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TROPICAL DISEASES OF MOZAMBIQUE (B GRAU, SECTION EDITOR)

Tuberculosis in Mozambique: Where Do We Stand?

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Abstract

Purpose of Review Tuberculosis (TB) is a global health concern, and Mozambique is one of the few high burden tuberculosis countries where the estimated TB incidence has not improved in recent years. The objective of this review is to provide a snapshot of the current situation of the TB epidemic in Mozambique, highlighting the main epidemiological features and particularities of TB care and control in the country.

Recent Findings Despite several efforts aimed at improving diagnosis and treatment success, the overall burden of TB, HIV-TB, and multidrug-resistant (MDR)-TB is enormous, with high TB-associated mortality. Improving surveillance is a key step for understanding the TB epidemic in the country, and the first TB prevalence survey is underway. Overall, drug-sensitive and MDR-TB notifications have increased markedly over the last 5 years, likely due in part to a more active case finding approaches, but the diagnosis gap is still substantial. The roll-out of Xpert technology to decentralized settings is improving TB diagnosis in the country, particularly for MDR-TB.

Summary Although some progress has been made in TB control in Mozambique, the challenges for TB control and elimination are enormous. More actively finding cases at health facilities and in communities via contact tracing, improving national surveillance/monitoring and evaluation systems, expanding TB molecular diagnosis, implementing shorter MDR-TB treatments, and improving HIV-TB case management (including rigorous TB screening and higher coverage of preventive therapies in people living with HIV) are considered key priorities for the National TB Control Program.

Keywords Tuberculosis · Mozambique · HIV · Incidence · Xpert · Challenges

Introduction

Tuberculosis remains a global health concern in this twenty-first century. It is among the top 10 causes of death worldwide and is the leading infectious cause of death globally, with higher mortality than HIV and malaria. In 2017, there were an estimated 10 million new (incident) tuberculosis (TB) cases worldwide and 1.6 million people died of the disease. Around 10% of cases are thought to occur in the pediatric age group, and about 9% of all cases occur among people living with HIV [1].

The World Health Organization includes Mozambique in the list of countries with three concurrent epidemics: TB, TB/HIV, and multidrug-resistant (MDR)-TB [1]. Mozambique has the eighth highest HIV prevalence globally among the general population, with around 13.2% of the population between 15 and 49 years of age being positive (15.2% in women and 10.1% in men) [1]. In addition, there are some geographic hotspots and subpopulations where HIV prevalence reaches 40% in some adult age groups in southern Mozambique [2–4].

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Topical Collection on *Tropical Diseases of Mozambique*

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According to the WHO, the country has one of the lowest TB and MDR-TB case detection rates in the world, with around half of expected cases being diagnosed and reported to the health authorities [1]. The uncertainty about the magnitude of the TB epidemic, given the historical absence of a national TB prevalence survey, adds an extra layer of complexity for prioritizing control interventions.

The objective of this review is to provide a snapshot of the current situation of the TB epidemic in Mozambique, highlighting the main epidemiological features, the particularities of TB care and control in the country as well as the challenges and prospects ahead to downsize this public health emergency.

Context

Mozambique is a country in Southeast Africa bordered by Zimbabwe, Swaziland, South Africa, Tanzania, Malawi, Zambia, and the Indian Ocean. In 2017, Mozambique has an estimated population of 28.8 million [5]. The average life expectancy of Mozambicans is only 54.5 years, due to the high burden of transmissible diseases such as malaria, HIV, TB, or diarrheal diseases and increasingly by non-transmissible diseases too [6–8]. High levels of poverty (more than half of the population lives in extreme poverty) [9], chronic malnutrition in a context of high food insecurity, low levels of education among women, poor access to safe water and poor sanitation, and poor access to quality health services are several of the main health determinants in Mozambique [10].

The health system organization corresponds to the administrative division of the country with 11 provincial delegations (including Maputo City which has provincial status) of health and over 154 functional health districts. Health infrastructure is fragile and with limited access, with more than 50% of the Mozambicans must walk an hour or more to the nearest health facility [10]. The ratio population/healthcare professionals is below the threshold of minimum standards set by WHO, and there is an urgent need for physicians and nurses in the country, let alone specialists [11–13].

