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REPÚBLICA DE MOÇAMBIQUE
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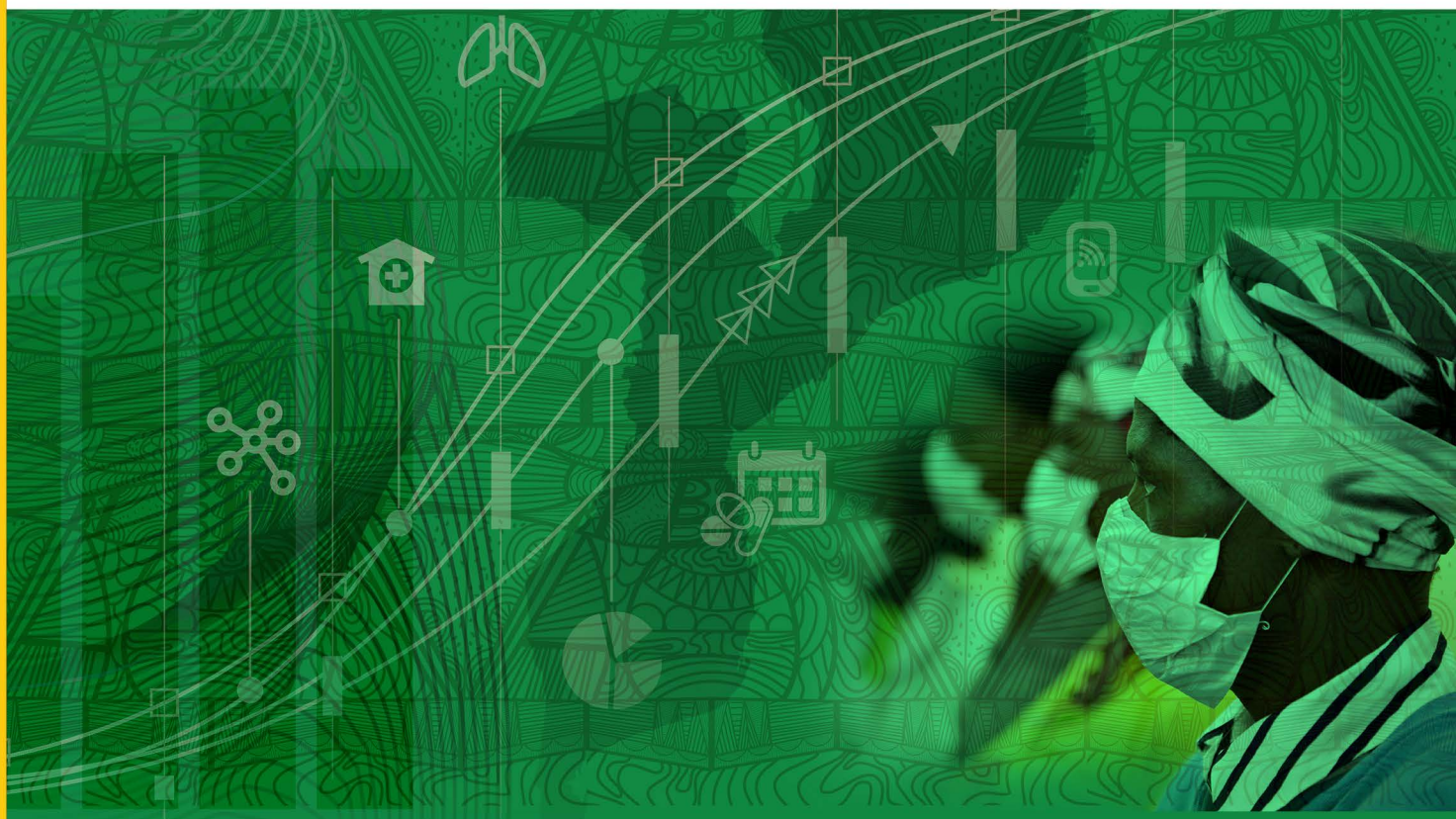
PNCT
PROGRAMA NACIONAL DE CONTROLO DA TUBERCULOSE



OPTIMIZING INVESTMENTS IN MOZAMBIQUE'S TUBERCULOSIS RESPONSE:

RESULTS OF A TUBERCULOSIS ALLOCATIVE EFFICIENCY STUDY

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OPTIMIZING INVESTMENTS IN MOZAMBIQUE'S TUBERCULOSIS RESPONSE:

RESULTS OF A TUBERCULOSIS EFFICIENCY STUDY

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ACRONYMS

ART	Antiretroviral therapy
BCG	Bacillus Calmette-Guérin
CHW	Community health worker
DOT	Directly observed treatment
DR	Drug resistant
DS	Dug susceptible
HIV	Human immunodeficiency virus
LTBI	Latent TB infection
MDR	Multi-drug resistant
NSP	National Strategic Plan
NTP	National Tuberculosis Programme
PEPFAR	U.S. President's Emergency Plan for AIDS Relief
PHC	Primary health care
PLHIV	People living with HIV
RR	Rifampicin resistant
TB	Tuberculosis
UN	United Nations
USD	United States Dollar
XDR	Extensively drug-resistant
Xpert	GeneXpert MTB/RIF, detecting DNA sequences specific for M. tuberculosis and rifampicin resistance
WHO	World Health Organization

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KEY MESSAGES

1. Epidemiological projections using the Optima TB model **indicate a declining future trend in TB incidence, TB prevalence and TB-related deaths in Mozambique**. However, the total number of new cases is projected to remain fairly stable due to the rapid increase in population size

2. The country is currently working on the 2020–25 strategic plan with a goal of reaching TB diagnosis rate of 90%. **Our model suggests that reaching this 90% diagnosis target by 2025 and sustaining it would, by 2035 reduce the total number of TB cases and TB-related deaths by up to 80% and reduce DR-TB by up to 50%**

3. An optimized allocation of resources could have a substantial impact on key TB indicators. Relative to the current allocation, **an optimized allocation of spending could**, in 2025:
   - Reduce the annual number of active TB cases by 19%
   - Reduce the annual number of TB-related deaths by 18%
   - Reduce the rate of TB incidence per 100,000 by 11%

4. Under an optimized allocation of current TB expenditure, TB treatment would receive more funding (in relative to the current condition) and would absorb approximately 28% of total TB spending in Mozambique compared with the current 19%, **enabling the NTP to treat the additional TB cases identified through accelerated case finding**

5. Latest available data suggests that the proportion of TB notifications that are clinically diagnosed is high (60%; 2017). This hinders accurate assessment of the progress made in improving case detection rate in Mozambique. **Expanding the use of rapid and sensitive drug resistance testing methods such as GeneXpert would strengthen accurate TB diagnosis for both DS and DR-TB.** The effectiveness, cost, and operational aspects of universal GeneXpert use in TB suspects could be investigated through implementation science research for decision support.

6. **An optimized allocation of resources would decrease funding for screening and diagnosis programs from 25.4 million (2017 level) to 23.9 million USD** by relocating resources to cheaper and more effective case findings activities: screening PLHIV at outpatient visits, expanding initiatives such as cough monitors, reducing community outreach case findings (e.g., general house to house screening), increase coverage of programs targeting key high-risk groups such as prisoners, and doubling coverage of household contact tracing. In contrast, **an optimized allocation would increase funding for TB treatment programs from 10.6 million to 11.9 million USD** to ensure that the cases found with this combination of efficient diagnosis programs can also get treatment.

7. Although mainly managed by the HIV program, ART provision is a key factor in the TB response as treatment reduces the probability of progression from latent to active TB. For example, **scaling up to 90% ART coverage by 2035 is projected to reduce the number of new TB cases among adult PLHIV in 2035 by 35% (compared to an ART coverage of 70%)**

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Mozambique is one of the 30 highest TB burden countries in the world

Reaching and sustaining a 90% diagnosis rate by 2025 would reduce the total number of TB cases and TB-related deaths by up to 80% and reduce DR-TB by up to 50% by 2035.

Mozambique can cut TB prevalence and TB deaths by 20%, and TB incidence by 11% by allocating resources optimally.

Increasing investments in active case finding programs are essential to improve the estimated case detection rate of 52%.

EXECUTIVE SUMMARY

CURRENT STATUS AND FUTURE PROJECTIONS OF THE TB EPIDEMIC IN MOZAMBIQUE

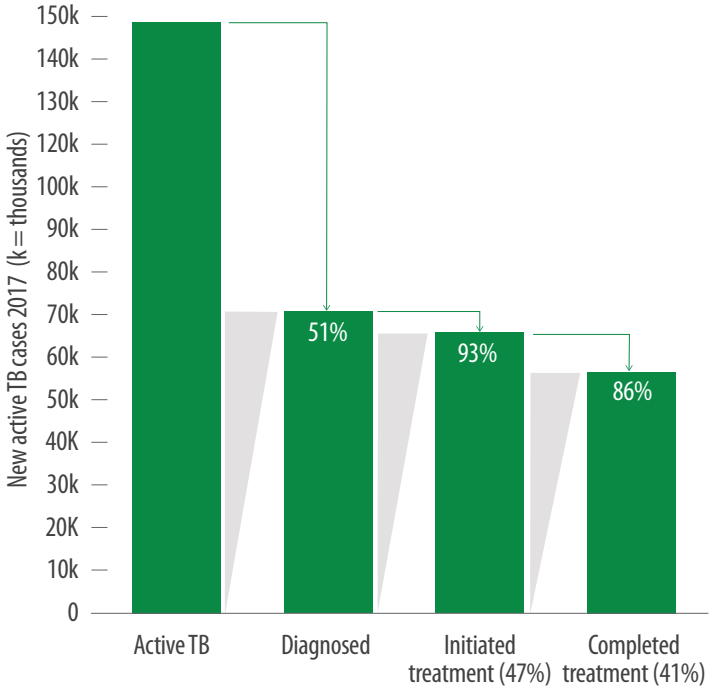
Mozambique is one of the 30 highest tuberculosis (TB) burden countries in the world with an estimated 551 new TB cases per 100,000 population, a low TB detection rate of just above 50%, and a low DR-TB diagnosis and treatment success rate (38%) (Global TB Report, 2018). Overall, historical data from the National Tuberculosis Programme (NTP) shows an increasing trend in TB case detection rate (36% in year 2010 to 53% in 2017) coupled with a high treatment success rate for drug susceptible tuberculosis (DS-TB) (90%). However, it is still far from the 2020 global target of identifying and placing 90% of all TB patients on treatment, indicating challenges for the country to reach NTP targets for 2025 as well as End-TB targets for 2035.

Epidemiological projections using the Optima TB model indicate a declining future trend in TB incidence, TB prevalence and TB-related deaths in Mozambique. At the time of this analysis, the country was working on the 2020–25 Strategic Plan with a goal of reaching 90% TB diagnosis rate. Our model outputs suggest that reaching and sustaining a 90% diagnosis rate by 2025 would reduce the total number of TB cases and TB-related deaths by up to 80% and reduce DR-TB by up to 50% by 2035. Furthermore, reaching 90% ART coverage (at 55% in 2017) by 2035 would contribute to a reduction of new TB cases of 35%. To reach the (global) END-TB targets, the country must (i) increase TB detection rates, and at the same time, (ii) improve ART coverage and (iii) reduce HIV infection rates. Mozambique has already achieved high coverage of HIV services in TB clinics and among TB patients with 97% of TB patients registered aware of their HIV status and 95% of TB patients living with HIV on ART. Overall, ART coverage was at 55% in 2017 (UNAIDS, 2017).

TB CARE CASCADES

We estimated that 51% of active TB cases got diagnosed, using routine data available in 2016/17 (Figure 0.1). Among the diagnosed cases, 93% initiated treatment, and of those initiated treatment, 86% completed treatment. As a result, despite high treatment success rates, only about 41% of all new active TB cases successfully completed treatment.

Figure 0.1 TB care cascade



Source: Populated Optima TB model, Mozambique.
Note: TB = tuberculosis.

OPTIMIZED ALLOCATIONS

Assuming same amount of funding as for 2017 (USD 36.8 million) remains available each year up to 2035, the optimized budget allocation differs from current allocations in several areas, including:

- Increasing annual funding for outpatient screening from USD 10.8 million to USD 13.2 million, including regular TB screening for all PLHIV at outpatient clinics (currently at 74% coverage)
- Prioritizing investments in case-finding programs for key risk groups, such as prisoners and health workers
- Increasing funding for treatment programs to accommodate increased number of notifications

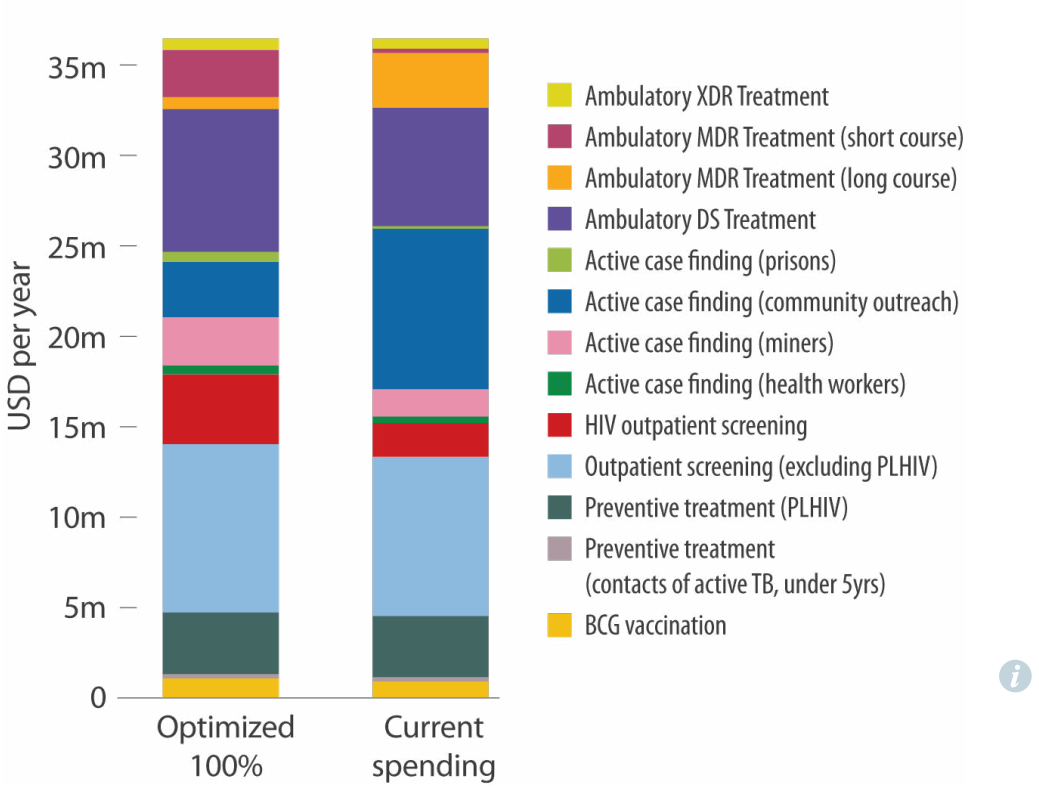
SCALE-UP SCENARIOS

- Mozambique can cut TB prevalence and TB deaths by 20%, and TB incidence by 11% by allocating resources optimally. Specifically, this can be done by (i) doubling the rate of household contact tracing for notified cases, (ii) screening all PLHIV during their routine outpatient visits, and (iii) focusing on the community outreach activities among key populations such as prisoners, cross-border miners and community health workers.
- Compared to current resource allocation across programs, the optimized resource allocation scenario indicates a need to significantly increase active case finding programs. Increasing investments in active case finding programs are essential to improve the estimated case detection rate of 52%. In addition to allocative efficiency arguments, there is also an equity argument for funding active case finding programs, as it means that populations targeted by outreach activities would receive care that would otherwise not be available to them.
- **Changes across screening, diagnosis and prevention interventions:** An optimized allocation of resources would result in increased funding for screening, diagnosis and intervention programs

from 23.9 million to 25.4 million USD and increase funding for treatment from 10.6 million to 11.9 million USD.

- **Shifts within treatment interventions:** In an optimized intervention mix, TB treatment would receive more funding and would absorb approximately 28% of total TB spending in Mozambique compared with the current 19%.

Figure 0.2 Optimized allocations of the current TB funding



Source: Populated Optima TB model, Mozambique.
Note: BCG = Bacille Calmette-Guerin; DS = drug susceptible; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

RECOMMENDATIONS

Based on the key findings, we make the following recommendations:

1 **Intensify contact-tracing of notified cases**
The number of traced contacts should increase by 50–100% the current coverage (estimated 1.32 contacts traced per 1 notified case). In addition, the yield data of contact-tracing of notified cases for Mozambique varied highly and should be monitored to inform future program planning and similar exercise.

2 **Screen all PLHIV at each outpatient visit**
An estimated 74% of new cases enrolled in HIV treatment were screened for TB in 2017. Given high TB prevalence in PLHIV and low costs, screening all HIV patients regularly for TB as per global recommendation, will likely improve TB case finding and save costs.

3 **Expand active case finding programs for high-risk populations**
Health care workers, prisoners, and cross-border miners should be screened annually, as these groups are at higher risk of TB infection.

4 **Increase yield from outpatient screening activities**

About 75% of notified cases are found in the outpatient setting in Mozambique. As only 60% of cases are currently clinically diagnosed (2017), the NTP should aim to increase the proportion of TB cases that are bacteriologically confirmed by increasing coverage of rapid diagnostic tests such as GeneXpert. Without increasing bacteriological confirmation rate, it is difficult to assess true progress in the TB response in Mozambique. We recommend small-scale implementation science research project to assess the effectiveness, cost, and operational aspects of an implementation of universal use of GeneXpert.

5 **Closely monitor the pilot of MDR regimens to inform future MDR treatment recommendations**

The NTP is planning to move away from all injectable based regimens starting in late 2019. The oral short course regimen is currently being studied in several high volume MDR-TB sites in the Maputo City area. By the time of this analysis, data from this research was not yet available. Final discussions about regimen and protocol should be based on operational research data available from studies such as the ongoing on in Maputo city.

6 **Expand ART coverage, aiming to reach UNAIDS/WHO's 95-95-95 targets by 2030 (new global targets)**

Increasing ART coverage has a significant impact on TB incidence amongst PLHIV. Continued expansion of ART care, including adherence support to keep people in care and achieve and maintain viral suppression, will significantly reduce the number of new active TB infections.

7 **Continue ambulatory-focused care for both DS-TB and DR-TB patients**

The country should continue this approach and avoid unnecessary hospitalisation. This approach reduces costs without affecting outcomes, provided directly observed treatment (DOTS) is in place.

