2017)	Potential regimen changes based on WGS-derived DST, benefits of routine access to WGS-derived resistance prediction
Mark Bateman *et al.* [28]	Adherence Measured Using Electronic Dose Monitoring is Associated with Emergent Antiretroviral Resistance and Poor Outcomes in People with Human Immunodeficiency Virus/AIDS and Multidrug-Resistant Tuberculosis	KwaZulu-Natal, South Africa	Not specified	Prospective cohort study	198 MDR-TB and HIV patients (November 2016–February 2018)	Adherence using EDM, emergent antiretroviral resistance, treatment outcomes
Melaku Tilahun *et al.* [29]	Phenotypic and genotypic drug susceptibility patterns of Mycobacterium tuberculosis isolates from pulmonary tuberculosis patients in Central and Southern Ethiopia	Central and Southern Ethiopia	Not specified	Cross-sectional study	315 culture-positive PTB patients (July 2021 - April 2022)	Drug susceptibility patterns, genotypic versus phenotypic DST discordance
Mahamadou Bassirou Souleymane *et al.* [29]	Safety, effectiveness, and adherence of a short and all-oral treatment regimen for the treatment of rifampicin-resistant tuberculosis in Niger: a study protocol of a pragmatic randomised clinical trial with stratified block randomisation	Niger	Not specified	Randomised clinical trial	Ongoing (April 2021–March 2024)	Safety, effectiveness and adherence of all-oral BDQ/LZD-containing STR versus Niger's RR-TB treatment strategy

Table 1 (*Continued*)

Ref.	Title	Study setting	MDR-TB/HIV co-infection proportion	Design	Confirmed MDR-TB cases	Outcome explored
Iruedo *et al.* [30▪]	Time-to-Treatment Initiation in a Decentralised Community-Care Model of Drug-Resistant Tuberculosis Management in the OR Tambo District Municipality of South Africa	OR Tambo district municipality of Eastern Cape Province, South Africa	Not specified	Prospective cohort study	454	Time-to-treatment initiation (TTTI)
Pietersen *et al.* [31▪]	Variation in missed doses and reasons for discontinuation of antituberculosis drugs during hospital treatment for drug-resistant tuberculosis in South Africa	Multisite study in South Africa	Not specified	Retrospective data analysis	242	Missed doses and reasons for discontinuation
Ejo *et al.* [32]	Strain diversity and gene mutations associated with presumptive multidrug-resistant Mycobacterium tuberculosis complex isolates in Northwest Ethiopia	Northwest Ethiopia	Not specified	Not specified	130	Genetic diversity and gene mutations
Abebaw *et al.* [33]	Pulmonary tuberculosis case notification and burden of drug resistance among children under 15 years of age in Ethiopia: sub-analysis from third-round drug resistance tuberculosis survey	Ethiopia	Not specified	Retrospective secondary clinical and laboratory data analysis	102	Bacteriologically confirmed childhood PTB and drug resistance burden
Kamara *et al.* [34]	Social and health factors associated with adverse treatment outcomes among people with multidrug-resistant tuberculosis in Sierra Leone: a national, retrospective cohort study	Sierra Leone	Not specified	Retrospective cohort study	365	Adverse treatment outcomes
Kilale *et al.* [35]	Economic burden of tuberculosis in Tanzania: a national survey of costs faced by tuberculosis-affected households	Tanzania	80.0% among households of patients with MDR-TB	Cross-sectional survey	777 TB-affected households	Economic burden of TB care, catastrophic costs
Loukman *et al.* [36]	Epidemiology of tuberculosis and susceptibility to antituberculosis drugs in Reunion Island	Reunion Island	1.4% multidrug-resistant TB	Retrospective observational study	265 cases of TB disease	Epidemiological, demographic, microbiological, clinical, and social characteristics
de Araujo *et al.* [37▪▪]	Implementation of targeted next-generation sequencing for the diagnosis of drug-resistant tuberculosis in low-resource settings: a programmatic model, challenges, and initial outcomes	Namibia	Not specified	Programmatic model	Not specified	Implementation challenges of targeted next-generation sequencing
Ali *et al.* [38]	QT Interval Prolongation with One or More QT-Prolonging Agents Used as Part of a Multidrug Regimen for Rifampicin-Resistant Tuberculosis Treatment: Findings from Two Pediatric Studies	Cape Town, South Africa	Not specified	Prospective observational studies	88 children with RR-TB	QT interval prolongation in children with RR-TB receiving QT-prolonging drugs