The National Tuberculosis Control Program (NTP) in Mozambique was launched in 1977 and expanded nationwide in 1985 [14]. The TB patient registration system began in 1984 and short-course therapy (6 month) for drug-sensitive TB (DS-TB) followed in the late 1980s, despite a civil war (1977–1992) which resulted in a shortage of qualified medical staff and supplies, and fragile deployment systems. The war ended in 1992, and by 2000, the NTP introduced the directly observed therapy (DOTS) strategy for DS-TB and then declared TB a national emergency in 2006 [15].

Most of the funding of the NTP comes from external sources. During 2014–2017, the NTP was granted funds from the Global Fund and the World Bank in 2017 to combat TB. This has allowed for the significant expansion of Xpert MTB/RIF testing, MDR/rifampicin-resistant TB (RR-TB) diagnosis and treatment, and a more integrated approach to HIV/TB care/treatment using a "one-stop model." Despite increased funding, the NTP did struggle with fund absorption, and executing some activities planned for the 2014–2017 period [16]. The NTP is planning to significantly increase the technical and administrative staff at the central and provincial levels in order to maximize the impact of funds allocated to fight TB in the country.

Burden of TB in Mozambique

In 2017, the WHO estimated TB incidence of 551 (uncertainty interval [UI], 356–787) per 100,000 population. From the estimated 163,000 (UI 106,000–233,000) absolute number of new TB cases in 2017, 66,000 (UI 42,000–95,000) (40%) occurred in people living with HIV. In the last 5 years, the NTP has increased the annual number of TB case notifications by 61%: from 53,585 in 2013 to 86,515 in 2017 (Fig. 1). Based on WHO estimates, children below 15 years of age contribute between 10 and 15% of all TB cases and the sex ratio is about 2:1 (male/female). Ninety-three percent of TB cases have pulmonary disease, 40% of them with bacteriological confirmation. Although the prevalence of HIV among TB patients seems to be decreasing at national level [1, 17], in some regions of the south of the country, the proportion of TB patients coinfected with HIV can reach up to 70% of all cases [18•] (Table 1). An observational study using data from 2011 showed that among men aged 38–47, the notification rate of laboratory confirmed TB (with sputum smear) among people living with HIV was 1884 per 100,000 [19]. The same study showed that the population attributable fraction to HIV in adults was 61.7%, and the incidence risk ratio of confirmed TB among HIV-positive compared to HIV-negative adults was around 5 [19].

As some studies have shown, the estimated trend in TB notification rate has been increasing during the first decade of this century [18•] although the incidence rate seems to have stagnated in the recent years at around 550 per 100,000 [1]. Studies conducted in southern Mozambique showed a marked disproportion on sex and age distribution of the disease, with higher burden in males below 5 and after 25 years of age (Fig. 2). The peak in rate of notifications seems to occur later for male (in 40–44 age group) than in women (30–34 age group) [20].

WHO estimates 49,000 people died of tuberculosis in Mozambique during 2017, around two fifths of them coinfected with HIV, accounting for a case fatality rate (CFR) of 31%—one of the highest in the world. High TB/HIV mortality has also been shown in autopsy studies and surveillance-based analyses [20, 21]. That entails a mortality rate (TB/HIV) of 90 per 100,000 population (UI 70–167) [1].