8 **Collect data on community case finding programs to inform decision making**

Community case finding programs contribute around 25% of notified cases in Mozambique. Currently, several community case-finding programs are underway with fragmented implementation and lack of data on cost, coverage, and impact. We recommend the NTP collects data, especially cost data, of these pilot projects in order to inform cost-effectiveness estimates and guide future policy recommendations.

9 **Maximize the collection and use of TB routine data to inform programming and policies**

The quality and availability of cost and coverage data in Mozambique provided a challenge for this analysis and results in uncertainty in model parameters. Key data sources include tracking of TB-specific expenditures, reporting of how TB cases are identified (by intervention modality) and keeping better records of often fragmented implementation of activities. Therefore, monitoring and evaluation systems should be streamlined, and spending and coverage data should be collected for all TB programs (NTP led and non-NTP led)

10 **More funding is needed for TB programs**

The TB response in Mozambique is not on track to meet the 2025 milestones or 2035 End-TB targets—a revised target or timeline and more funding for the TB program are needed.

TB has been diagnosed in the country predominantly through passive case-finding programs, meaning that TB is only diagnosed after a person seeks healthcare.

Active case finding in Mozambique has been expanding and community-based efforts now account for around 25% of detected cases.

The primary objective of the national TB response therefore remains to increase the case detection rate, which was estimated at just 53%.

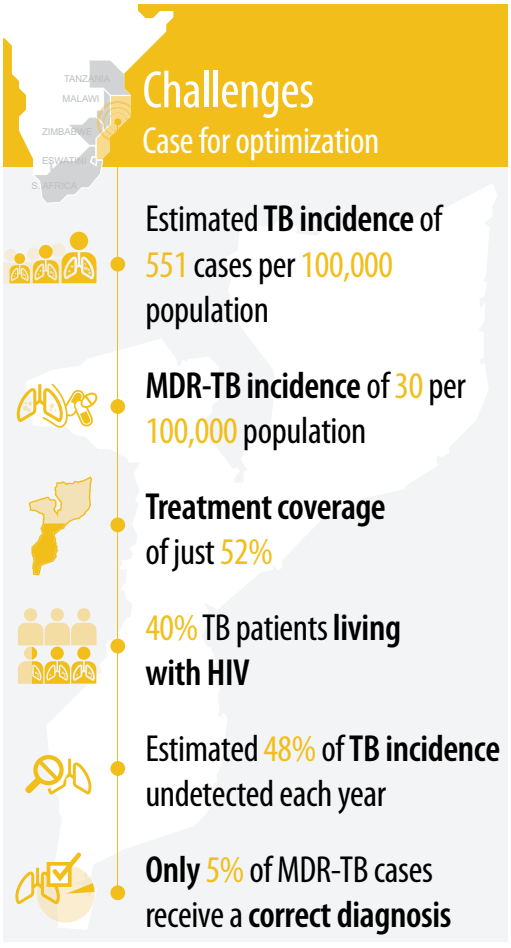
Allocative efficiency modelling focused on a national level analysis to provide guidance on how to use existing resources and identify TB care models towards maximizing the impact of the TB response in Mozambique.

1 INTRODUCTION

Mozambique is located in Southern Africa bordering Tanzania, Malawi, Zambia, Zimbabwe, South Africa, and eSwatini. Mozambique's estimated population is about 28 million (UN Population Division, 2017) and the majority of its population lives in rural areas. Despite recent economic growth, it is estimated that about half of the population lives under the poverty line. Main economic activities in the country include agriculture, fishing tourism, mining and oil industry. The whole country has about 1,600 health facilities and 398 laboratories located in a vast territory of 800.000 km^2.

1.1 OVERVIEW OF THE TB EPIDEMIC

Mozambique is amongst the 30 high burden countries for TB, TB/HIV and MDR-TB. The Global TB Report 2018 estimated that Mozambique has (i) a TB incidence of 551 cases per 100,000 population, (ii) MDR-TB incidence of 30 per 100,000 population, (iii) treatment coverage of just 52%, and (iv) 40% TB patients living with HIV (WHO, Global TB report 2018). There is a gap between the estimated TB burden in the community and the case detection by the National Tuberculosis Program (NTP), for both drug susceptible TB (DS-TB) and multi-drug resistant TB (MDR-TB). It is estimated that 48% of incident TB cases are undetected each year and only 5% of MDR-TB cases receive a correct diagnosis (WHO, Global TB report, 2018). Additionally, treatment success rates for MDR-TB are low at 48%. Among new TB cases, an estimated 3.7% are MDR whereas among previously treated cases, about 20% are MDR. The NTP has been able to achieve and maintain the treatment success rates at 90% for DS-TB (2018 Global TB Report).

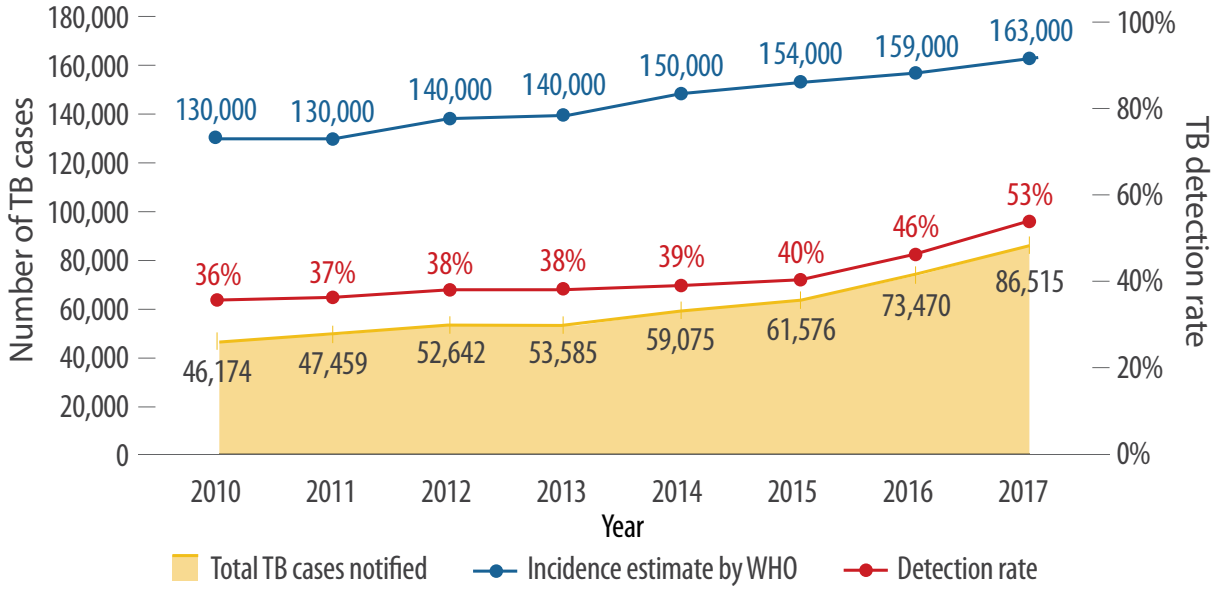


TB case finding programs

TB has been diagnosed in the country predominantly through passive case-finding programs, meaning that TB is only diagnosed after a person seeks healthcare. An

estimated 75% of cases were notified in this way. Passive case-finding generally results in diagnosis at a later stage of disease than diagnosis through active case-finding. Ongoing efforts are being made to train healthcare workers to screen people who are attending for non-TB related health conditions. These healthcare workers are called "cough monitors" or cough officers. A more proactive approach to TB diagnosis at this level could facilitate more diagnoses at an earlier stage of disease and reduce the time of TB transmission prior to diagnosis.

Figure 1.1 Trends in TB notification and detection rate



Source: NTP TB desk review, 2018.
Note: Detection rate increased from 36% (2010) to 53% (2017); TB = tuberculosis; WHO = World Health Organisation.

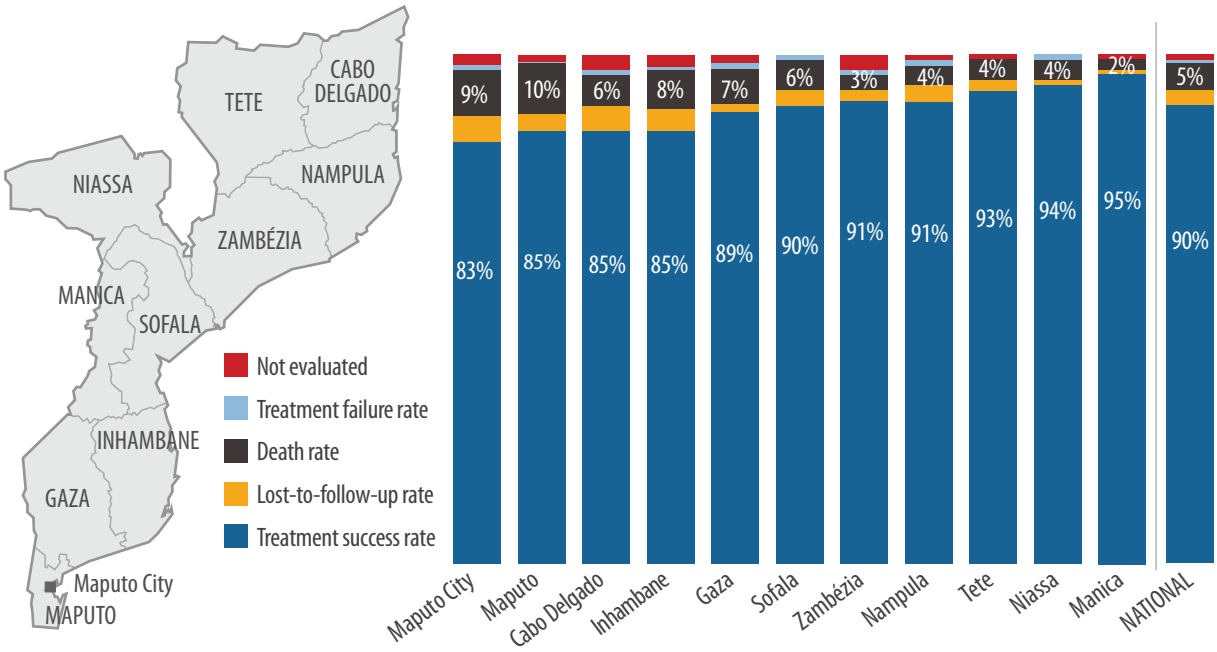
Active case finding in Mozambique has been expanding and community-based efforts now account for around 25% of detected cases. This involves both contact tracing of notified cases, and other community-level interventions such as active house-to-house case finding in TB hotspots. However, there are opportunities for further expansion. For example, currently, just 1.3 contacts are traced per notified case on average, whereas the average household size is 4.4 (WHO LTBI Dataset). Other smaller active case finding programs focus on key populations of prisoners, miners, health workers and PLHIV. It is estimated that TB screening is carried out in 74% of newly registered HIV patients. All new enrolees should be screened for TB, and there should be regular routine TB screening for all HIV patients. Similarly, there are an estimated 50,000 healthcare workers in Mozambique, of which approximately only 27% were screened for TB in 2017 (NTP Desk Review, 2018). Although screening for TB has been conducted annually in prisons, this also does not cover all prisoners—it was estimated that only a small proportion of prisoners (15%) received a bacteriological exam for TB in 2017. For miners, the World Bank is supporting screening programs in two regions—Gaza and Maputo. However, the total cases found from these programs was small (544 cases in 2017).

In all of the above screening settings, there remain issues of bacteriological confirmation and lab capacity. Around 60% of pulmonary TB notifications were clinically diagnosed in 2017, a proportion which has increased from around 51% in 2014. This is despite increasing use of GeneXpert, which was used 167,162 times in total for monitoring and diagnosis in Mozambique (2017). Although use of GeneXpert is increasing, there are no records of total number who were screened, received a lab test, types of lab test used, and positivity rates.

TB Treatment

The Mozambique NTP has achieved a treatment success rate of 90% among new and relapsed DS-TB cases (WHO, 2018). The primary objective of the national TB response therefore remains to increase the case detection rate, which was estimated at just 53% (WHO 2018). Treatment of TB in Mozambique is delivered in outpatient settings, with patients receiving inpatient care only for the treatment of adverse events or complications even for drug resistant cases. The use of community health workers has improved access to treatment but access still remains uneven. DOT has been implemented nationwide, with patients being required to attend outpatient clinics daily for the first two months of the treatment regimen, after which they attend twice per month. Improving access to supervised treatment through community-based initiatives therefore remains a priority.

Figure 1.2 Treatment outcomes for DS-TB



Source: NTP TB desk review, 2018.

Treatment outcomes for DR-TB remain sub-optimal; only 48% of MDR-TB cases and 38% of XDR-TB cases beginning second line treatment in 2015 successfully completed treatment. A transition from the use of injectables to newer, oral drugs, such as bedaquiline, as recommended by WHO, could improve outcomes, but would also incur higher drug costs. Most MDR-TB patients are currently treated with a regimen of 18 months. A smaller cohort of patients are receiving the short-course oral regimen of 9 months. Finally, Mozambique has started to implement integrated psychosocial and adherence support packages and counselling for DR-TB patients. These packages include support such as reimbursement of transportation costs and nutritional support.

TB program expenditure

The vast majority of the National TB Program (NTP) budget in Mozambique is funded by international donors, primarily the Global Fund (53%) and the World Bank (31%). Domestic funds cover 5% of total expenditure, with the remaining 11% funded by other sources. Based on data provided by the individual funding sources, it is estimated that the total NTP budget in 2017 amounted to approximately USD 27 million in Mozambique.

Table 1.1 Mozambique: NTP budget by source of financing (2017)

Funding source	2017 spending (USD)	% share
Global Fund	14,176,960	53%
World Bank	8,206,204	31%
Domestic	1,361,600	5%
Other sources	2,920,512	11%
Grand Total	**26,665,276**	

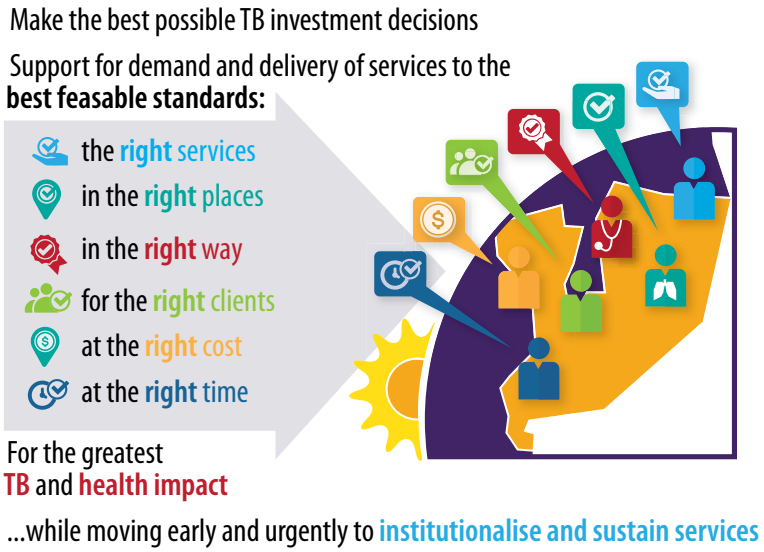
Source: NTP; latest data source was 2017.

1.2 RATIONALE FOR ALLOCATIVE EFFICIENCY ANALYSIS

To achieve the 2030 SDG target and the UN/WHO's goal of ending TB by 2035, it is crucial to determine which models of TB care and treatment should be prioritized, especially in the context of limited resources. Mozambique's NTP budget was an estimated 27 million USD, of which 95% was internationally funded, indicating the high reliance on donor funding of the Mozambique TB response. In addition, as the country is moving on from the National Strategic Plan (NSP) for 2015–19 to the NSP 2020–25, an understanding what targets can be achieved under a given resource envelope is essential. This allocative efficiency study aims to support Mozambique in assessing advancements towards the strategic targets and provide inputs into the country's decision-making on strategic TB investments to attain the 2035 End TB targets.

Any resource-constrained efforts to improve health outcomes are inevitably faced with the need to allocate resources judiciously to achieve better results with the available resources. Moreover, any additional resources allocated in a resource-constrained context as is the Mozambique's TB program, also merits optimized allocation across case finding strategies, diagnosis and treatment regimens as well as management and surveillance activities. This makes strategic decisions in prioritization of which programs to fund (allocative efficiency) and how they should be implemented (implementation efficiency) critical to maximize health outcomes.

Figure 1.3 Allocative efficiency in the TB response



Source: World Bank.
Note: TB = tuberculosis

The concept of allocative efficiency refers to the maximization of health outcomes with the least costly mix of health interventions. Implementation efficiency can be enhanced by a range of measures relating to service delivery modalities, management arrangements, unit costs in procurement and service delivery, and several other areas. Cascade models have been successfully applied in different

contexts to identify breakpoints in health care, compare service delivery models and identify effective interventions to address patient drop-off in the service delivery continuum.

Further to the request from the Government of the Republic of Mozambique and with the understanding of these two dimensions of improving TB efficiency, detailed consultations were held with program managers and experts in the National TB Program and the Ministry of Health.

From these discussions, it was determined that the allocative efficiency modelling should focus on a national level analysis, aiming to:

1. Understand the current and future (predicted) TB epidemic and care cascade; and
2. Provide guidance on how to use existing resources and which models of TB care can maximize impact of the TB response in Mozambique.

Photo: National Tuberculosis Programme. Used with permission.

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To assess how incremental changes in spending affect TB epidemics and determine an optimized funding allocation, the optimisation model parameterises relationships between the cost of TB interventions, the coverage level attained by these interventions, and the resulting outcomes.

Costs of all treatment programs were estimated using a 'bottom-up' approach, including outpatient care as well as hospitalisation.

2 POLICY QUESTIONS AND METHODOLOGY

This section outlines the study questions posed and the accompanying analyses conducted and presented in this report. Additional details are available in Annexes 1, 2, 3, 4, 5 (Technical summary of Optima TB and Data inputs into the model).

2.1 POLICY QUESTIONS

To support Mozambique in allocating TB resources, the analyses presented in this report set out to answer five key policy questions developed together with key stakeholders in the initial planning and methodology workshop. These are:

1. **What is the status of the TB epidemic and TB care cascade for Mozambique using the most recent available data?**

   What are the current estimated numbers of active TB infections, latent TB infections, TB incidence, TB prevalence and TB-related deaths by population group and resistance type:

   i. Children aged 0–14 years
   ii. Adults 15+ years not living with HIV
   iii. Adults 15+ years living with HIV
   iv. By resistance type

   What is the status of the current TB care cascade?