Table 1 (*Continued*)

Ref.	Title	Study setting	MDR-TB/HIV co-infection proportion	Design	Confirmed MDR-TB cases	Outcome explored
Desta Watumo *et al.* [39]	Predictors of loss to follow-up among adult tuberculosis patients in Southern Ethiopia: a retrospective follow-up study	Southern Ethiopia	Not specified	Retrospective follow-up study	37 LTFU cases observed	Factors predicting LTFU: Age, Education, Lack of family/nutritional support, Distance to health facility
Clara Wekesa *et al.* [40]	Comparing adherence to MDR-TB treatment among patients on self-administered therapy and those on directly observed therapy: noninferiority randomized controlled trial	Uganda	Not specified	Noninferiority randomized controlled trial	164 newly diagnosed MDR-TB patients	Adherence rates between self-administered therapy (MEMS technology) and health facility-based DOT
Joseph Baruch Baluku *et al.* [41]	Association between biomarkers of inflammation and dyslipidemia in drug resistant tuberculosis in Uganda	Uganda	69.0%	Cross-sectional	N/A	Association between inflammation biomarkers and dyslipidemia in patients with DR-TB
Sirak Biset *et al.* [42]	Trends of Mycobacterium tuberculosis and Rifampicin resistance in Northwest Ethiopia: Xpert® MTB/RIF assay results from 2015 to 2021	Northwest Ethiopia	N/A	Retrospective	N/A	Trends in TB and RR-TB prevalence over time, association with age and anti-TB drug exposure
Kamara *et al.* [34]	Social and health factors associated with adverse treatment outcomes among people with multidrug-resistant tuberculosis in Sierra Leone: a national, retrospective cohort study	Sierra Leone	19.4%	Cohort	365	Risk factors for adverse MDR-TB treatment outcomes
Baluka *et al.* [10]	Molecular snapshot of drug-resistant Mycobacterium tuberculosis strains from the Plateau State, Nigeria	Nigeria	Not reported	Cross-sectional	35	Genetic diversity of MDR-TB
Chizimu *et al.* [43]	Genetic Diversity and Transmission of Multidrug-Resistant Mycobacterium tuberculosis strains in Lusaka, Zambia	Zambia	Not reported	Cross-sectional	85	Genetic profile and transmission of MDR-TB
Sebastiao *et al.* [44]	Epidemiological Characteristics and Risk Factors Related to Drug-resistant Tuberculosis in Luanda, Angola	Angola	16.4%	Cohort	55	Risk factors associated with MDR-TB
Mpoh *et al.* [45]	Safety of antituberculosis agents used for multidrug-resistant tuberculosis among patients attending the Jamot Hospital of Yaounde, Cameroon	Cameroon	36.4%	Cohort	107	Adverse drug effects of MDR-TB treatment
Afful *et al.* [46]	Predictors of multidrug-resistant tuberculosis in a teaching hospital in Ghana: A case-control study	Ghana	Not reported	Case–control	37	Risk factors for MDR-TB
de Dieu Longo *et al.* [47]	Risk factors for multidrug-resistant tuberculosis in the Central African Republic: A case-control study	Central African Republic	27.3%	Case-control	70	Risk factors for MDR-TB

Table 1 (*Continued*)