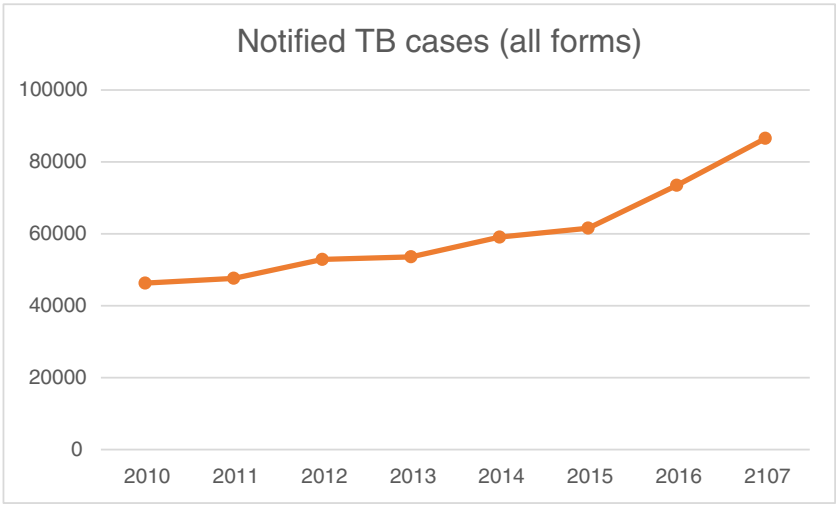


Fig. 1 Trends in national TB notifications for Mozambique (all forms, all ages). Source: Global Tuberculosis Reports (2011-2018)

Available estimates from the Institute of Health Metrics and Evaluation (IHME) for 2015, however, report less than half of the deaths attributable to tuberculosis than the WHO for the same year [22, 23, 24], which highlights the high uncertainty on TB attributable mortality. A report from the district of Manhiça (Maputo province) estimated that around 6.5% of all deaths by natural causes in the district occurred in patients under TB treatment [20].

Pediatric Tuberculosis

Young children and those with immunodeficiencies such as HIV or severe malnutrition are at highest risk of developing active TB disease following infection [25]. TB diagnosis is particularly challenging in this population, given the lack of specific symptoms, the difficulty in obtaining samples for microbiological examination, and the often paucibacillary

Table 1 Epidemiological features of TB in Mozambique. Adapted from Global Tuberculosis Report 2018

TB incidence	Rate per 100,000 population		
Total TB incidence	551 (356–787)		
Incidence (HIV + TB only)	221 (141–319)		
Incidence (MDR/RR-TB)	30 (15–48)		
Estimated TB incidence by age and sex (thousands)	0–14 years	> 14 years	Total
Females	11 (9.6–12)	51 (40–63)	62 (47–77)
Males	12 (11–13)	90 (64–115)	101 (70–133)
Mortality (HIV + TB only)	90 (56–131) per 100,000 population		
Mortality (excludes HIV + TB)	73 (43–111) per 100,000 population		
TB case notifications			
Total cases notified	86,515		
Total new cases and relapse	85,376		
-% with known HIV status	*96%*		
-% pulmonary	*93%*		
-% bacteriologically confirmed among pulmonary	*40%*		
Drug-resistant TB care			
Estimated MDR/RR cases among notified pulmonary TB cases	4100 (2500-5700)		
	New cases	Previously treated	
Estimated % of TB cases with MDR/RR-TB	3.7% (2.4–5)	20% (2.1–37)	
% notified TB cases tested for rifampicin resistance (2016)	48%	55%	
Treatment success rate	Success	Cohort (size)	
New and relapse cases registered in 2016	90%	70,510	
Previously treated cases	86%	1593	
HIV-positive TB cases registered in 2016	87%	30,572	
MDR/RR-TB cases started on second-line treatment in 2015	48%	646	