2. **What is the projected future trend of the TB epidemic in Mozambique under current levels of budget and assuming status-quo programming?**

   What are the future numbers of active TB infections, latent TB infections, TB incidence, TB prevalence and TB-related deaths up to 2035 if current programs are implemented with constant coverage in:

   i. Children aged 0–14 years
   ii. Adults 15+ years not living with HIV
   iii. Adults 15+ years living with HIV
   iv. By resistance type

3. **What is the projected impact on the TB epidemic of meeting key national and international targets?**
    i. TB incidence
    ii. TB prevalence
    iii. TB deaths
4. **What is the projected future trend of the country's TB epidemic with optimized allocation of currently available resources? How can the TB care cascade be improved?**
    i. Is the projected future trend of the country's TB epidemic with optimized allocation of currently available resources?
    ii. What are the key interventions for addressing break points in the cascade and what is the evidence for their effectiveness?
    iii. Which steps of the cascade should be prioritized in resource allocation and programming?
5. **What resources are required to achieve key targets of the national TB response?**

2.2 METHODOLOGY

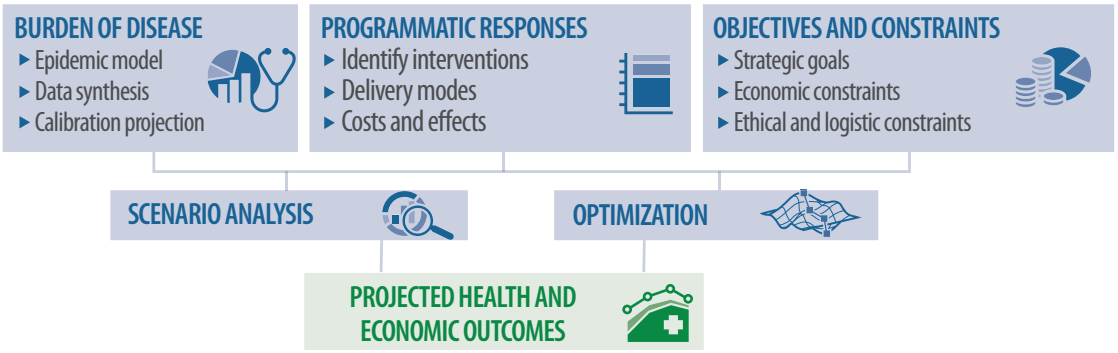
Collaboration and stakeholder involvement

The analysis was a collaboration between the Government of the Republic of Mozambique, the Mozambique National Tuberculosis Program, the World Bank, and University College London as part of the Optima Consortium of Decision Sciences (OCDS). Focal Points were assigned within each organisation to implement the analyses and coordinate contributions. A group of experts and key informants was brought together in two workshops to provide input into the policy questions and analytical framework, share data and expertise, and review the outputs. Epidemiological, program and cost data were collected in a joint effort using an adapted Excel-based Optima TB data entry spreadsheet. Input data, model calibration and cost-coverage-outcome relations were reviewed and validated by the in-country study group. The team also consulted with government experts and other in-country partners on preliminary results.

Optima TB model

To carry out the analyses, the team used Optima TB, a mathematical model of TB transmission and disease progression integrated with an economic and program analysis framework. (Figure 2.1).

Figure 2.1 The Optima approach to TB modelling



Source: Optima Consortium for Decision Science.

Optima TB incorporates evidence on biological transmission probabilities, detailed infection progression and population mixing patterns, in a compartmental mathematical model, which

disaggregates populations into different model compartments including susceptible, vaccinated, early latent, late latent, undiagnosed active TB, diagnosed active TB, on treatment and recovered populations. In addition, compartments are further disaggregated by drug resistance types: drug susceptible (DS), multi-drug resistant (MDR) and extensively drug resistant (XDR). These compartments change in size based on yearly transition rates. A detailed illustration of the compartmental model structure is included in Annexes 1–5.

A national TB prevalence survey is currently underway in Mozambique. In the absence of survey results, Optima TB was calibrated primarily based on data on TB case notifications and WHO estimated TB incidence (2018 Global TB report) with guidance from NTP. The model was calibrated to closely match the yearly number of notified TB cases, as well as estimates of key TB indicators such as active-TB incidence and prevalence and latent TB prevalence. Parameters with high levels of uncertainty, such as force of infection were adjusted to closely match notifications, as well as other indicators including TB incidence and prevalence.

To assess how incremental changes in spending affect TB epidemics and determine an optimized funding allocation, the model parameterises relationships between the cost of TB interventions, the coverage level attained by these interventions, and the resulting outcomes (cost-coverage-outcome relations). These relationships are specific to the place, population, and intervention being considered.

Using the relationships between cost, coverage, and outcome in combination with Optima TB's epidemic model, it is possible to calculate how incremental changes in the level of funding allocated to each intervention will impact the overall epidemic indicators. Furthermore, by using a mathematical optimization algorithm, Optima TB is able to determine an optimized allocation of funding across different TB interventions. Additional details of the Optima TB model and the Mozambique application are included in Annexes 1–5.

Cost estimates

Total expenditure in the TB response was also estimated. In addition to the core TB budget (26.67 million in 2017), this includes funding from other sources that support the management of TB/HIV cases and TB prevention among HIV patients. For example, a bottom-up costing of expenditure on TB-preventive treatment for PLHIV suggests that this intervention costs 12 million USD annually, and is funded by the HIV department. Similarly, ambulatory care for TB patients and BCG vaccinations for children are funded by the Ministry of Health. Estimated total expenditure across program areas and funding streams amounted to around 39 million USD in 2017, nearly double the actual TB budget.

Table 2.1 Mozambique: total estimated expenditure on the TB programmatic response included in this analysis by area (2017)

Program areas	2017 spending (USD)	% share
Screening and diagnosis	21,778,771	55%
Prevention	4,480,459	12%
Treatment	10,524,949	27%
Management, HR and other	2,514,886	6%
Total	**39,299,066**	**100%**

Source: Optima TB analysis estimates.

Note: HR = human resources

Although the NTP budget (Table 2.1) is USD 27 million, the modelled programs include expenditure on TB from other sources. This applies to an estimated USD 3.4 million on preventive therapy (funded by

the HIV program), estimated USD 11 million of state funding for ambulatory care and other services, and an estimated USD 0.9 million on the BCG vaccination program. As data on TB spending by expenditure category was not available, estimates were made used using a bottom-up costing approach. Both total expenditure and unit costs for interventions are therefore subject to some uncertainty

In addition to the total expenditure reported above, a detailed breakdown of expenditure on drugs, diagnostics and other supplies was provided by the NTP. All of these sources facilitated the estimation of program costs for inclusion in the analysis in this report.

Analytical framework

Model parameters are summarised in Table 2.2 and detailed in Annex 5. All DR-TB treatment programs include financial support to improve patient adherence.

Table 2.2 Model parameterisation

Category	Parameterization in the Optima model	Description / Assumptions
Populations defined in the model	Children (0–14 years)	Male and Female Children aged 0-14
	Adults (15+)	Male and Female Adult Population aged 15+ (HIV-negative)
	Adults (15+ HIV+)	Male and Female Adult Population aged 15+ (HIV-positive)
Program expenditure areas defined in the model and included in optimization analysis	Ambulatory-focused DS treatment	Current treatment delivery for DS-TB implemented in Mozambique, 6 months of treatment with daily outpatient visits for the first two months followed by twice-monthly outpatient visits thereafter.
	Ambulatory-focused MDR treatment (long course)	Treatment delivery for MDR-TB, 18 months of treatment with daily outpatient visits for the first two months followed by twice-monthly outpatient visits thereafter. Treatment regimen includes bedaquiline. Severe MDR cases, re-treatments and adverse drug reactions may require some hospital care.
	Ambulatory-focused MDR treatment (short course)	Treatment delivery for MDR-TB, 9 months of treatment with daily outpatient visits for the first two months followed by twice-monthly outpatient visits thereafter. Oral treatment regimen includes bedaquiline or delamanid. Very sick MDR cases, re-treatments and adverse drug reactions may require some hospital care.
	Ambulatory-focused XDR treatment	Treatment delivery for XDR-TB, 24 months of treatment with daily outpatient visits for the first two months followed by twice-monthly outpatient visits thereafter. Very sick XDR cases, re-treatments and adverse drug reactions may require some hospital care.

Table 2.2 continued...

Table 2.2 Model parameterization (continued)

Category	Parameterization in the Optima model	Description / Assumptions
Program expenditure areas defined in the model and included in optimization analysis	BCG Vaccination	Vaccination with Bacillus Calmette-Guérin targeting newborns within the 0–14 population
	Preventive treatment (contacts of active TB - under 5)	6-month Isoniazid Preventive Therapy given to children aged under 5 identified through contact tracing of people with active TB
	Preventive treatment (PLHIV)	6-month Isoniazid Preventive Therapy given to adults living with HIV
	Outpatient screening (excluding PLHIV)	Includes the cost of complete symptom screen delivery, as well as the cost of available TB-testing for diagnosis
	HIV outpatient screening	Includes the cost of complete symptom screen delivery, as well as the cost of TB-testing for diagnosis
	Active case finding (health workers)	Includes the cost of complete symptom screen delivery, as well as the cost of available TB-testing for diagnosis
	Active case finding (miners)	Includes outreach costs in addition to the cost of complete symptom screen delivery, as well as the cost of available TB-testing for diagnosis
	Active case finding (contact tracing)	Includes outreach costs, in addition to the cost of complete symptom screen delivery, as well as the cost of available TB-testing for diagnosis
	Active case finding (community outreach at hotspots)	Includes outreach costs in addition to the cost of complete symptom screen delivery, as well as the cost of available TB-testing for diagnosis
	Active case finding (prisons)	Includes outreach costs in addition to the cost of complete symptom screen delivery, as well as the cost of available TB-testing for diagnosis
Expenditure areas not optimized	The components of TB spending that were not included in the optimization analysis:	Some program areas have not been optimized but instead were fixed at agreed amounts. This was done for different reasons: due to an unclear relationship between an intervention and its effect on TB incidence, morbidity or mortality, or because there was no detail on what the expenditure was for. ART coverage was held fixed as the budget is very large and, once on ART, treatment should never be withdrawn. The importance of ART coverage was instead explored in scenario analyses (see results).
	Management, HR and other costs	Fixed at USD 2,514,886

Table 2.2 continued...

Table 2.2 Model parameterization (continued)

Category	Parameterization in the Optima model	Description / Assumptions
Expenditure areas not optimized	ART for adult PLHIV	Fixed at USD 165,606,756 (Note that this is not included in the TB budget estimate)
Years and time horizons	2001	Year of model initiation, start year for data entry
	2017	Base year
	2025	Milestone year for End TB Strategy and target year for achievement of Stop TB partnership targets
	2035	Target year for End TB Strategy
Baseline scenario funding	As per authors' expenditure analysis	Total spending on modelled TB programs in 2017 as per this study's expenditure analysis (estimated approximately USD 36.8 million, excluding management, HR and other costs.)

Source: World Bank.

Note: ART = antiretroviral therapy; BCG = Bacille Calmette-Guerin; DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

Costs of all treatment programs listed above were estimated using a 'bottom-up' approach, including outpatient care as well as hospitalisation. Although treatment is delivered in the outpatient setting in Mozambique, DR-TB cases often require hospitalisation, for example due to adverse effects of treatment regimens. Data from one province was used to inform the length of hospitalisation. In Maputo province, 58% of DR-TB cases received some inpatient treatment, with an average length of stay of 35 days. An average cost per ambulatory interaction was also derived and applied to both screening programs and to outpatient treatment following the initial hospitalisation period. Based on spending per person reached with an intervention, cost-coverage-outcome relations were developed. Calibrations and cost-coverage outcome relations were produced in collaboration with in-country experts and are further explained in Annexes 1, 2, while unit costs are shown in Annexes 9–15.

Modelling the impact of the HIV epidemic

In recognition of the importance of the HIV epidemic in the high-prevalence and incidence setting of Mozambique, the most recent Spectrum modelling estimates for Mozambique (conducted by AvenirHealth and PEPFAR partners) from 2000 to 2021 were used to inform ART coverage, HIV prevalence and HIV incidence.

Several Optima TB model parameters are impacted by HIV. Co-infection directly impacts nine model parameters whereby each parameter was influenced differently depending on co-infection rates and ART coverage (see Appendices on Optima TB and on TB epidemiological parameters for further details):

1. Mortality rates (excluding TB-related deaths)
2. Mortality rates (including TB-related deaths)
3. Susceptibility to TB infection
4. TB infectiousness
5. Departure rate from early TB latency
6. Probability of latent TB infection versus active TB infection
7. Proportion of new active TB cases with different smear/strain combinations

8. Rate of TB diagnosis (by population which may be targeted differently)
9. Proportion of TB treatment outcomes for each smear/strain combination

Strategic TB targets used in the analysis

The national 2025 targets and global 2025 STOP TB targets both aim to improve diagnosis rates and treatment success rates. The targets used in the modelling analyses are shown in Table 4.

Table 2.3 National and international TB care cascade targets

Impact of improved care cascade	Baseline ('current conditions', 2017)	NSP targets (2025)	STOP TB target (2025)
DS-TB care			
Diagnosis	52%	90%	90%
Treatment success	90%	90%	90%
MDR-TB care			
Diagnosis	5%	80%	90%
Treatment success	48%	70%	90%
XDR-TB care			
Diagnosis	5%	80%	90%
Treatment success	38%	70%	90%

Sources: WHO Mozambique TB country profile; Mozambique National Strategic Plan 2015–19 STOP-TB.
Note: MDR and XDR diagnosis rates are calculated on the basis of number of cases diagnosed and treated for DR-TB (i.e., not those who receive a TB diagnosis but receive treatment for DR-TB). The model's "diagnosis rate" was calculated using notified as a proportion of total prevalence and not incidence in the absence of data on treatment initiation, an arbitrary pre-treatment loss to follow up of 2% was assumed in consultation with local experts.

Limitations of the analysis

As with any mathematical modelling analysis it is necessary to make assumptions about data that are not routinely collected or available, and about some of the expected relationships between variables. These assumptions necessarily imply certain limitations:

Active TB prevalence: This parameter includes diagnosed and undiagnosed active TB cases and is of key importance in TB modelling. Routine data on TB notifications formed the basis for estimating this parameter. WHO estimates of total TB prevalence in 2000 formed the baseline estimate for prevalence in the model, while prevalence for the following years is estimated based on yearly transition rates in the model. Prevalence is also disaggregated across populations based on reported notifications of TB cases. This means that prevalence may be underestimated in populations with lower diagnosis rates. Empirical data from the TB prevalence survey will improve the accuracy of future TB modelling in Mozambique.

TB expenditure: There was limited data on the coverage and costs of key TB interventions in Mozambique, affecting the estimation of TB expenditure. At the same time, TB spending data was reported in broad expenditure areas only, while this analysis uses discrete TB interventions. Unit costs for interventions were subject to some levels of uncertainty. While data triangulation of intervention cost, coverage, and program expenditure used all available information from different funding sources, it had data limitations.

Implementation efficiency: The analysis included considerations of implementation efficiency in a limited way only, as detailed modelling of implementation efficiency was beyond the scope of the study.

For instance, reduced drug prices (leading to lower unit costs, better efficiency and cost-effectiveness) were not modelled, although treatment regimens were carefully costed by component cost. Lower unit costs can influence resource allocation recommendations.

Intervention effectiveness: Allocative efficiency modelling depends critically on the availability of evidence-based parameters for the effectiveness of individual interventions. Although these estimates were derived from global systematic literature reviews where possible, they may vary in specific countries and populations. In particular, the quality of implementation and levels of adherence may vary by context and population. All interventions and spending categories for which effectiveness parameters could not be obtained were treated as fixed spending in the mathematical optimization.

Non-TB benefits: Effects outside of TB indicators, such as the non-TB benefits of different TB treatment modalities are not considered in these analyses. Given the range and complexity of interactions among interventions and their non-TB benefits, the model did not consider wider health, social, human rights, ethical, legal, employment-related or psychosocial implications; but acknowledges that they are important aspects to be considered in planning and evaluating TB responses.

Photo: National Tuberculosis Programme. Used with permission.

The Optima estimate of TB prevalence is much higher than previous WHO 2014 estimate of 150,000 Assuming constant conditions of TB intervention coverage and outcomes, and that ART coverage in Mozambique will reach 90% by 2035, the projected TB incidence rates per 100,000 are on a downward trajectory, decreasing by an average of approximately 2.5% per year between 2017 and 2035.

The incidence of TB in children remains far lower than in the adult populations. TB incidence is projected to reduce significantly in PLHIV as ART coverage increases.

Treatment for HIV significantly reduces the probability of progression from latent to active TB. It is expected that Mozambique would achieve a 90% target for ART coverage by 2035.

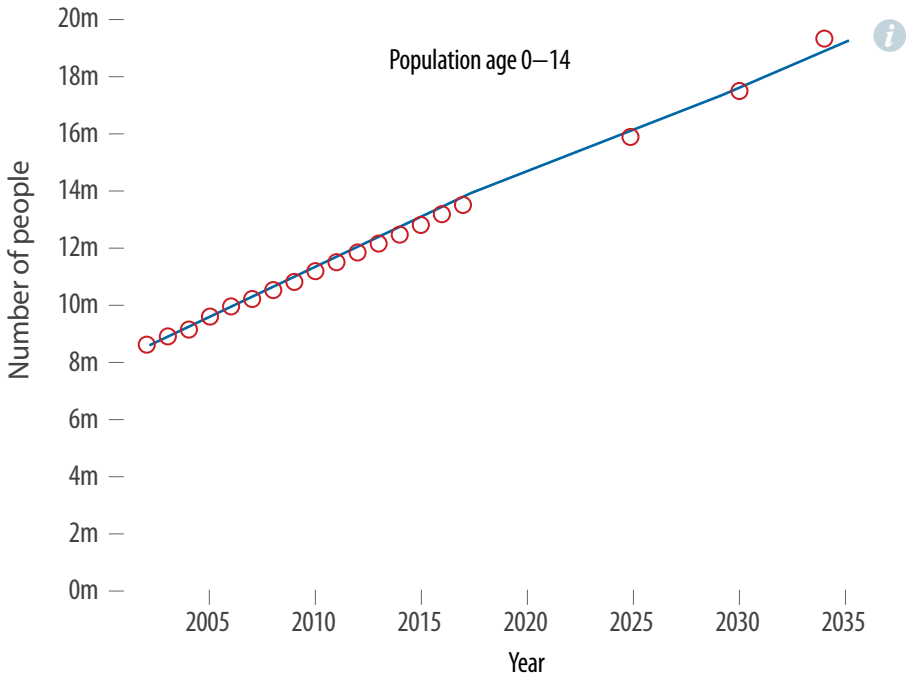
3 RESULTS

3.1 DEMOGRAPHIC TRENDS

The following key observations can be made:

Children: The number of children in Mozambique has been increasing. UN Population Division projections suggest that the number of people under 15 years old in Mozambique will increase from around 13.4 million in 2017 to 19.2 million in 2035. Children are vaccinated with BCG at birth in Mozambique (99% in 2016). For modelling purposes, the analysis is based on the assumption of 50% efficacy of vaccination at birth (Mangtani et al. 2014).