Ref.	Title	Study setting	MDR-TB/HIV co-infection proportion	Design	Confirmed MDR-TB cases	Outcome explored
van de Water *et al.* [48]	The Effect of HIV and Antiretroviral Therapy on Drug-Resistant Tuberculosis Treatment Outcomes in Eastern Cape, South Africa: A Cohort Study	South Africa	63.4%	Cohort	246	Treatment outcomes of MDR-TB/HIV coinfection
Said *et al.* [49▪▪]	Determining the risk factors for molecular clustering of drug-resistant tuberculosis in South Africa	South Africa	60.3%	Cohort	2029	Risk factors for MDR-TB patient clusters
Abdul *et al.* [50▪]	Resistance patterns among drug-resistant tuberculosis patients and trends-over-time analysis of national surveillance data in Gabon, Central Africa	Gabon	35.3%	Cohort	334	Resistance pattern of MDR-TB

Examining the country-specific trends (Fig. 2) in the estimated number of incident cases of multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) from 2015 to 2021 reveals noteworthy variations in Sub-Saharan Africa. South Africa consistently reports a high burden of MDR/RR-TB. Nigeria experienced fluctuations, starting at 16 000 cases in 2015, and reaching 15 000 in subsequent years. Mozambique shows a gradual increase from 4100 cases in 2015 to 4800 in 2021. Conversely, Zimbabwe exhibits a concerning decline from 2200 cases in 2015 to 780 in 2021. These country-specific trends underscore the dynamic nature of MDR-TB incidence, emphasizing the need for tailored interventions and targeted public health strategies [57].

HIV/AIDS CO-AFFECTED COUNTRIES

Among the high-burden countries, four also grapple with a high prevalence of HIV/AIDS (Zimbabwe, South Africa, Zambia, Mozambique) [63–65]. The global burden of MDR-TB and HIV/AIDS specifically has been difficult to ascertain. It has been reported that this lack of global data is because up-to-date anti-TB drug susceptibility testing (DST) and HIV testing are not sufficiently accessible for joint surveillance under routine conditions [66]. As such, the burden in sub-Saharan Africa where the highest burden of TB and HIV co-infections are reported (71%) seems to also be lacking.

This intersection of MDR-TB and HIV/AIDS magnifies the intricacies within healthcare delivery systems. The potentially weakened immune system of people living with HIV (PLHIV) being infected with MDR-TB, the possibility of drug-drug interactions, and the magnified side effects of both treatments pose significant health challenges. It not only amplifies the clinical complexities in managing each condition individually but also introduces unique and compounded challenges at the intersection of MDR-TB and HIV/AIDS [67]. A recent study in South Africa showed that patients being treated for both HIV and MDR-TB had an 8% treatment completion proportion (11/137) and 18% mortality (25/137) [50▪]. Concurrent with this finding, a systematic review of HIV and MDR-TB outcomes in sub-Saharan Africa reported an increased risk of death among HIV-positive patients compared to negative patients (Relative Risk (RR) 1.50, 95% CI 1.30–1.74) [7▪]. It should be noted that this review included 19 studies all conducted exclusively in Southern and East African countries.

DATA-DEFICIENT REGIONS

Despite the overall burden, existing literature reveals significant gaps in comprehensive reporting,

Table 2. Global and African characteristics of MDR/RR-TB, 2015–2021 [56]

Years	Proportion among new TB patient (%)	Proportion among TB patient previously treated (%)	Global trend of incident cases (1000 per year)	African regional trends of incident cases (1000 per year)
2015	3.9 [2.8–5.0]	20 [9.5–31]	517 [432–603]	90 [67–112]
2016	3.8 [2.8–4.8]	20 [9.8–30]	499 [425–573]	84 [65–104]
2017	3.8 [2.8–4.7]	19 [10–29]	480 [414–547]	82 [62–102]
2018	3.7 [2.8–4.6]	19 [10–28]	465 [402–528]	81 [61–101]
2019	3.7 [2.7–4.6]	19 [10–28]	450 [390–511]	79 [59–100]
2020	3.6 [2.8–4.4]	19 [11–26]	437 [390–483]	78 [57–99.0]
2021	3.6 [2.7–4.4]	18 [11–26]	450 [399–501]	77 [55–99.0]

particularly in certain regions of Sub-Saharan Africa. These data-deficient areas pose a challenge to understanding the true extent of MDR-TB and hinder the formulation of targeted interventions [68]. These data deficiencies are not uniformly distributed but are particularly pronounced in certain regions of Sub-Saharan Africa [69].