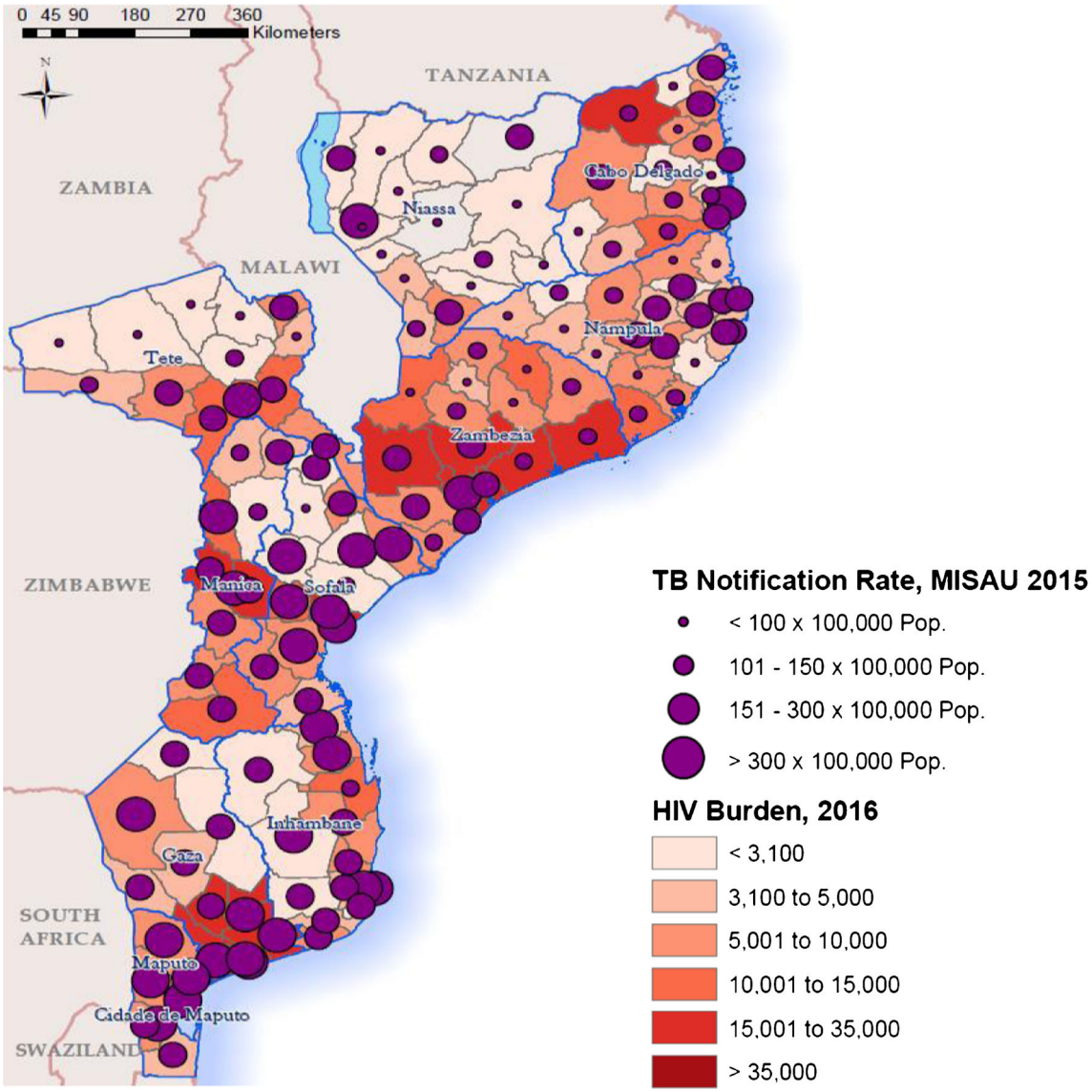


Fig. 2 HIV burden by district versus TB notification rates (MOH, 2017)

disease [26]. In Mozambique, children aged 0–15 years constitute around 50% of total national population (around 15 million) [27]; thus, the contribution of pediatric TB to overall TB is expected to be higher than in other countries. Mozambique adheres to the BCG universal vaccination policy, although monitoring its coverage, particularly with recent global and national shortages, needs to continue and prospective vaccination registries need to be implemented [28, 29].

The notifications of pediatric TB in Mozambique almost tripled from 3214 cases in 2011 to 9254 cases in 2016, and the percentage of total TB cases notified increased from 7 to 13% during this time period [30, 31]. Although a real increase in TB incidence might be possible, the increase in pediatric case detection and specific activities directed to improve pediatric TB diagnosis might explain these increase in notifications. This contribution of pediatric TB to overall TB incidence is in line with global estimates.

One of the few studies in Africa providing prospective population-based incidence data of childhood tuberculosis was conducted in southern Mozambique. The minimum community-based incidence rate of TB (laboratory confirmed plus probable cases) in children under 3 years of age was 470 of 100,000 person-years in 2012 [32•]. HIV coinfection was present in 44% of the TB cases, and the case detection rate was estimated to be around 40% in this age group [33]. The high prevalence of non tuberculous mycobacteria could hinder TB diagnosis in young children investigated for TB, although these findings do not seem to have clinical relevance [34, 35].