Figure 3.1 Projected demographic trends in Mozambique for children aged 0–14 years (2002–35)

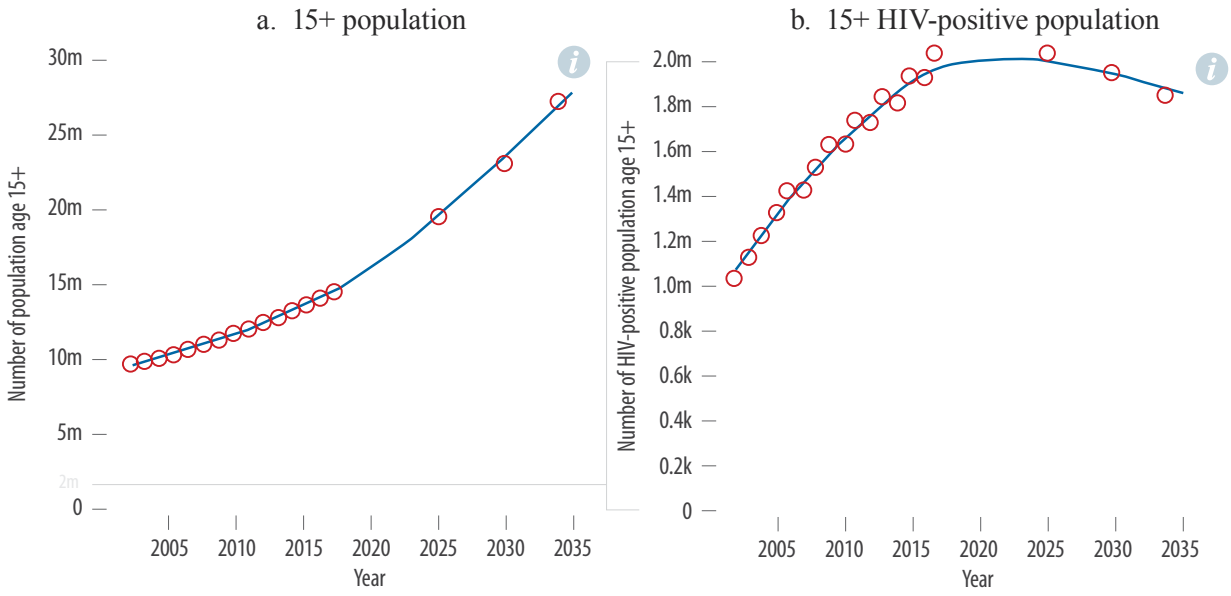


Source: Optima TB model output

Adults: UN Population Division projections suggest that the total number of people age 15 years and over in Mozambique will increase from around 14.3 million in 2017 to 28 million in 2035. Currently, an estimated 2 million adults are living with HIV in Mozambique (UNAIDS). To ensure alignment with

existing HIV projections in Mozambique, SPECTRUM data on future HIV prevalence was used in this analysis. These projections suggest adult prevalence of 1.8 million in 2035. Future HIV prevalence and incidence remain highly uncertain and will depend on future coverage of ART. In 2017, adult coverage of ART was 55%.

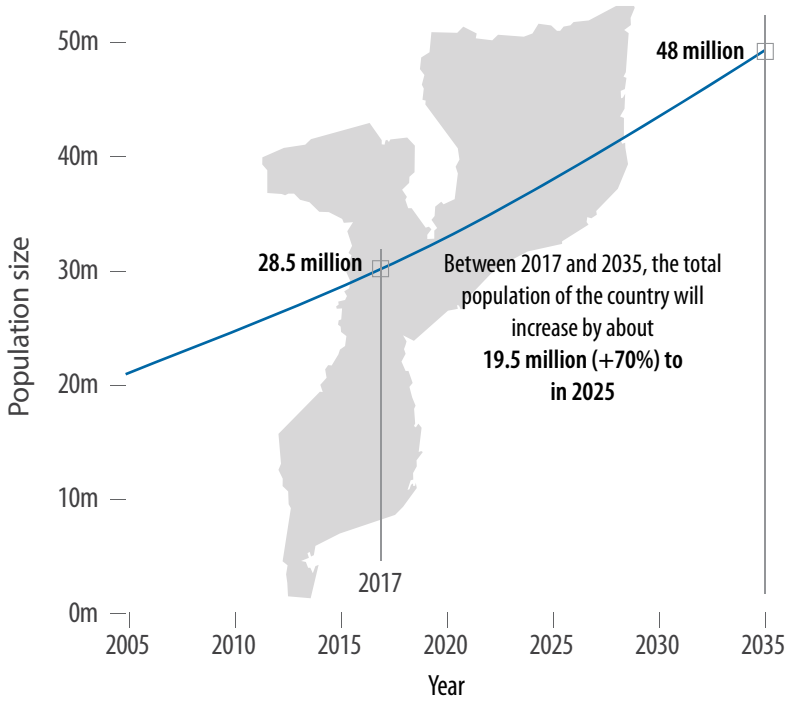
Figure 3.2 Projected demographic trends in Mozambique for HIV-negative and HIV-positive adults aged 15 years and older (2002–35)



Source: Optima TB model output.

Total population: It is estimated by the UN that between 2017 and 2035, the total population of the country will increase by about 19.5 million (+70%) and would reach 48 million in 2025.

Figure 3.3 Total population



Source: Optima TB model output.

3.2 PAST AND FUTURE TB EPIDEMIC TRENDS

What is the projected future trend of the TB epidemics in Mozambique under current budget levels and assuming status-quo programming?

This section outlines the epidemic trajectory for DS-, MDR- and XDR-TB across the three sub-populations in Mozambique.

Estimates for the 2017 base year of the Mozambique analysis

Given that 2017 was used as the base year for the analysis, Table 3.1 and Table 3.2 below present Optima TB estimates of active TB prevalence, incidence, latent infections and TB-related deaths by sub-population for 2017.

Table 3.1 Model estimates of number and prevalence of active pulmonary TB infections by sub-population (2017)

Population	Active TB cases	Active DS-TB cases	Active MDR-TB cases	Active XDR-TB cases	Active TB prevalence
0-14 years	32,826	32,165	651	9	0.24%
15+ years HIV-	163,538	155,036	8,323	179	1.15%
15+ years HIV+	197,435	186,992	10,228	214	10.26%
Total	**393,799**	**374,193**	**19,938**	**403**	**1.32%**
In percent	**100%**	**95.0%**	**4.8%**	**0.1%**	–

Source: Optima TB model output.
Note: DS = drug susceptible; TB = tuberculosis; MDR = multi-drug resistant; XDR = extensively drug-resistant.

Table 3.2 Model estimates of active pulmonary TB incidence, latent infections and TB-related deaths, by sub-population (2017)

Population	Incidence per 100,000	Latent TB cases	TB-related deaths
0–14 years	144	976,635	2,052
15+ years	542	6,032,670	20,880
15+ years HIV+	2,592	583,964	37,406
Total	**491**	**7,593,269**	**60,339**

Source: Optima TB model output.
Note: TB = tuberculosis.

Past trends in Mozambique's TB epidemic

Historical TB notifications data for Mozambique were used to calibrate the model and assess past epidemic trends. Although the number of notifications and the estimated case detection rate in Mozambique increased rapidly, WHO estimates suggest that TB incidence also increased. Accounting for pulmonary TB only, there were:

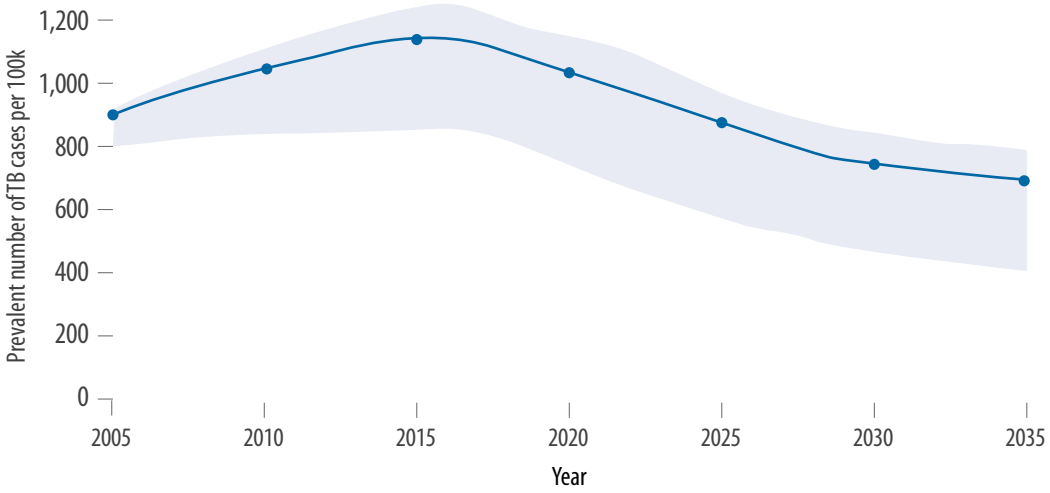
- 79,658 notified TB cases in 2017, of which 1.25% were DR-TB
- 0,140 notified TB cases in 2015, of which 1.40% were DR-TB
- 66,187 notified TB cases in 2013, of which 1.52% were DR-TB

Past TB epidemic trends for the period 2002 to 2017 show significant differences across sub-populations included in the analysis. Results are presented for children aged 0–14, adults aged 15 and over (HIV-negative) and adults aged 15 and over (HIV-positive) (Table 3.2).

TB prevalence estimates over time

Actual TB prevalence in Mozambique is currently unknown. In 2014, WHO estimated TB prevalence of approximately 150,000 [80,000– 243,000]. In this analysis, Optima TB estimate is much higher than previous WHO estimate (about 352,000 for year 2017). Figure 3.4 shows the temporal trend of TB prevalence per 100,000 population over 30 years.

Figure 3.4 Prevalence of pulmonary TB per 100 thousand



Source: Optima model output.
Note: TB = tuberculosis.

Future TB incidence projections

Future projections for TB incidence, assuming TB intervention coverage and outcome conditions as per 2015, are shown below in Table 3.3, Figure 3.5 (a–c), and Figure 3.6 for 2025 and 2035. Given the importance of ART coverage on TB incidence in this context, in consultation with local experts, a figure of 90% adult ART coverage by 2035 (compared to 55% of adult PLHIV in 2017; UNAIDS) was used to inform a realistic target for the purposes of this analysis. ART coverage has a significant impact on modelled TB incidence. For PLHIV on ART, the probability of progressing from latent to active TB is assumed to be the same as for the general population. For PLHIV not on ART, the probability of progression is significantly higher.

Assuming constant conditions of TB intervention coverage and outcomes, and that ART coverage in Mozambique will reach 90% by 2035, the projected TB incidence rates per 100,000 are on a downward trajectory, decreasing by an average of approximately 2.5% per year between 2017 and 2035 (Figure 3.6). The incidence of TB in children remains far lower than in the adult populations. TB incidence is projected to reduce significantly in PLHIV as ART coverage increases (Table 3.3 and Figure 3.5 (a–c).

Table 3.3 Modelled pulmonary TB incidence per 100,000 in Mozambique, by sub-population (2017, 2025 and 2035)

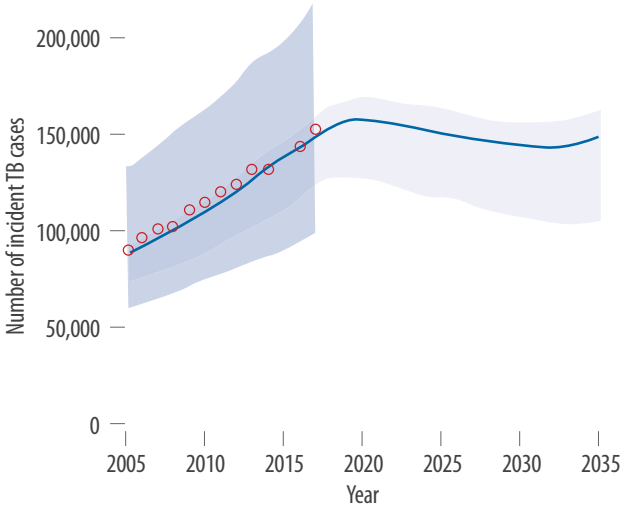
Sub-population	TB incidence 2017	TB incidence 2025	TB incidence 2035
0-14 years	144	156	127
15+ years	519	499	406
15+ years HIV+	2,752	1,356	545
Total	**495**	**401**	**303**

Source: Optima model output.

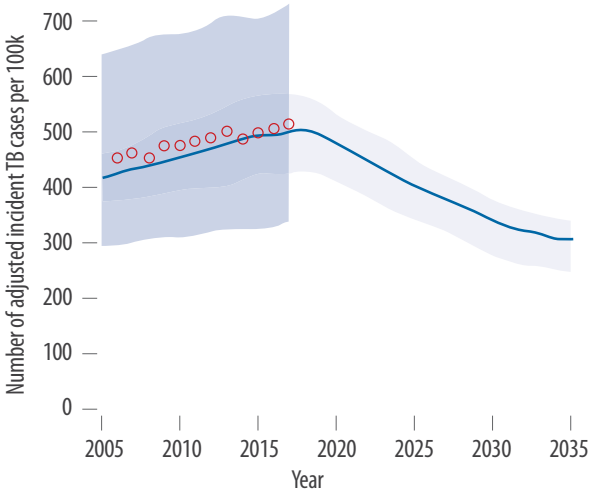
Note: TB = tuberculosis.

Figure 3.5 Projected future TB incidence (a–c)

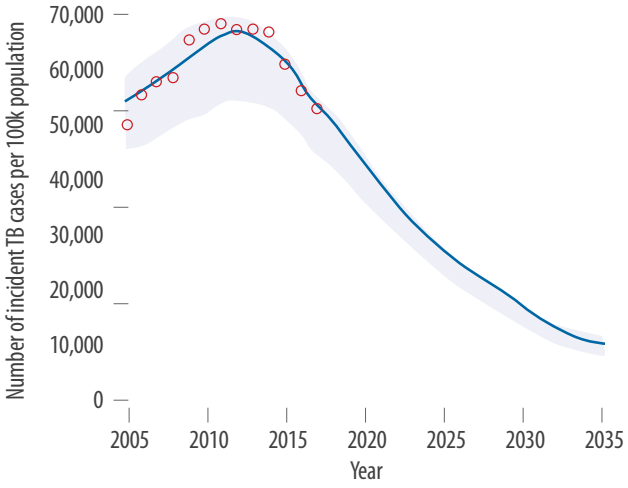
a. Projected new TB cases (total cases)



b. Projected new TB cases per 100,000 population



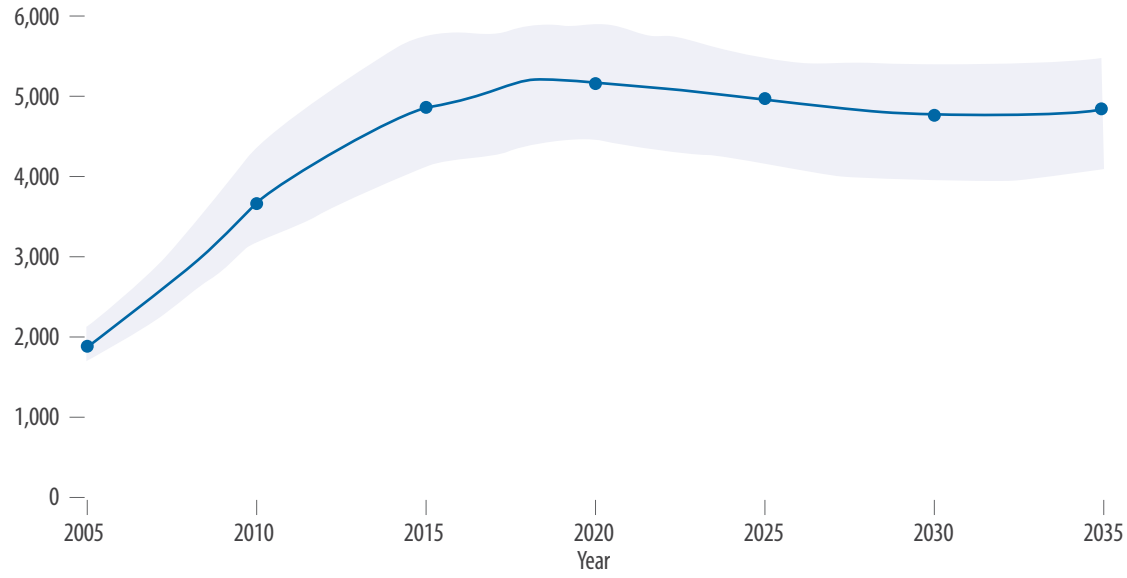
c. Projected TB cases/100,000 population among adults 15 years and older living with HIV



Source: Optima model output.

Note: k = thousands; TB = tuberculosis.

Figure 3.6 Projected future DR-TB (total cases)



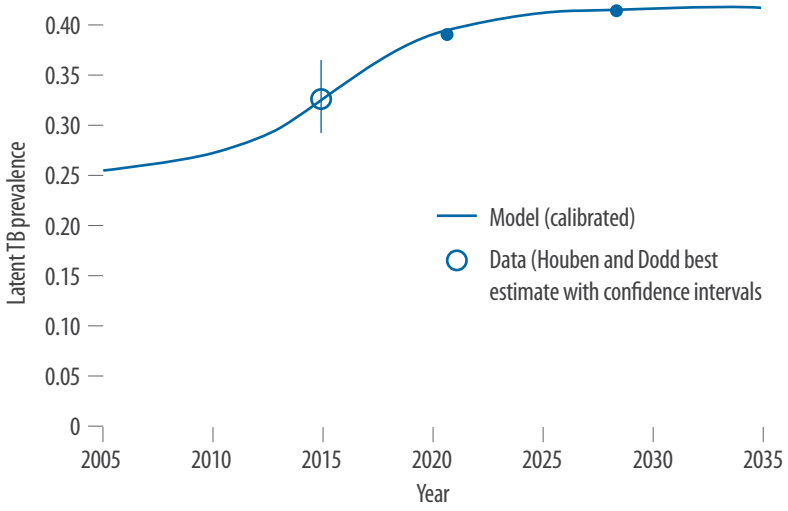
Source: Optima model output.
Note: TB = tuberculosis.