CHALLENGES IN DIAGNOSIS AND TREATMENT

The surge in MDR-TB cases across Sub-Saharan Africa stems from a constellation of factors, prominently including treatment defaulting [70]. This phenomenon exacerbates the difficulties in achieving timely diagnoses and subsequent treatment initiation. The protracted

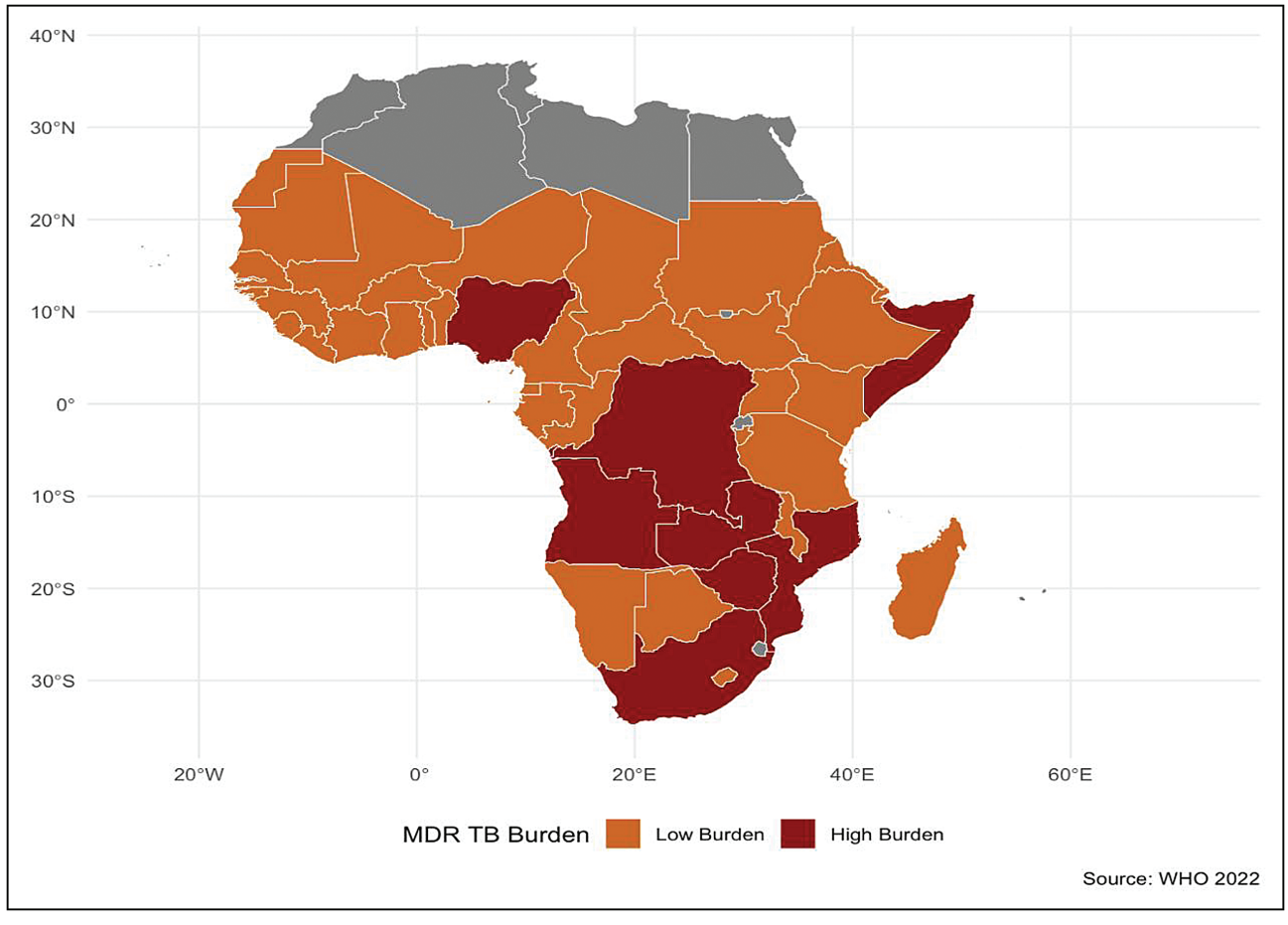

FIGURE 1. MDR-TB burden in Sub-Saharan African countries in 2022. This figure was created using data on the burden of MDR-TB published in the WHO 2022 report.