Screening and Diagnosis

Historically, patients diagnosed with TB in Mozambique have primarily self-presented to health facilities with symptoms and

if noted by the consulting healthcare provider were referred for testing with Ziehl-Neelsen (ZN) smear microscopy, possibly chest radiograph if available, or for clinical diagnosis of TB [14]. This passive approach, insensitive tests for TB, and other patient and health system factors (distance to health facilities, high prevalence of other concomitant diseases, such as AIDS, among others) led to an average delay to diagnosis of 150 days in one study [36]. Delays in diagnosis and treatment of TB have important individual and public health implications. At individual level, patients with long delays in initiation of treatment may have increased risk of developing severe disease and death. At a public health level, these delays increase TB incidence by increasing the risk of transmission. In recent years, with funding from USAID and Global Fund, there have been active case finding campaigns focusing on prisoners, miners, patients living with HIV, and other high-risk populations, but there has not been a sustained and systematic national focus on contact tracing.

This is beginning to change, as the NTP and partners pursue a more aggressive case-finding approach to identify missing TB cases. A initial pilot with "cough officers" increase the coverage of community based health care workers involved in screening all patients that present to health facilities. This is also in line with the rising proportion of patients that were diagnosed from a community referral, which increased nationally from 9% in 2015 to 21% in 2016 and was over 30% in Sofala, Nampula, and Zambézia in 2016 [37].

Earlier and improved TB case detection as well as expanded capacity to diagnose MDR-TB are not only global priorities for TB control but also highly important for the Mozambican context.

The Mozambique NTP and lab department piloted LED microscopy in 2012 which showed increased sensitivity for MTB relative to Ziehl-Neelsen, similar to what has been reported in the literature, approximately 10–15% increased sensitivity [38] (HAI, NTP, unpublished data). LED microscopy was rapidly scaled up to an estimated 380 laboratories as a replacement for ZN.

Mozambique has three functional TB reference labs in Maputo (NRLT), Beira, and Nampula and one BSL3 lab at Manhiça Health Research Center which covers the TB diagnostic needs at the district of Manhiça (Maputo province). Aligned with WHO recommendations, the Mozambique NRLT has started offering first- and second-line DST using LPA at their facility in Maputo and is in the process of expanding this capacity to Nampula. In addition, the NRLT in Maputo does first- and second-line phenotypic DST.

In December 2010, WHO first recommended the use of the Xpert MTB/RIF assay. Until 2010, the diagnosis of TB in Mozambique was performed by Ziehl-Neelsen smear microscopy and the culture with DST was available at the national TB reference laboratory in Maputo [39]. In 2011, the Xpert MTB/RIF assay was first implemented in pilot settings in Mozambique. This number has risen to approximately 71 four-module GeneXpert's (on December 2017) dedicated to TB testing that ran over 100,000 tests in 2017. There are plans to implement an additional 96 machines in 2018 to decentralize Xpert MTB/RIF testing to every district in Mozambique (Fig. 3). Xpert MTB/RIF is now the first-line tests for patients at health facilities with a machine, and samples from patients with additional eligibility criteria (PLHIV, retreatment TB cases, MDR-TB contacts, children, pregnant women, other immunosuppression, miners, health care workers) are referred to centers with Xpert testing.

In parallel with the expansion of the GeneXpert, a connectivity and results management and analysis solution called GxAlert was piloted and expanded. This technology have the potential to improve patient treatment, such as linkage to care in TB care cascade, programmatic monitoring and evaluation of test results and key indicators, and logistics management of Xpert cartridges and machine performance/maintenance. To date, GxAlert is installed on almost all Xpert-associated computers in the country via a national connectivity contract [40•].