Incidence of drug-resistant TB is projected to follow the same overall trend. The WHO estimate 3.7% [2.5%–5.2%] of new TB cases are MDR/RR-TB (2017). These projections assume constant TB care coverage and outcomes to 2035 and ART coverage increasing to 90% by 2035.

Temporal trends in latent TB infections

The actual prevalence of latent TB in Mozambique is unknown. Our analysis, based on observed active TB infections in Mozambique, estimated latent TB prevalence of around 34% in Mozambique for 2016 (Figure 3.7). This is consistent with published national estimates of between 31% and 38% latent TB prevalence in Mozambique, with a best estimate of 34% (Houben and Dodd 2016). The projections for future years are inherently uncertain due to probable changes in disease burden and program coverage.

Figure 3.7 Model-derived total latent prevalence in Mozambique, 2005-35 (% of total population)

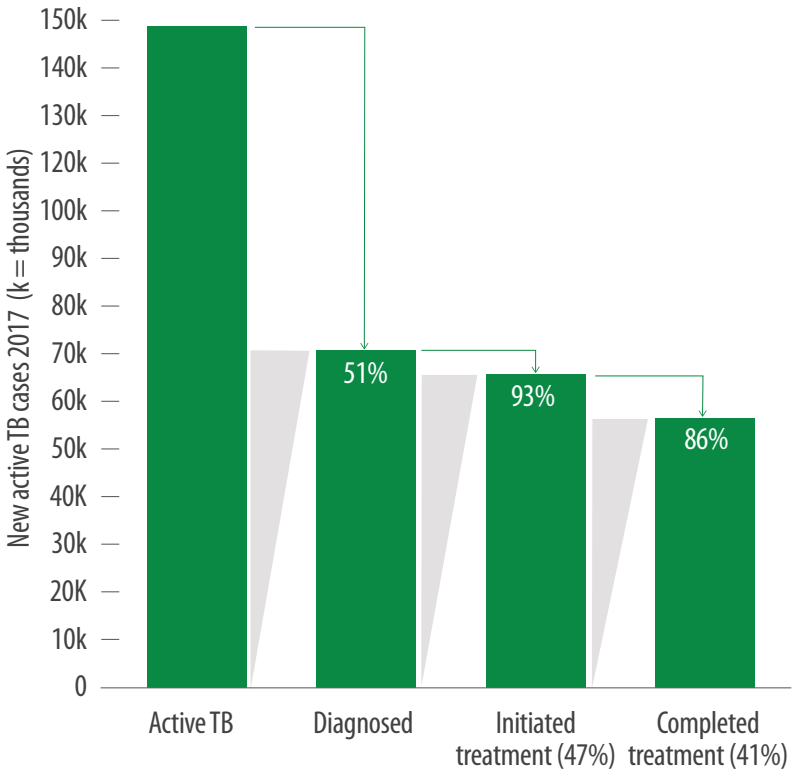


Source: Optima TB model output.
Note: Data for comparison represents range of estimate from Houben and Dodd (2016); TB = tuberculosis.

What is the current status of the TB epidemic and TB care cascade for Mozambique using the most recent available data?

Figure 3.8 shows outcomes from each stage in the TB care cascade based on total modelled pulmonary TB incidence (2018). It shows that TB diagnosis remains suboptimal with an estimated 51% of all active pulmonary TB incidence diagnosed. As a result, despite high treatment success rates, only about 41% of all new active TB cases attain treatment success. Improved screening and diagnosis are therefore a priority for Mozambique's TB response.

Figure 3.8 TB care cascade (2017; all cases)



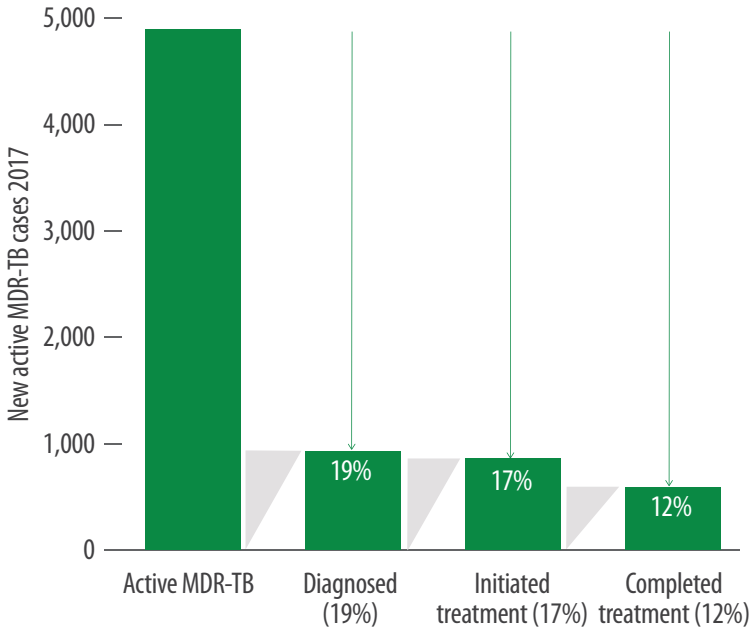
Source: Optima TB model output.

Note: This cascade is probabilistic rather than cohort-based. It shows the probability of final outcomes from each stage in the cascade, e.g., for people with active TB, how many of those will be diagnosed prior to natural recovery or succumbing to a TB-related death. This cascade is based on modelled incidence of TB for 2018 and rates of flow through the stages of the cascade. The green color in each column indicates total cases, diagnosed, initiated treatment, and completed treatment.

Figure 3.9 shows the 2018 care cascade for MDR-TB. Results show a low diagnosis rate of about 19% (of new active MDR-TB). This leads to a very low percentage of cases with treatment success (12%). Increased coverage of drug susceptibility testing, either using GeneXpert or other diagnostic testing is essential to improve the care cascade for MDR-TB.

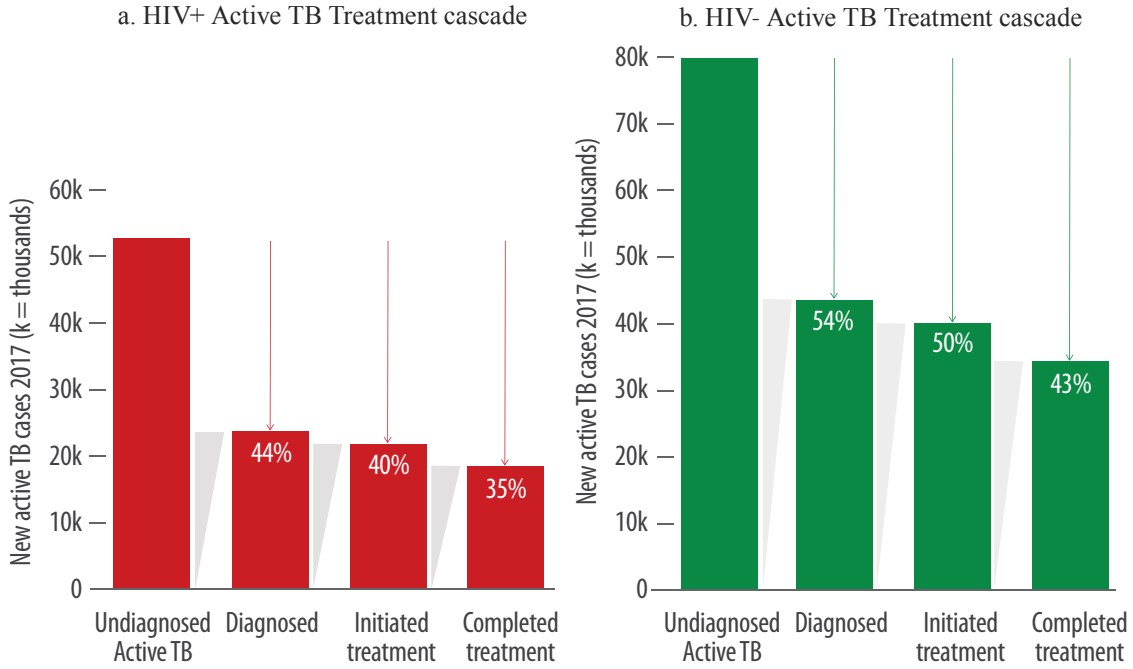
Figure 3.10 show outcomes from each stage in the care cascade based on total modelled pulmonary TB incidence (2018) in adults disaggregated by HIV status. Our finding suggests that PLHIV have a significantly higher undiagnosed TB mortality rate—40% of total incident TB in adult PLHIV died without receiving a TB diagnosis—compared to around 20% amongst HIV-negative adults. Improved screening and timely diagnosis in PLHIV are therefore a priority for preventing deaths amongst coinfected cases.

Figure 3.9 MDR-TB treatment cascade (2017)



Source: Optima TB model output.
Note: MDR-TB = multi-drug resitant TB; TB = tuberculosis.

Figure 3.10 TB Care cascade by HIV status



Source: Optima TB model output.
Note: TB = tuberculosis.

3.3 IMPACT OF MEETING NATIONAL AND INTERNATIONAL TB CARE TARGETS ON THE TB EPIDEMIC?

A scenario analysis was performed to understand the impact of meeting international care cascade targets set for 2025 on key TB indicators. For each scenario, there is a time frame for programmatic change to occur, which is the time period over which programmatic targets are achieved, and another

time frame for tracking impact, which is the time period for which the effect of these achievements is estimated. For example, in the 2025 target scenario, coverage targets are achieved by 2025 and the impact of achieving and sustaining 2025 coverage levels is tracked up to 2035.

Testing and treatment scenarios to meet 2025 STOP-TB targets

This group of scenarios models the impact of meeting 2025 NSP and STOP TB targets separately for:

- TB screening/testing
- TB treatment outcomes

These effects are then considered simultaneously to assess what impact on key TB indicators can be obtained by meeting 2025 STOP TB targets. Although the 2025 STOP TB targets also aim for treatment initiation rates amongst diagnosed cases of 100%, there was insufficient data on treatment initiation rates in Mozambique to conduct a meaningful scenario analysis.

Improved TB screening/testing

What is the impact of reaching 2025 targets for case detection? The parameters modified in the model to assess the effect of the scenario are summarised in Table 3.4.

Table 3.4 Scenario parameters: improved TB screening/testing

Improved TB screening/testing	Current conditions (2017)*	NTP 2025 Targets	STOP-TB 2025 Targets
Case detection for DS-TB	52%	90%	90%
Case detection for MDR-TB	5%	80%	90%
Case detection for XDR-TB	5%	80%	90%

Source: WHO (2018); STOP-TB.

Note: * = MDR and XDR diagnosis rates are calculated on the basis of number of cases diagnosed and treated for DR-TB (i.e., not those who receive a TB diagnosis but receive treatment for DR-TB). The model's "diagnosis rate" was calculated using notified as a proportion of total prevalence and not incidence. In the absence of data on treatment initiation, an arbitrary pre-treatment loss to follow up of 2% was assumed in consultation with local experts; DS = drug susceptible; TB = tuberculosis; MDR = multi-drug resistant; XDR = extensively drug-resistant..

Improved treatment outcomes

Table 3.5 presents various targets related to improved treatment outcomes in the TB care cascade.

Table 3.5 Scenario parameters: Improved treatment outcomes

Improved treatment outcomes	Current conditions (2017)	NTP 2025 Targets	STOP-TB 2025 Targets
Treatment success rates for DS-TB regimens	90%	90%	90%
Treatment success rates for MDR-TB regimens	48%	70%	90%
Treatment success rates for XDR-TB regimens	38%	70%	90%

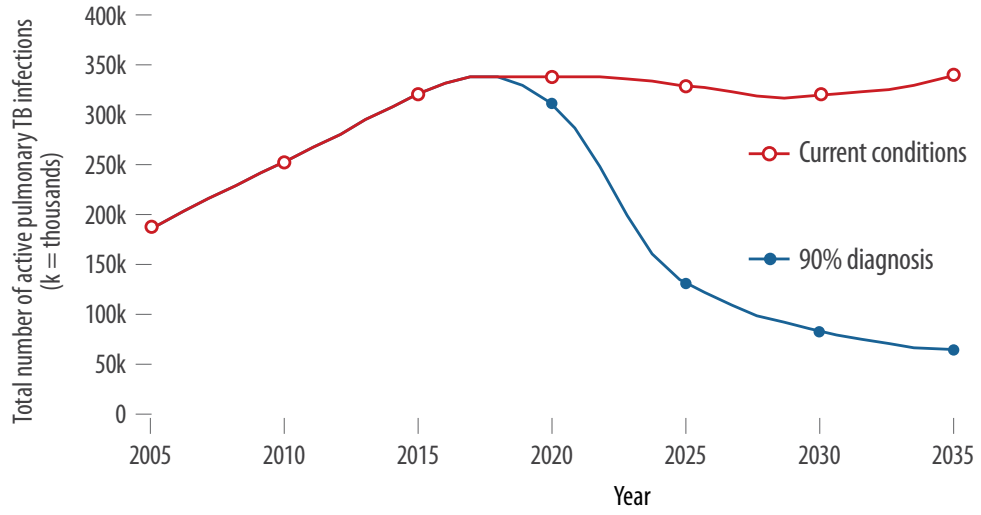
Source: WHO (2019); STOP-TB.

Note: DS = drug susceptible; TB = tuberculosis; MDR = multi-drug resistant; XDR = extensively drug-resistant.

Figure 3.11 presents the impact of meeting and sustaining the NTP and STOP-TB care cascade target of 90% diagnosis rate by 2025 on all active pulmonary TB prevalence. Although treatment success rate in Mozambique is high (90% for new and relapsed cases, WHO 2017), the estimated case detection is low

(52%; WHO, 2017). Therefore, improving case detection is a priority for Mozambique's TB response – both NTP targets and Stop-TB targets aim for 90% diagnosis rate by 2025. We modelled the impact of meeting the 2025 targets of diagnosis rate and our results show significant reductions in the total number of active TB cases and TB-related deaths of up to 80% relative to current conditions by 2035.

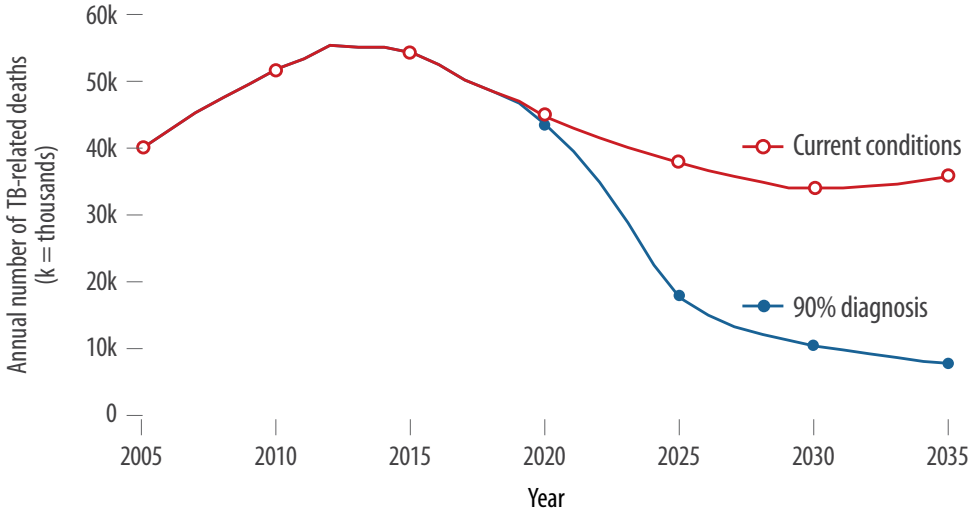
Figure 3.11 Modelled impact of reaching 90% diagnosis rate by 2025 on the number of people with active pulmonary TB (TB prevalence) (2001–35)



Source: Optima TB model output.
Note: TB = tuberculosis.

Similarly, Figure 3.12 presents the impact of meeting the 90% diagnosis rate by 2025 on annual TB-related deaths. Meeting and sustaining the proposed care cascade would yield significant reductions in the total number of deaths, of up to 80% relative to current conditions by 2035.

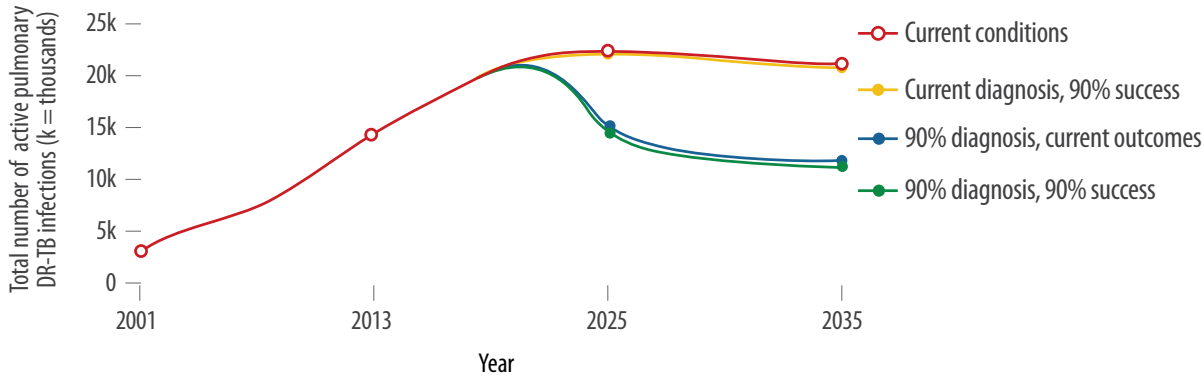
Figure 3.12 Modelled impact of reaching 90% diagnosis rate by 2025 on the annual number of pulmonary TB-related deaths (2001–35)



Source: Optima TB model output.
Note: TB = tuberculosis.

Figure 3.13 presents the impact of meeting the STOP-TB care cascade targets for all types of drug-resistant TB. Simultaneously, meeting the proposed targets can reduce 50% new DR-TB infections by 2035.