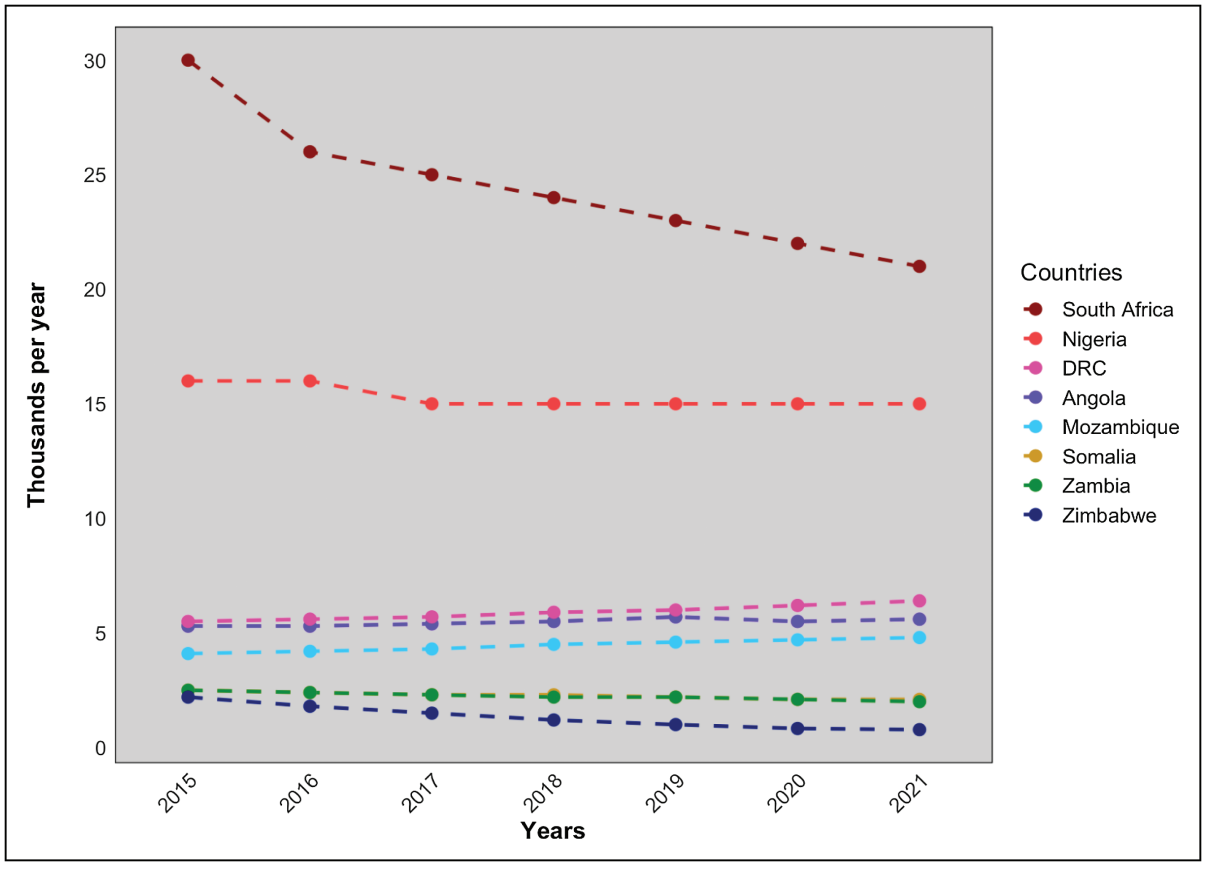

FIGURE 2. Country-specific trends in the estimated number of incident cases of MDR/RR-TB. This figure illustrates the burden over 7 years (2015–2021) in the eight most affected Sub-Saharan African countries. It was constructed using data from the WHO 2022 report.