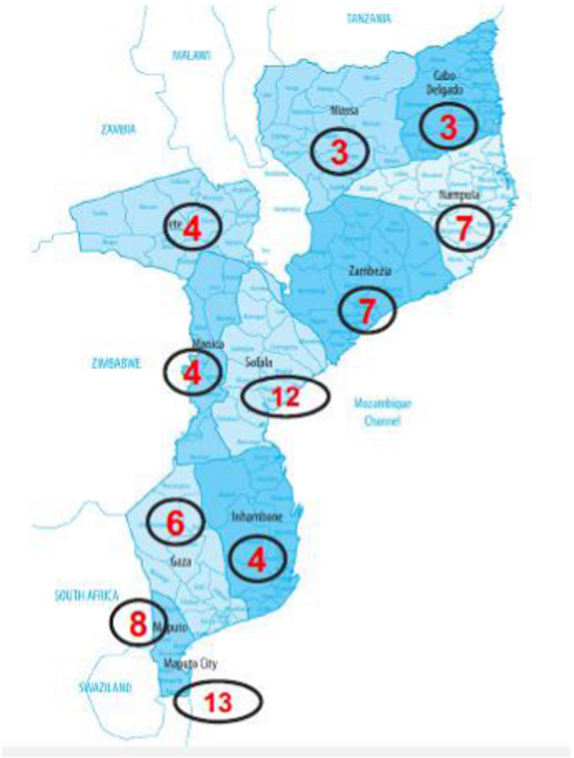
LF-LAM (lateral flow urine lipoarabinomannan assay) has shown usefulness in the diagnosis of TB in highly immunocompromised patients and in reducing mortality [], however is not yet implemented in Mozambique as a routine test.

Treatment Outcomes

In Mozambique, the treatment success rate among new cases has increased from 76% in 2003 to 79% in 2007 to 90% in 2017 [41], reaching the global targets for treatment success, set at 90% [42]. These are notable improvements and should be applauded, especially in light of the rising number of total notified patients during this time [1, 17].

Most patients are treated at one of the more than 1500 health facilities that provide TB treatment in Mozambique. A relatively recent innovation in service delivery was the integration of TB and HIV care through the one-stop model in which TB nurses treat patients both for TB and also for HIV (instead of patients visiting the TB and separate HIV clinics). This has introduced more work for TB nurses, but significantly simplified treatment for patients, and eliminates the risk of having patients with active TB wait in areas with patients living with HIV.

Ninety-six percent of TB patients in Mozambique are tested for HIV, and 95% of coinfected patients consent to early initiation of ART. However, the percentage of newly diagnosed HIV-positive patients who were screened for TB in 2016 is still low at 67.1% and only 52% are started on isoniazid preventive therapy (IPT). This needs to improve in order to reach the End TB Strategy targets, which aim at screening 90% of all patients [42].



*Last update: December 2017

Fig. 3 Number of GeneXpert platforms allocated in Mozambique per province. *Last update: December 2017

Province	Number of GeneXpert Platform
Maputo City	13
Maputo	8
Gaza	6
Inhambane	4
Sofala	12
Manica	4
Zambezia	7
Tete	4
Nampula	7
Niassa	3
CaboDelgado	3
	Total 71

Despite these successes, there is still low coverage of community-based DOTs or other innovative DOTs and care delivery platforms such as video-dots, 99dots. Given the geographical and demographic heterogeneity of Mozambique, there is some variability in how DOTs is implemented from facility to facility.

Despite overall good treatment outcomes reported at national levels, reports from some subpopulations show a high rate of fatal outcomes, especially among HIV-positive TB patients [20, 43]. A better understanding of factors influencing poor treatment outcomes may allow the development of tailored treatment support strategies. In general, predictors for unsuccessful treatment are considered socio-demographic, behavioral, disease-related, and treatment-related factors [44]. In a study in Maputo province, HIV status, being male, and lack of laboratory confirmation were factors associated with a higher risk of death during the TB treatment. A recent study conducted in Beira, Mozambique's second largest city, identified factors associated with treatment failure in newly diagnosed patients with pulmonary TB: young males, malnutrition, low income, low educational degree, and HIV-coinfected patients were all more likely to fail treatment [44]. These results suggest that pharmacological prescription in itself is not sufficient to guarantee a reduction of TB adverse outcomes and further policies with a multidisciplinary psychosocial support will need to be implemented. The NTP currently updated their psychosocial support guidelines.

Drug Resistance

In 2017, there were an estimated 600,000 new cases of MDR-TB and RR-TB who were eligible for MDR-TB treatment worldwide, yet only 130,000 were diagnosed and started treatment, and of those treated in 2014, only 54% had a successful treatment outcome [1, 45, 46].