Figure 3.13 Total modelled number of people with DR-TB

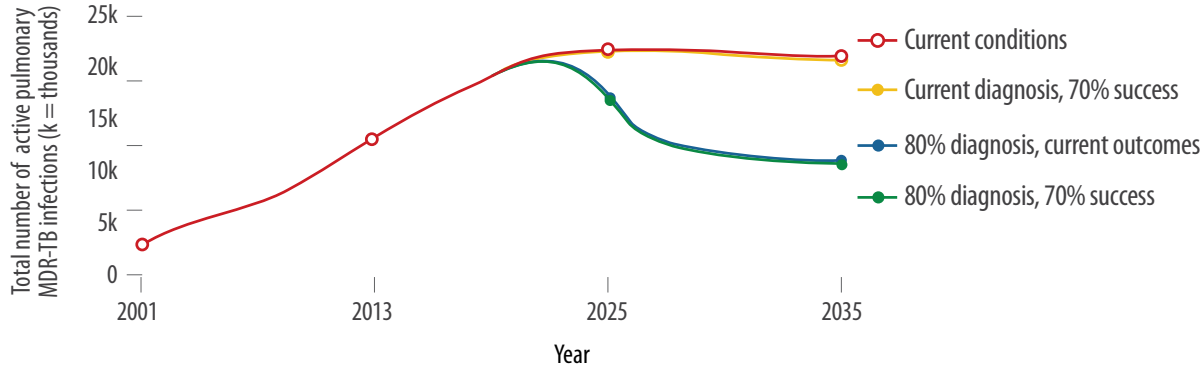


Source: Optima TB model output.
Note: DR-TB = drug resistant tuberculosis.

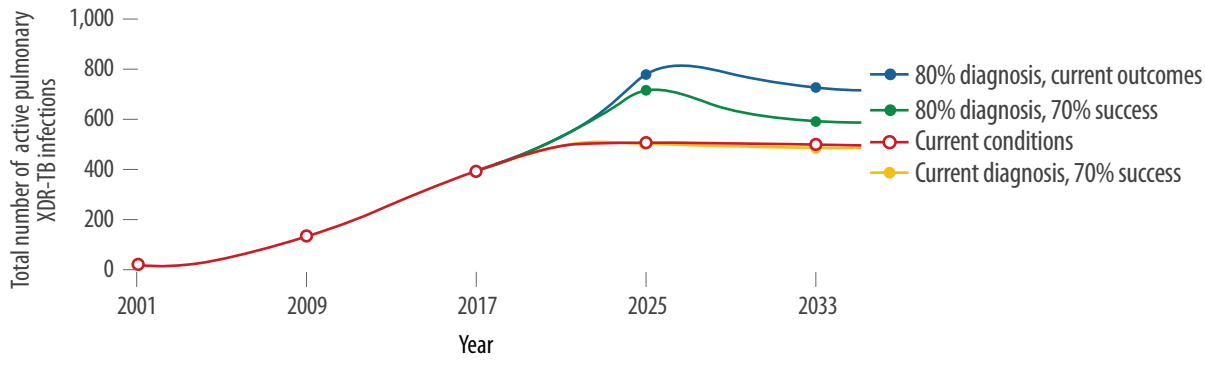
Figure 3.14 presents the impact of meeting and sustaining the NTP 2025 care cascade targets for drug-resistant TB. These targets show similar trends to those observed under the Stop TB scenarios. As the targets for diagnosis and treatment success are lower than the Stop TB targets, the impact on DR-TB prevalence is correspondingly less. Simultaneously meeting NTP targets for diagnosis and treatment of MDR-TB by 2025 could reduce MDR-TB prevalence in 2035 by 50% relative to current conditions.

Figure 3.14 Projected impact of meeting NTP care cascade targets on the number of people with pulmonary a. DR-TB and b. XDR-TB (2015–35)

a. Modelled number of people with MDR-TB



b. Modelled number of people with XDR-TB



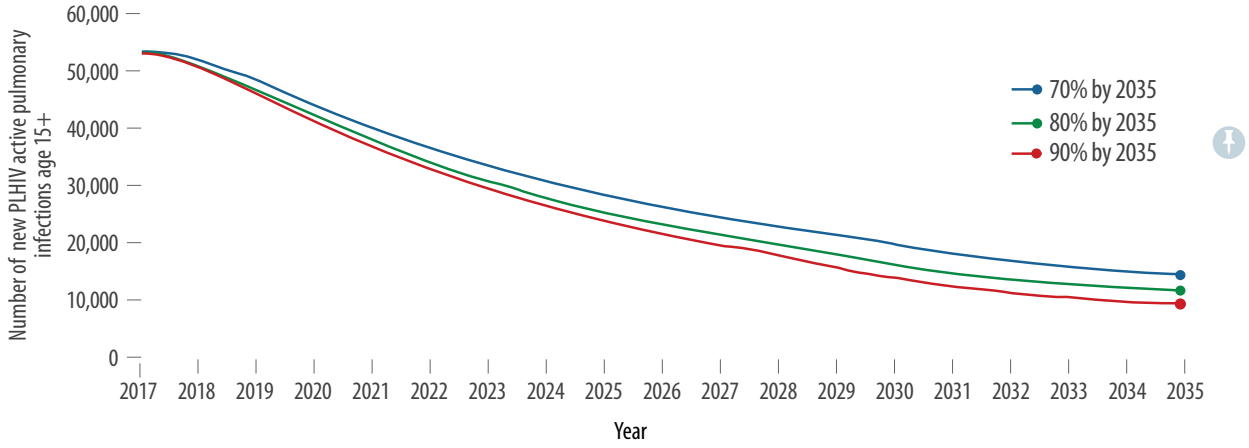
Source: Optima TB model output.
Note: MDR-TB = multi-drug resistant tuberculosis; XDR-TB = extensively drug-resistant tuberculosis.

3.4 WHAT IS IMPACT OF REACHING 90% ART COVERAGE ON FUTURE HIV INCIDENCE?

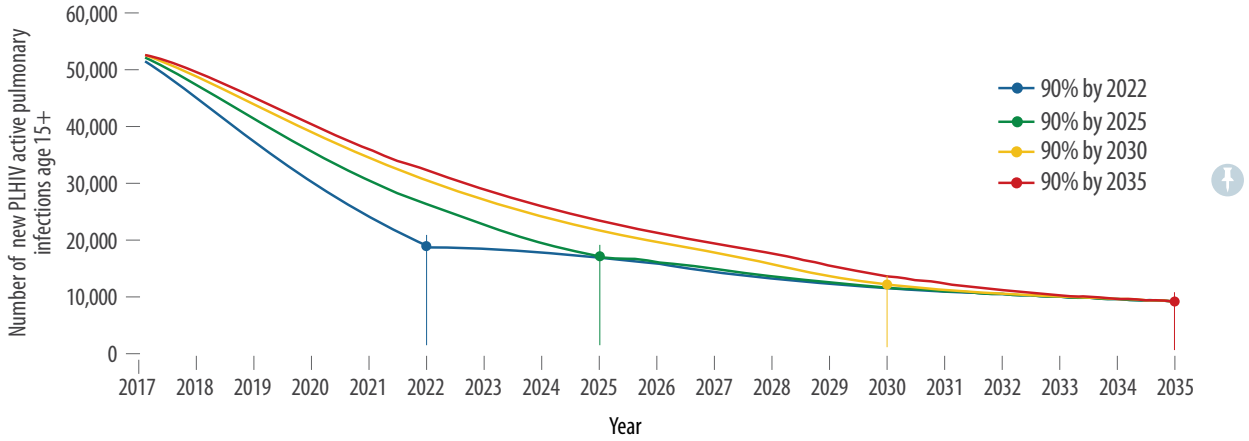
Treatment for HIV significantly reduces the probability of progression from latent to active TB. In consultation with local experts, it is expected that Mozambique would achieve a 90% target for ART coverage by 2035. Scaling up to 90% ART coverage by 2035 is projected to reduce the number of new TB cases among adult PLHIV in 2035 by over 50% compared to current ART coverage (55%). Additionally, the timeframe for ART scale-up is important for reducing TB incidence. Reaching 90% ART coverage more quickly reduces incident TB in PLHIV very rapidly (Figure 3.15 b). This highlights the importance of expanding access to treatment for HIV to as many people as possible and as soon as possible in order to minimize TB incidence in Mozambique.

Figure 3.15 Estimated impact of reaching a. different ART coverage levels and b. 90% ART coverage levels on the annual number of new active pulmonary TB infections (2017–35)

a. Impact of different scale-up assumptions by 2035 among HIV positive adults



b. Impact of timing of reaching 90% coverage among HIV positive adults

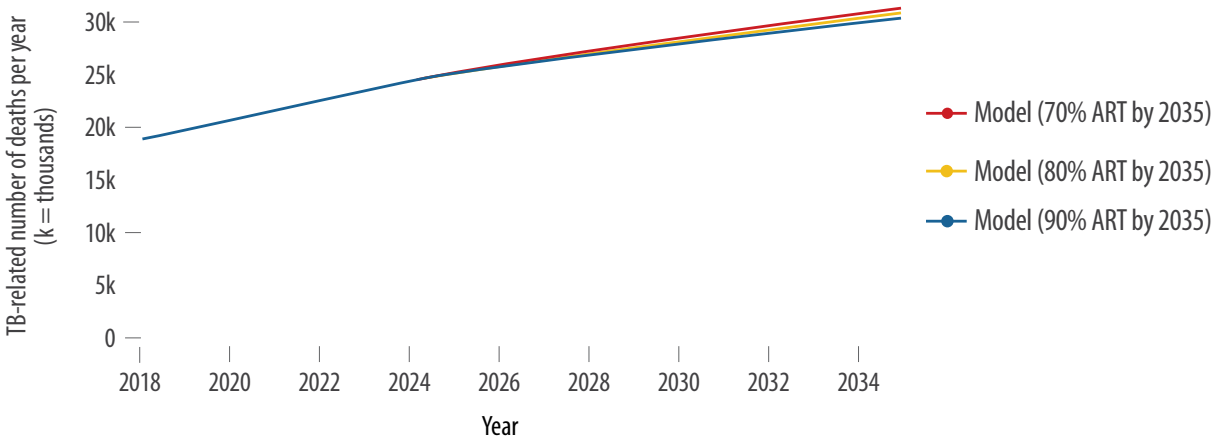


Source: Optima TB model output.
Note: PLHIV = people living with HIV.

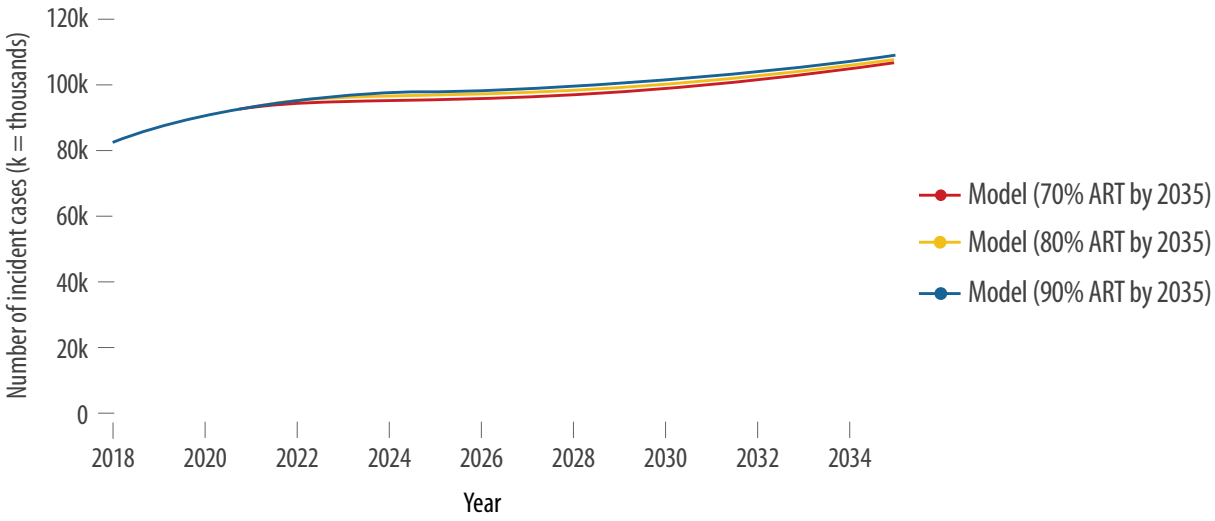
Although the effect is far smaller compared to the effect of ART coverage among HIV positive adults, increased ART also indirectly reduces active TB incidence in the HIV-negative population, as a result of reduced transmission probability.

Figure 3.16 Importance of ART coverage for future a. TB-related deaths and b. TB incidence in HIV-negative adults

a. TB-related deaths, adults 15+



b. TB incidence adjusted for notified EPTB, adults 15+



Source: Optima TB model output.
Note: ART = antiretroviral therapy; EPTB = extrapulmonary TB; TB = tuberculosis.

3.5 HOW TO OPTIMALLY ALLOCATE CURRENTLY AVAILABLE RESOURCES FOR TB TREATMENT?

The analysis presented in this section addresses the core questions of this allocative efficiency study, looking at the entire TB response and determining how resources could be allocated to maximize health outcomes.

- How can the TB care cascade be improved and resource allocation be optimized?
- How is Mozambique's TB epidemic projected to change if we optimize the allocation of current funding available?
- How close will Mozambique get to international targets with an optimal allocation of funding?

As outlined in above section, current TB spending and allocation patterns in Mozambique are projected to lead to a steady decline in TB incidence rates. The scope of this section is therefore to explore whether greater reductions in key indicators can be achieved by optimally re-allocating TB spending.

Optimized allocations of resources are only optimal relative to a specific set of objectives and within a given time frame. The optimization analysis was performed for a combination of three objectives:

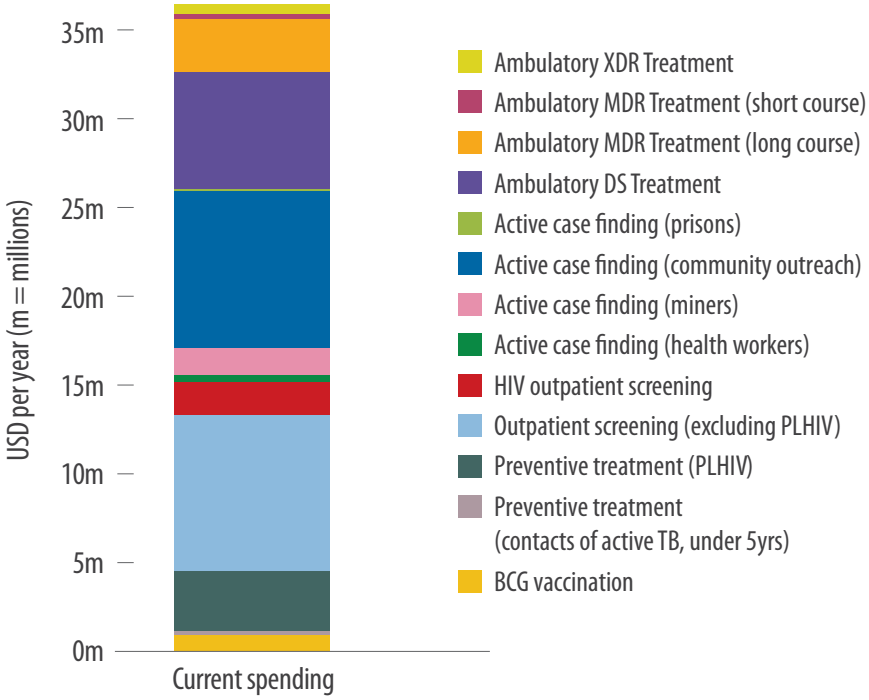
- Avert more new infections
- Further reduce prevalence
- Prevent additional TB deaths

Overview of TB budget and spending in Mozambique

Total national spending on TB prevention and care was estimated at ~USD 36.8 million in 2017 (Table 2.1), including:

- NTP funding for diagnosis and treatment of pulmonary TB
- Estimated expenditure: USD 3.4 million on preventive therapy for PLHIV (funded by the HIV program)
- Estimated state funding through Ministry of Health hospital care and other services: USD 11 million
- Estimated BCG vaccination: USD 0.9 million
- Estimated expenditure on ART for PLHIV was USD 166 million (not included in this exercise)

Figure 3.17 Overview of estimated TB expenditure (2017)



Source: Optima TB model output.
Note: As data on TB spending by expenditure category was not available, estimates were made using a bottom-up costing approach; Both total expenditure and unit costs for interventions are therefore subject to some uncertainty; BCG = Bacille Calmette-Guerin; DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

Optimizing Mozambique's TB program funding allocations

Figure 3.18 and Table 3.6 show the overall optimized allocation of expenditure to minimize TB incidence, prevalence and deaths. In this analysis it was assumed that the same USD 36.8 million that were available for TB-related interventions in 2017 would remain available each year up to 2035. The

optimized budget allocation differs from current allocations in several areas, including:

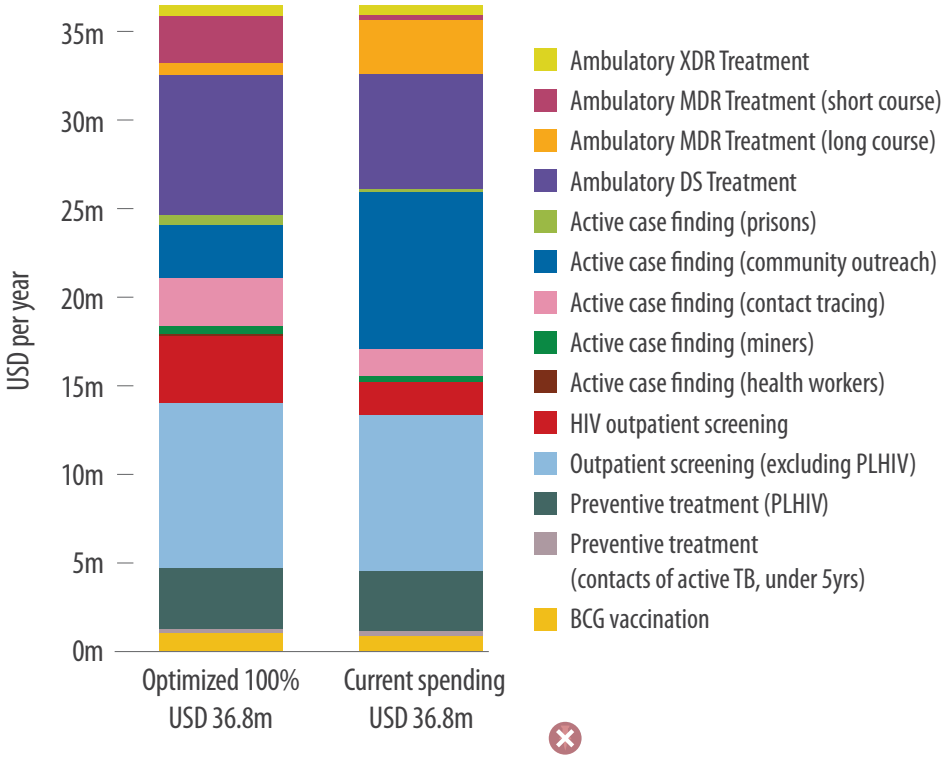
- Increasing annual funding for outpatient screening from USD 10.8 million to USD 13.2 million, including regular TB screening for all PLHIV at outpatient clinics (currently at 74%)
- Prioritizing investment in case-finding programs for key risk groups, such as prisoners and health workers
- Increasing funding for treatment programs to accommodate increased number of notifications

Unit costs estimated using bottom up costing approach

Table 3.6 Estimated unit cost per person (treatment)

	Unit cost (USD)
Preventive TB treatment (contacts of active TB - under 5)	8.1
Preventive TB treatment (PLHIV)	19.7
Ambulatory-focused DS treatment	87
Ambulatory-focused MDR treatment (long course)	3,493
Ambulatory-focused MDR treatment (short course)	1,573
Ambulatory-focused XDR treatment	13,198

Figure 3.18 Optimizing Mozambique's TB program funding allocations



Source: Optima TB model output.