treatment duration required for MDR-TB, coupled with the increased economic burden on healthcare systems and affected individuals, underscores the urgent need for targeted interventions. Exploring the diagnostic terrain for drug-resistant tuberculosis (DR-TB) in Africa reveals a dual narrative, one of policy progress and another of substantive implementation challenges. Despite the widespread availability of the Xpert MTB/RIF assay in 91% of African countries, the actual utilization, as inferred from testing site density adjusted for population size, reveals considerable variations [71]. This hints at a significant discrepancy between the availability of diagnostic tools and their practical implementation [68].

Furthermore, the identification of primary drug-resistant TB cases poses a considerable challenge. The fact that only 35% of newly diagnosed TB cases undergo rifampicin drug susceptibility testing indicates a substantial number of undetected cases. In many countries, this critical diagnostic step is available for less than 10% of new cases, raising concerns about missed opportunities for early detection [69]. Policies advocating universal drug susceptibility testing are notably absent in 60% of countries, emphasizing the need for a more comprehensive approach to diagnostic strategies. The availability of second-line drug susceptibility testing, while existent in 60% of countries, does not necessarily translate into effective utilization, with only 43% of these countries testing more than half of their notified rifampicin-resistant TB cases [72].

The challenges extend to the laboratory front, where only 55% of national reference laboratories report ISO 15189 accreditation status [73]. However, the actual number of reference laboratories officially recognized as accredited based on external evaluation remains limited, questioning the accuracy of reported accreditation. Beyond diagnostics, the treatment landscape raises concerns about the capacity to meet WHO End TB Strategy targets. While introducing the short-course regimen is a step forward, treatment success rates in Africa remain at 59%, indicating the need for ongoing improvements [74].

IMPACT ON HEALTHCARE SYSTEMS

MDR-TB exacts a toll on healthcare systems throughout Sub-Saharan Africa, reshaping resource

allocation dynamics and straining existing infrastructure. The repercussions extend far beyond individual patients, permeating the broader public health landscape. There are multifaceted challenges faced by health systems, encompassing issues related to diagnosis, treatment, resource distribution, and the overall resilience of healthcare structures. The transformative effects of MDR-TB on healthcare infrastructure require a nuanced understanding to develop targeted interventions that can mitigate these challenges and foster sustainable improvements in disease management.

CONCLUSION

The multifaceted challenge of MDR-TB in Sub-Saharan Africa demands a comprehensive and nuanced approach to address its impact on public health. The epidemiological landscape, characterized by a significant regional burden and intersecting challenges with HIV/AIDS, underscores the urgency of targeted interventions. The existing gaps in comprehensive reporting and knowledge dissemination on MDR-TB in certain regions further highlight the imperative nature of this review. The far-reaching impact of MDR-TB on healthcare infrastructure necessitates a concerted effort to mitigate its cascading effects. The dynamics of resource allocation and the overall public health landscape are affected, requiring a resilient healthcare response. By unravelling the intricate relationship between MDR-TB and healthcare systems, this review serves as a guide for identifying interventions that can fortify the health ecosystem against the challenges posed by this resilient pathogen.

Moving forward, collaborative efforts are essential to bridge data gaps, enhance reporting mechanisms, and implement evidence-based practices. A holistic approach encompassing prevention, diagnosis, and treatment strategies tailored to the unique regional context is paramount. Through sustained commitment to research, education, and healthcare infrastructure development, Sub-Saharan Africa can progress towards achieving the ambitious global targets set by the WHO's 'END TB' strategy. The goal is not only the reduction of MDR-TB incidence but the establishment of resilient healthcare systems that can withstand the complex challenges presented by infectious diseases in the region.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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