WHO data for Mozambique estimates that in 2016, there were 7600 (4500–11,000) new MDR/RR-TB cases nationally, translating into a MDR/RR rate of 26 (15–36) per 100,000 population [29]. Case notification for drug-resistant TB (DR-TB) increased from 313 in 2013 to 911 cases in 2016 [29]. While MDR/RR-TB case notification is improving, primarily due to the expansion of GeneXpert and MTB/RIF testing, it continues to be substantially below global targets at just 12% of the total 7600 estimated MDR-TB cases each year in Mozambique. Treatment success rates for MDR-TB remains low, at 48% for the 2015 cohort [1].

In Mozambique, there have been two previous drug resistance surveys (most recently in 2007–2008), and based on these, the WHO estimates that 3.7% of new and 20% of previously treated TB cases had RR/MDR-TB in 2016 [47]. In 1998–2000, the first drug-resistant survey conducted in Maputo City showed an MDR-TB prevalence of 3.5% [48]. In 2002–2003, a study performed in Maputo showed an MDR-TB prevalence among PLHIV of 5.8% among new cases [45]. In 2013–2014, a study performed in Manhiça

district showed that the overall prevalence of MDR-TB was 5.1%: 3.8% among newly diagnosed TB cases and 13.2% among those previously treated [46].

MDR-TB treatment in Mozambique is decentralized and free of charge. Guidelines and management tools are available and are in the process of being updated to align with new WHO recommendations for the use of short treatment regimens for MDR-TB, Bedaquiline, Delamanid, and other accompanying drugs. MDR focal points and TB supervisors have been trained in the new MDR treatment guidelines. Mozambique is using a standardized treatment regimen for MDR-TB cases including 8Cm(Km)-Lfx-Eto-Cs-E-Z/12Lfx-Eto-Cs-E but in 2018 is introducing phase-wise the 9–11-month short-course ("Bangladesh") regimen for its MDR-TB cases: 4(+)Cm-Mfx-Eth-Cfz-H-E-Z/5Mfx-Cfz-E-Z. A few dozen patients in Mozambique have been started on Bedaquiline and or Delamanid containing regimens—each of these cases is reviewed by a newly established central DR-TB Clinical Review Committee.

Prospects and Challenges

Tuberculosis remains an important public health concern and leading cause of disease and death in Mozambique. The reductions of 90% in incidence, 95% in mortality, and 100% in catastrophic costs by 2035 set by the End TB strategy [49] seem hard to be accomplished at a national level, if the gap in missing cases is not closed rapidly. In the last several years, we have witnessed a marked increase in the total notifications for DS and RR/MDR-TB, higher notifications in children, and improved treatment success rates for DS-TB. The NTP has move to a one-stop model for TB/HIV coinfected patients and the vast majority are on ART. Lab capacity has expanded substantially, particularly for Xpert MTB/RIF testing, LED microscopy, and the introduction of the first- and second-line LPA testing. The NTP and its partners should be commended for these improvements.

However, the challenges are enormous. Improving surveillance and effective M&E systems is a priority. The country needs to know the true burden of TB in order to prioritize health interventions and to this end has launched the first ever national TB prevalence survey in the fall of 2017. Furthermore, the TB epidemic and its associated mortality cannot be downsized when more than half of the TB patients remain undiagnosed. Most of the estimated mortality in the country comes from those who are not diagnosed [1, 50, 51].

Along these lines, the NTP recently implemented new DS-TB and drug-resistant MDR-TB registries, as well as laboratory registries for TB that conform with WHO M&E recommendations. Currently, the NTP is also in the process of transitioning from Excel spreadsheet reporting of facility-level data into DHIS2/SISMA, the new official aggregate data management solution for the MOH that will provide better analytics and real-time feedback to each level of the healthcare system for both TB and HIV program management. This will also be the first time that the TB program will have access to facility-level data at the national level (previously only district-level aggregate data was reported to the NTP). These health information systems need to be expanded to create digital patient level registries, together with the implementation of innovative mHealth platforms which can improve the surveillance at all levels of care (from central level to community based healthcare workers or activists).

The roll-out of Xpert (and associated electronic data management systems such as GxAlert) needs to continue and logistical hurdles (platforms maintenance, cartridge deployment, training of technologists) tackled with standardized procedures. If successfully executed, decentralizing molecular diagnosis and drug resistance testing to the district level may improve the proportion of TB cases that are confirmed, reduce delays to diagnosis, and help increase notification of bacteriologically confirmed TB cases, particularly those with RR-TB [36, 52].