Note: 2017 = base year (current allocation); Optimized budget: It was assumed expenditure of USD 36.8 million available for TB-related programs in 2017 would remain available on an annual basis up to 2035; BCG = Bacille Calmette-Guerin; DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

Table 3.7 Current and optimal allocations of 2017 TB spending, by intervention (in million USD)

Program	Optimized 100% (USD)	Current spending (USD)	Change (USD)
Active case finding (contact tracing)	2,800,000	1,700,000	1,100,000 ▲
Active case finding (health workers)	130,000	38,000	92,000 ▲
Active case finding (miners)	370,000	250,000	120,000 ▲
Active case finding (community outreach)	3,100,000	8,900,000	-5,800,000 ▼
Active case finding (prisons)	560,000	120,000	440,000 ▲
Ambulatory DS treatment	7,900,000	6,700,000	1,200,000 ▲
Ambulatory MDR treatment (long course)	680,000	3,100,000	-2,420,000 ▼
Ambulatory MDR treatment (short course)	2,600,000	92,000	2,508,000 ▲
Ambulatory XDR treatment	710,000	670,000	40,000 ▲
Outpatient screening (excluding PLHIV)	9,500,000	8,900,000	600,000 ▲
HIV outpatient screening	3,700,000	1,900,000	1,800,000 ▲
Preventive treatment (contacts of active TB - under 5)	220,000	210,000	10,000 ▲
Preventive treatment (PLHIV)	3,500,000	3,400,000	100,000 ▲

Source: Optima TB model output.
Note: DS = drug susceptible; HR = human resources; MDR = multi-drug resistant; PLHIV = people living with HIV; TB = tuberculosis; USD = United states dollar; XDR = extensively drug-resistant.

Shifts within screening and diagnosis interventions

Gaps in diagnosis represent a major break point in the TB care cascade in most countries and finding the "missing cases" is a key challenge for Mozambique's TB program. An optimized allocation of resources would reduce total funding for screening and diagnosis, mainly due to reallocating resources to cheaper activities, including: (1) screening of PLHIV at each outpatient visits, (2) increasing funding for other outpatient screening such as cough monitors, (3) increasing coverage of programs targeting key high-risk groups such as prisoners, (4) doubling coverage of household contact tracing, and (5) reducing the house-to-house screening activities (Table 3.7 and Figure 3.19). Screening and diagnosis would then consume about 51% of total TB spending.

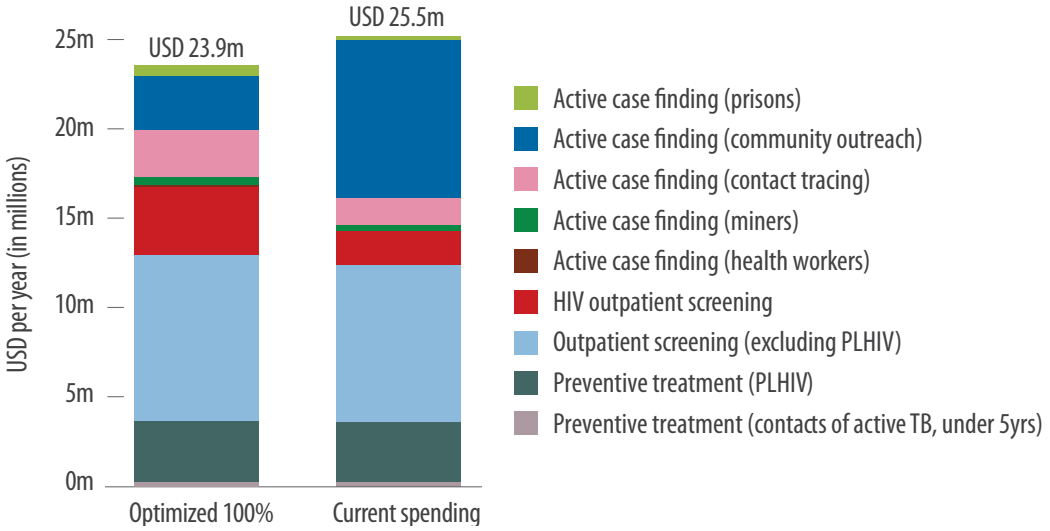
Shifts within treatment programs

In an optimized intervention mix, TB treatment would receive more funding and would absorb approximately 32% of total TB spending in Mozambique compared with the current 29%. This is due to the increased number of cases diagnosed as a result of increased funding for active case finding programs.

- An optimal allocation increases annual funding for treatment programs as a result of a greater number of people diagnosed
- Mozambique already treats all patients in the ambulatory setting, reducing costs, impacting on patients' lives and the risk of nosocomial TB transmission
- Both long-course and short-course regimens for MDR-TB in Mozambique now use bedaquiline (in-line with WHO guidance)

- Short-course regimens for MDR-TB are currently used for just a small number of patients
- Although short-course regimens will not be suitable for all people with MDR-TB, increased coverage of the short-course regimen could significantly reduce costs
- Future policy decisions on the choice of DR-TB regimens in Mozambique should be closely monitored and made based on local evidence when results for each cohort become available

Figure 3.19 Optimal reallocation of current TB screening and prevention expenditure to minimize active pulmonary TB prevalence between 2017 and 2035 in Mozambique



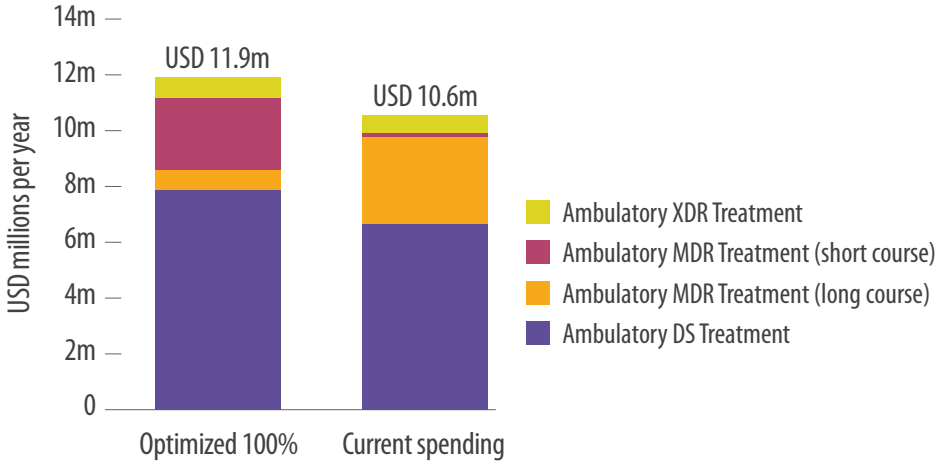
Source: Optima TB model output.
Note: 2017 = base year (current allocation); Optimized budget: It was assumed expenditure of USD 36.8 million available for TB-related programs in 2017 would remain available on an annual basis up to 2035; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

Table 3.8 Estimated impact of reaching 90% coverage of screening for key risk groups

Target population	Estimated population size	Estimated % screened for TB 2017	Estimated yield	Estimated current spending (USD)	Target for screening	Potential additional yield from reaching target coverage	Estimated additional cost (USD)
Adult PLHIV (on ART)	1,100,000	48%	21,021	1,880,392	90%	18,579	1,661,948
Health workers	50,000	27%	395	38,030	90%	932	89,692
Household contact tracing	270,836	42%	6,224	1,657,168	90%	7,646	1,893,130
Miners	70,000	29%	506	252,400	90%	1,069	533,357
Prisoners	80,000	15%	776	123,221	90%	3,755	596,493

Source: Optima TB model output.
Notes: ART = antiretroviral therapy; PLHIV = people living with HIV; TB = tuberculosis; USD = United states dollar.

Figure 3.20 Optimal reallocation of current TB treatment expenditure to minimize active pulmonary TB prevalence between 2017 and 2035 in Mozambique



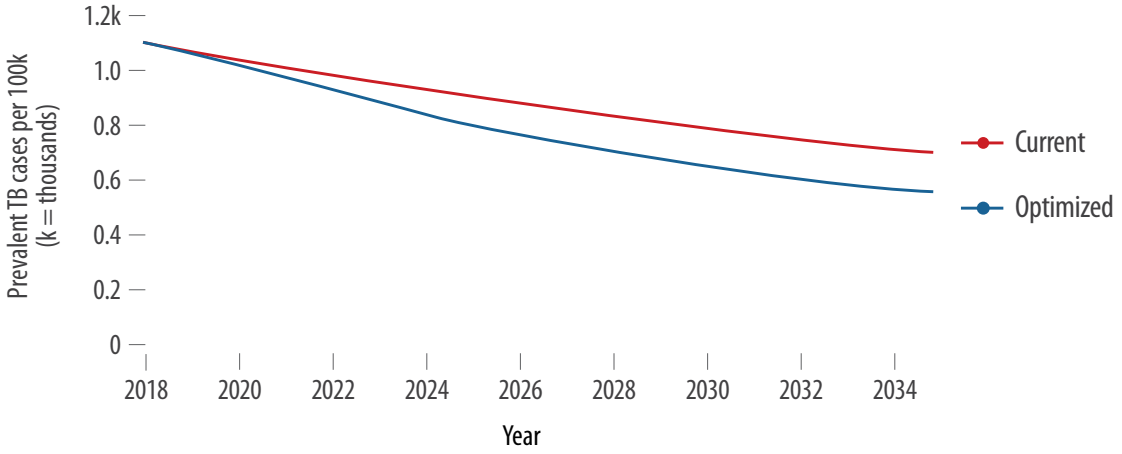
Source: Optima TB model output
Note: DS = drug susceptible; HR = human resources; MDR = multi-drug resistant; XDR = extensively drug-resistant.

Improved TB outcomes under optimized resource allocation scenarios

As shown in Figure 3.21, an optimized allocation of resources could have a substantial impact on key TB indicators. Relative to the current allocation, an optimized allocation of spending could:

- Reduce the number of active TB infections in 2035 by 19%
- Reduce the number of TB-related deaths per year in 2035 by 18%
- Reduce the rate of TB incidence per 100k in 2035 by 11%

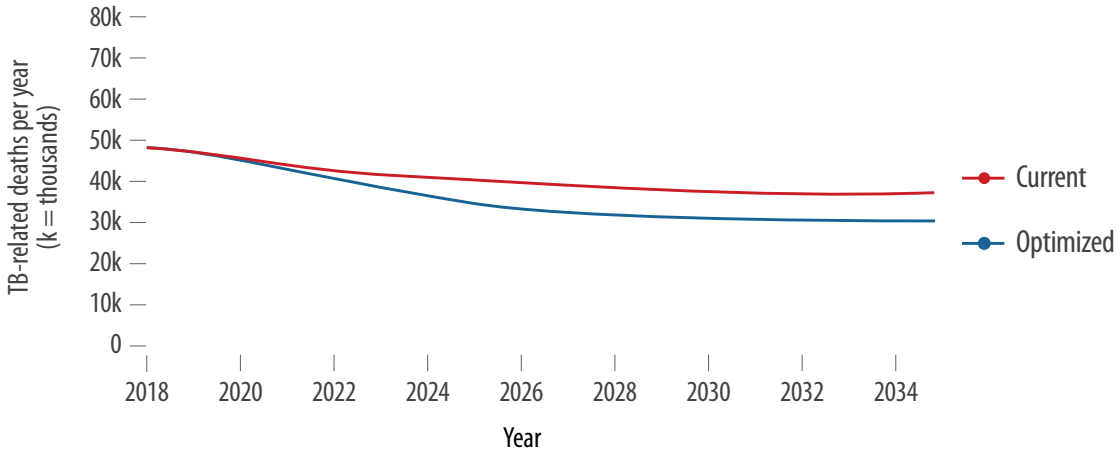
Figure 3.21 Estimated number of people with active pulmonary TB



Source: Optima TB model output.
Note: Total annual expenditure is assumed constant at USD 36.8 million until 2035.

Relative to the current allocation, an optimized allocation of spending could also reduce the annual number of TB-related deaths by 18% (by 2035) (Figure 3.22)

Figure 3.22 Estimated number of annual TB-related deaths

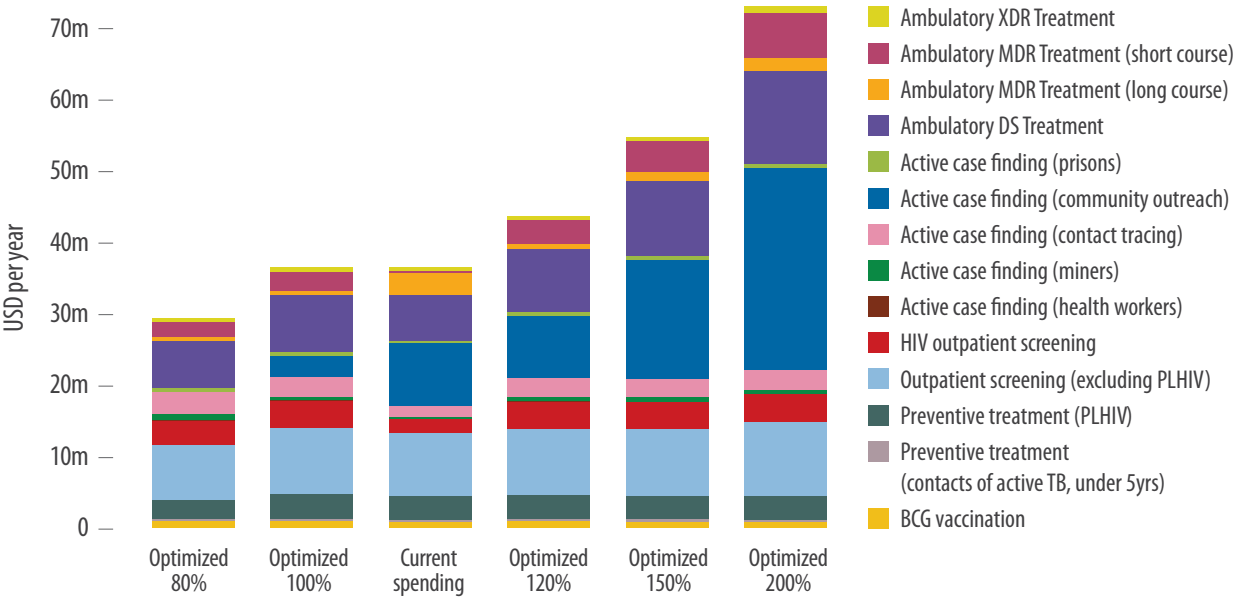


Source: Optima TB model output.
Note: Total annual expenditure is assumed constant at USD 36.8 million until 2035.

Optimized allocations under different amounts of spending and their impact

Figure 3.23 shows the optimal allocation at different spending levels. Screening of PLHIV in the outpatient setting is continuously prioritized under various amounts of spending relative to current spending (80%, 100%, 120%, 150%, 200%). The pattern of optimized treatment expenditure remains consistent across spending levels, with a shift towards expanding active case finding programs as the budget increases. Preventive TB treatment for PLHIV remains outside the optimal allocation mix even at 200% of budget. With reduced expenditures, funding for community case finding programs are no longer funded, with cheaper and more targeted programs prioritized such as screening of health workers.

Figure 3.23 Programs funded under different amounts of spending

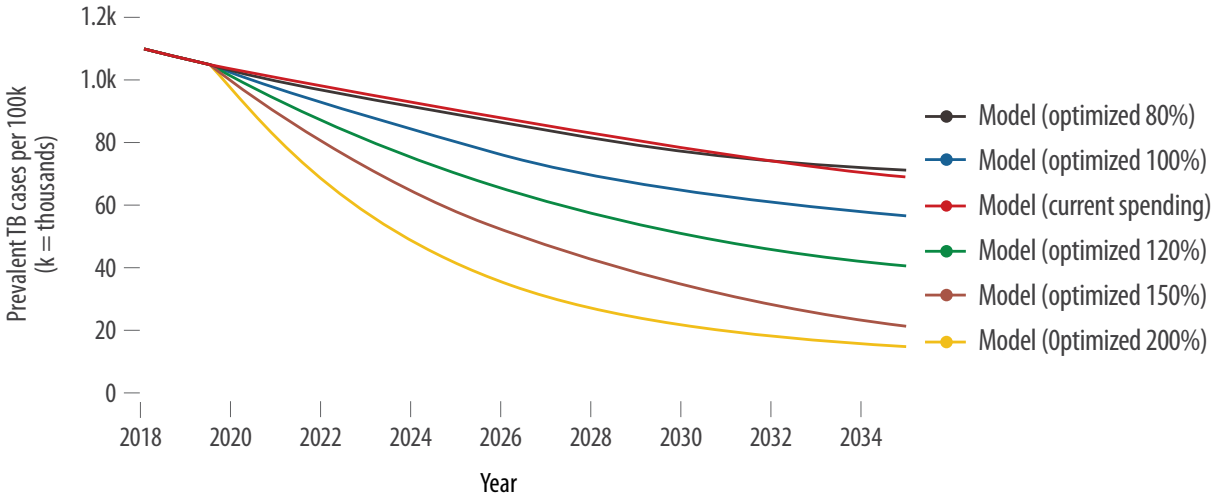


Source: Optima TB model output.
Note: BCG = Bacille Calmette-Guerin; DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; XDR = extensively drug-resistant.

Impact of different amounts of expenditure on TB outcomes (Figure 3.24 and 3.25).