Coordinating these efforts, ensuring that all funding sources are fully exploited for maximum impact needs to be a major focus for the NTP. The NTP has initiated this process but needs to further clarify their vision in an updated strategic plan. Further initiatives include harmonizing and strengthening sample transportation networks, introducing new tests such as TB LAM for immunocompromised HIV-positive patients, considering multiplexing for GeneXpert, improving the delivery of test results from referral facilities to the requesting physicians, and eliminating the pretreatment lost to follow-up gap, especially among RR/MDR-TB patients, are also top priorities.

The implementation of active case finding interventions among high-risk groups (people living with HIV, with diabetes, miners, healthcare workers, and TB contacts, among others) at a programmatic level needs to be more vigorously implemented. Some TB contact tracing projects, led by CTB/FHI360, CISM, HAI, in collaboration with the NTP, are paving the road for a more standardized implementation of these activities. In addition, the NTP started a program of "cough officers" in selected healthcare settings, in order to identify TB among users of the national health system. While it seems a potentially effective initiative for early TB diagnosis [53], there is a need to monitor its impact and cost effectiveness for more generalized roll-out of this intervention.

A major challenge is improving childhood TB diagnosis. Delay of diagnosis and treatment in children can increase the risk of rapid disease progression and mortality. The difficulty in reaching an accurate TB diagnosis is aggravated by the complex patterns of care seeking. Misconceptions of pediatric TB, associated complex care-seeking itineraries, and negative feelings of the diagnostic procedures may result in delays in diagnosis, low adherence, and lost to follow-up, which needs to be addressed by adequately framed health promotion approaches [54].

TB treatment can be further strengthened by providing more individualized care to patients, especially to those that are most vulnerable, maximizing the use of community health workers (APE) and implementation and monitoring of the "padrinho" program (which entails that a relative or close friend observed treatment in rural areas where patients cannot go to the clinic to have proper DOT). This includes better screening and identification of patients most at risk for failure and relapse, and implementing a standard package of psychosocial support services. This should be particularly emphasized for RR/MDR-TB patients, whose treatment success rate is currently only 50%. The roll-out of new pediatric formulations will also facilitate adherence among this vulnerable group [55]. Reducing mortality and adverse outcomes among HIV-positive patients needs to be seriously addressed [20]. It could also be achieved by better symptom screening at the HIV follow-up visits, early diagnosis (which can be aided by the use of LAM, Xpert), implementing early ART initiation and adjusting regimens among HIV patients, as well as managing other opportunistic infections properly.

Prevention strategies, including the expansion of latent tuberculosis infection (LTBI) treatment to all eligible individuals as recommended by updated guidelines from the WHO need to be fully implemented, it has significantly increased to 52% among HIV-positive patients, but is still below the 90% target [42]. Comprehensive infection control practices at health facilities to protect patients and health care providers (such as the cough officer program) are also needed. This will reduce the number of HCW diagnosed with TB, which have been increasingly [37]. In addition, the NTP needs to continue expanding educational and awareness campaigns to the lay population, but also to existing healthcare workers about TB, which have been shown to be undertrained [56].

Despite these health sector-oriented approaches, to be successful, the TB epidemic needs to be addressed vigorously using multisectoral approaches. Recent evidence suggests that addressing the social determinants associated with TB, reducing poverty and expanding social protection programs are critical for epidemic control [57, 58]. As a first step, studies on the social and economic burden of TB in the country are needed. No formal assessment on the costs of TB for patients has been conducted at a national level, and this information is critical to monitor one of the key indicators of the End-TB strategy (100% reduction in TB associated catastrophic costs) [49].

Acknowledging the substantial burden of TB in Mozambique, international donors have significantly increased funding for TB available to the NTP for TB during the last several years, mostly through The Global Fund, the World Bank, USAID (TB Care and Challenge TB), and PEPFAR. If this financial scenario continues, together with the availability of new diagnostics, treatments, delivery strategies and growing political will and awareness of this ancient disease, the pieces are in place for the Mozambican NTP and MOH to start approaching TB epidemic control.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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