Reductions in TB expenditure to 80% of current levels, if optimally allocated, would still result in reduced prevalence and TB-related deaths as a result of reallocation to more cost-effective interventions. The optimized allocation of current expenditure is projected to yield significant gains, and there are significant gains from increasing the budget further, enabling further increases in the case detection rate through increased expenditure on active case finding programs. However, a larger increase in spending has diminishing marginal returns of impact. Furthermore, based on model outputs, it is not feasible to meet End-TB 2035 targets for reductions in TB incidence and TB-related deaths with any budget amount with the modelled interventions. Modelled TB incidence for 2017 was 491 per 100,000 population, meeting the End-TB target would require reducing the incidence rate to 49.1 per 100,000 by 2035. Expenditure of twice the 2017 level is estimated to reduce TB incidence to 147 cases per 100,000 population by 2035, hence missing the END-TB target (Figure 3.24).

Figure 3.24 Impact of different amounts of expenditure on TB prevalence

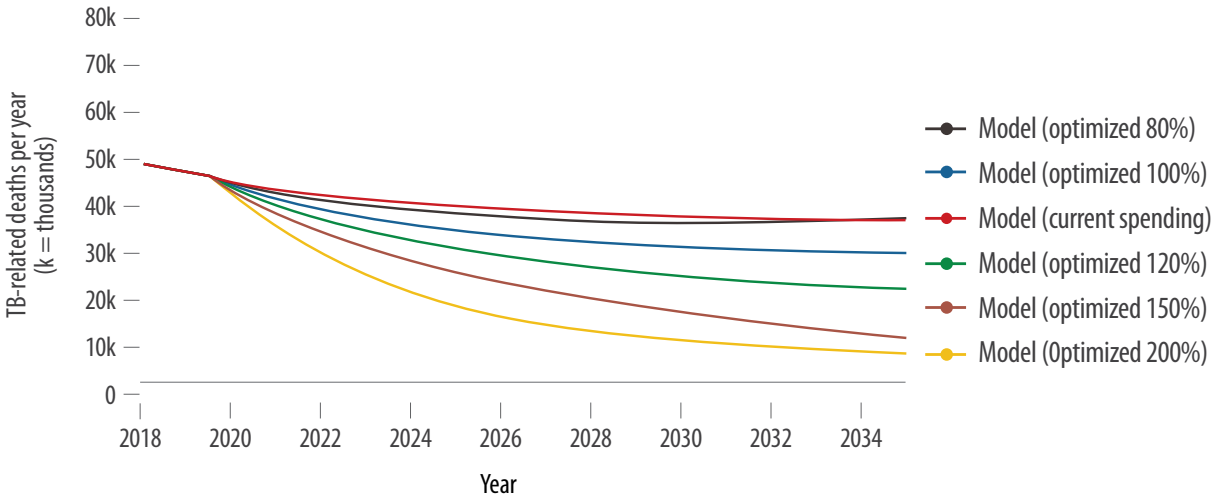


Source: Optima TB model output.
Note: TB = tuberculosis.

Impact of different amounts of expenditure on TB-related mortality (Figure 3.25).

- The number of modelled TB-related deaths for 2015 was around 54,000–meeting the End-TB target would require reducing the number of TB deaths to around 2,700 by 2035.
- When the allocation is optimized, reducing the current budget by 20% would still result in a comparable number of TB-related deaths in 2035
- Budget increases buy additional impact–expenditure of twice the 2017 level is estimated to reduce the number of TB-related deaths to 8,500 by 2035
- Increasing expenditure on a finite set of programs will likely result in diminishing marginal returns. Therefore, consideration could be given to new prevention and treatment modalities

Figure 3.25 Impact of different amounts of expenditure on TB-related mortality



Source: Optima TB model output.
Note: TB = tuberculosis.

Table 3.9 Impact of different amounts of expenditure on TB outcomes

	Optimized 80%	Optimized 100%	Current spending	Optimized 120%	Optimized 150%	Optimized 200%
TB prevalence in population						
0–14 years	47,385	41,790	44,498	36,461	29,304	19,776
15+ years	225,528	202,901	214,684	180,439	148,631	103,404
PLHIV	60,020	54,446	78,144	47,802	40,011	33,002
Total	332,933	299,136	337,325	264,701	217,946	156,183
TB related deaths						
0–14 years	2,809	2,587	2,723	2,377	2,079	1,625
15+ years	26,037	23,549	24,815	21,081	17,504	12,380
PLHIV	9,632	8,744	12,473	7,675	6,374	5,226
Total	38,477	34,880	40,011	31,132	25,957	19,232
TB incidence in population						
0–14 years	24,181	23,079	24,884	22,001	20,562	18,218
15+ years	98,171	96,384	99,870	94,366	91,577	86,119
PLHIV	34,216	32,928	32,426	31,721	29,656	25,586
Total	**156,568**	**154,391**	**157,179**	**148,088**	**141,795**	**129,924**

Source: Optima TB model output.
Note: PLHIV = people living with HIV; TB = tuberculosis.

This page is for collation purposes only.

Relative to the current allocation (2017), an optimized allocation of current spending could, by 2035 reduce the number of active TB infections by 19%, TB-related deaths per year by 18% and TB incidence rate (per 100,000 population) by 11%.

Expenditure of twice the 2017 level is estimated to reduce TB incidence to 147 cases per 100,000 population by 2035, hence missing the END-TB target.

Increasing expenditure on a finite set of programs will likely result in diminishing marginal returns. Therefore, consideration could be given to new prevention and treatment modalities.

4 CONCLUSIONS

This section summaries key findings in responding to each of the policy questions.

Policy question 1

What is the current status of the TB epidemic and TB care cascade for Mozambique using the most recent available data?

- TB incidence is amongst the highest in the world (551 cases per 100 000 in 2017) and 40% of TB cases are also HIV-positive
- Diagnosis remains the most significant breakpoint in the TB care cascade for Mozambique: only an estimated 50% of new active TB cases were diagnosed in 2018 and mortality prior to diagnosis is estimated to be particularly high among PLHIV (44%, vs. 21% in HIV-negative adults)
- As a result, despite high treatment success rates, only about 41% of all new active TB cases completed TB treatment (2018), emphasizing the importance of finding more cases

Policy question 2

What is the projected future trend of the TB epidemic in Mozambique under current level of budget and assuming status-quo programming?

- Assuming no changes in TB outcomes and TB program coverage (status quo), pulmonary TB incidence is projected to remain high, although decreasing, from 2017 (495 per 100,000) to 2035 (303 per 100,000)
- This is driven by the projected growth of the Mozambique population, estimated at a 70% increase in this time period
- While the TB incidence per 100 thousand population is decreasing, the number of new TB cases is projected to remain fairly constant at around 150,000 annually due to the rapid demographic growth
- New TB cases among PLHIV are projected to decrease as a result of ART coverage (anticipated to scale up to 90% by 2035)
- New TB cases in the HIV-negative adult population are projected to continue to increase – from ~76,000 in 2017 to ~113,000 by 2035

Policy question 3

What is the projected impact on the TB epidemic if meeting key national and international targets?

- Both NSP targets and Stop-TB targets aim for 90% diagnosis rate by 2025. Meeting and sustaining this target for 2025 is projected to yield significant reductions in the total number of active TB cases and TB-related deaths of up to 80% relative to current conditions by 2035
- Meeting NSP targets for diagnosis and treatment of DR-TB by 2025 could reduce DR-TB prevalence in 2035 by 50% relative to current conditions. With most DR-TB cases that are diagnosed with TB improving coverage of drug susceptibility testing is crucial to reaching this target
- Although mainly managed by the HIV program, ART provision is a key factor in the TB response as treatment reduces the probability of progression from latent to active TB. For example, scaling up to 90% ART coverage by 2035 is projected to reduce the number of incident TB cases among adult PLHIV in 2035 by around 35% compared to ART coverage of 70%

Policy question 4

What is the projected future trend of the country's TB epidemic with optimized allocation of currently available resources?

Relative to the current allocation (2017), an optimized allocation of current spending could, by 2035 reduce:

- The number of active TB cases by 19%
- The number of TB-related deaths per year by 18%
- TB incidence rate (per 100,000 population) by 11%

Policy question 5

What resources are required to achieve key targets of the national TB response?

- This analysis estimated that about USD 36.8 million was spent in 2017 by government on the TB response, including resources from dedicated TB funding streams and from the wider health sector
- The 2017 level of spending, even if allocated optimally, is unlikely to achieve End-TB targets of 95% reduction in deaths and 90% reduction in TB incidence by 2035
- Budget increases buy additional impact–doubling the 2017 spending level is estimated to reduce TB incidence to 147 cases per 100,000 population by 2035
- However, large increases of current spending have diminishing returns and it is not feasible to meet End-TB 2035 targets with any budget amount with the modelled interventions but instead requires additional and new tools

Increased tracing intensity would add to the yield of notified cases in Mozambique, and our optimization analysis indeed suggested that the effort of household contact tracing should be doubled.

Screening PLHIV for active TB at outpatient clinics represents a relatively inexpensive and high yield way to increase the number of diagnosed cases in Mozambique.

Expanding the use of rapid testing methods such as GeneXpert will reduce the number of false negatives and increase the notification rates for both DS and DR TB.

More data should be collected on the diagnostic yield of different case finding strategies, as well as their costs, in order to inform local best practice in Mozambique.

5 DISCUSSION OF KEY FINDINGS

Mozambique is one of the 30 highest TB burden countries in the world with an estimated 551 new TB cases per 100,000 population, a low TB detection rate of just above 50%, and a low DR-TB diagnosis and treatment success rates (38%). Overall, data from NTP suggests high treatment success rates for DS-TB (90%) and improvements in TB case detection rates over time. However, it is still far from the global target detection rates, indicating challenges for the country to reach NTP targets for 2025 as well as End-TB targets for 2035. More efforts and resources are needed for Mozambique to reduce the TB burden.

Our modelling exercise shows a declining trend in the risk of TB infections and the risk of TB related deaths, thanks to the rapidly improved HIV treatment coverage and TB services. However, due to the rapidly-increasing population size, the absolute number of TB cases continues to increase, especially among the HIV negative population. At the time of analysis, Mozambique was working on the National TB Strategic Plan 2020-2025 and our analysis shows that reaching a 90% diagnosis rate by 2025 would reduce the total number of TB cases and TB-related deaths of up to 80%, and reduce DR-TB of up to 50% (relative to current condition, by 2035). In addition, reaching 90% ART coverage by 2035 would contribute to a reduction of new TB cases of 35%. To reach END-TB targets, the country must increase TB detection rates, and at the same time, improve ART coverage and continue to prevent new HIV infections. The country has achieved high coverage of HIV services in TB clinics with 97% of TB patients registered aware of their HIV status and 95% of TB patients living with HIV on ART. Ongoing, regular TB screening and diagnosis among HIV patients remain critical, as is patient support for IPT which has been reported to suffer from low uptake and poor completion rates (Rodriques & Lisboa, 2019).

With the current level of budget and TB spending (2017), however, the country can cut TB prevalence and death by nearly 20%, and TB incidence by 11% by allocating resource optimally. Specifically, this can be done by doubling the average number of contacts traced per notified case, screening all PLHIV during their routine outpatient visits, and focusing on the community outreach activities among key populations such as prisoners, cross-border miners and health workers. Currently, an estimated 1.3 contacts per active TB case are traced. Increased tracing intensity would add to the yield of notified cases in Mozambique, and our optimization analysis indeed suggested that the effort of household contact tracing should be doubled. A study on systematic contact tracing of MDR patients in a rural area demonstrated the value of comprehensive contact investigations in finding additional cases and getting them on treatment early (Pires Machai, 2019).. However, the most effective way of conducting household contact tracing remains uncertain and is beyond the scope of this analysis.

In the optimal resource allocation scenario (compared to the status quo), both community case finding and active case finding amongst miners received less funding according to model outputs, but this was based on limited data on coverage and yield of these programs in Mozambique. Instead, we used global literature estimates for our modelling analysis. Generally, the delivery of case finding services in Mozambique remains fragmented, with multiple implementing partners operating to provide services. A study on active case finding approaches in the communities (using lay counsellors) and at health facilities (with cough monitors) demonstrated the importance of using combined approaches to find cases while ensuring high linkage to care rates of TB suspects identified in the community (Polana et al. 2019). Our optimization analysis suggested that increasing funding for outpatient TB symptom screening, through expanding initiatives such as cough monitors, is a recommended resource shift. In any case, more data should be collected on the diagnostic yield of different case finding strategies, as well as their costs, in order to inform local best practice in Mozambique.

Screening PLHIV for active TB at outpatient clinics represents a relatively inexpensive and high yield way to increase the number of diagnosed cases in Mozambique. In 2017, around 74% of new cases enrolled in HIV treatment were screened for TB. The total number of PLHIV in care screened for TB is unknown. On the basis of the estimated active case finding yield in this setting (Shapiro et al, 2013), we estimated that around half of PLHIV on treatment were screened for TB in 2017 for the purposes of this analysis. Although there is some uncertainty in this estimate, all PLHIV should nevertheless be regularly screened for TB in the outpatient setting. Other high-risk groups include prisoners and health workers. Both of these groups are relatively easy to find and should be screened for TB at least annually. The Challenge TB Project also concluded from an exercise extending HCW screening to community health workers that this is an essential occupational group to be included in regular HCW screening campaigns to find cases among them early and treat appropriately (Abdula, 2019).

Tackling low TB detection rates, especially for DR-TB, also requires laboratory capacity, which is beyond the scope of this analysis. Data and expert opinions in the country indicate low laboratory capacity, resulting in a high rate of TB patients identified by clinical symptoms (60% in 2017). Concerns were raised by local experts over the quality of sputum samples. A video created by TB Reach three years ago that has been translated into Portuguese and five local languages in Mozambique on best practices in collecting sputum could be shown to nurses, community health workers and presumptive TB cases. A pilot could be run in certain districts to see if using this video improves sputum quality and subsequent yield. Increased coverage of bacteriological testing would also require adequate sample transportation systems to ensure sputum quality. Such issues of implementation capacity should be carefully considered in any scale-up of laboratory testing.

Additionally, the country currently has about 100 GeneXpert machines and has planned to deploy more. Expanding the use of rapid testing methods such as GeneXpert will reduce the number of false negatives and increase the notification rates for both DS and DR TB. However, the overall impact of scaling up GeneXpert is difficult to estimate due to limited data available in Mozambique. We recommend that the NTP conducts operational research to investigate universal GeneXpert coverage in areas where it was previously unavailable, while also considering the necessary placement conditions. This would provide valuable information to the country on the roll-out of the technology, including its cost-effectiveness and impact. Several studies have also highlighted the importance of training on GenXpert use to address under-utilization of existing GenXpert test capacity (Jaintila et al., 2019) and the high rates of unsuccessful Xpert MTB/RIF results and associated financial costs (Teixeira et al., 2019).

During the course of this analysis, we were requested by local stakeholders to explore the impact of community-based interventions such as the use of CHWs and traditional healers in case finding.

However, due to insufficient data, we were not able to include this scenario in our analysis. Based on NTP data, community case finding programs already contribute around 25% of notified cases, playing a role in making progress towards case detection targets. It may be that that the increased rates of clinical diagnosis of TB may be due to the expanded use of CHWs and traditional healers who often work in rural areas with limited access to smear and Xpert testing. While accelerated TB case finding is essential in Mozambique, suitable capacity needs to be built to correctly diagnose cases, including resistance typing, so that the correct regimens can be prescribed and patients attain treatment success. These uncertainties can be answered by a small-scale implementation research study.

Photo: National Tuberculosis Programme. Used with permission.

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6 RECOMMENDATIONS

Based on the key findings, we make the following recommendations:

1. **Continue focusing on contact-tracing of notified cases**
As discussed above, the number of traced contacts should increase by 50–100% relative to current conditions. While all index patients should be followed up with contact tracing, those sputum-smear positive, those with (suspected) DR-TB, and those with children or immunocompromised people among household contacts should have greatest priority for comprehensive tracing of all contacts. In addition, the yield data of contact-tracing of notified cases for Mozambique is uncertain and should be monitored.

2. **Screen all PLHIV for TB symptoms at each outpatient visit**
About 74% of new HIV cases enrolled in ART were screened for TB in 2017. Given a high TB prevalence in PLHIV, screening all HIV patients regularly for TB as per global recommendation will likely increase yield.

3. **Expand active case finding programs for key high-risk populations**
Health care workers, prisoners, and cross-border miners should be screened annually as these groups are at higher risk of TB and are relatively easy to find.

4. **Increase yield of notified cases from outpatient screening and reduce clinical diagnosis**
About 75% of notified cases are found in the outpatient setting in Mozambique. As 60% of cases are clinically diagnosed (2017), increased funding should aim to increase the proportion of TB cases that are bacteriologically confirmed, by increasing coverage of tests such as GeneXpert. Without increasing bacteriological confirmation rate, it is difficult to assess true progress in the TB response in Mozambique. We recommend small-scale implementation science research to assess the effectiveness, cost, and operational aspects of the introduction and universal use of GeneXpert.

5. **Continue expanding ART coverage and ART adherence support**
Increasing ART coverage has a significant impact on TB incidence amongst PLHIV and continued expansion of ART care will significantly reduce TB infection.

6. **Closely monitor the pilot of MDR regimens to inform future MDR treatment recommendations**

The NTP is planning to move away from all injectable based MDR regimens from late 2019 onward. The oral short course regimen has been provided in several high volume MDR-TB sites in the Maputo City area. By the time of this analysis, data from these research studies was not yet available. Final discussions about investments in these short course regimen should be based on the outcomes from these studies.

7. Continue ambulatory-focused care for both DS-TB and DR-TB patients

The country should continue this approach and avoid unnecessary hospitalisation as long as it reduces costs without affecting outcomes, and provided directly observed treatment (DOT) and adherence support are in place. Community health workers are well placed to support TB patients during treatment in addition to their important role in contact tracing.

8. **Collect data on community case finding programs to inform decision making**

As discussed above, community case finding programs contribute to around 25% of notified cases in Mozambique. Currently, several community case-finding programs are underway with fragmented implementation and lack of data on cost, coverage, and impact. We recommend the NTP collects data, especially cost data, of these pilot projects in order to inform cost-effectiveness estimates and guide future policy recommendations.

9. **Maximize the collection and use of TB routine data to inform programming and policies**

The quality and availability of cost and coverage data in Mozambique provides a challenge for any allocative efficiency analysis, and results in uncertainty in epidemic and programmatic model parameters. Key data sources include TB-specific expenditures, reports on how TB cases are identified (by intervention modality), and better records of often fragmented implementation of service delivery activities. Therefore, monitoring and evaluation systems should be streamlined, and spending and coverage data should be collected for all TB interventions and programs (NTP led and non-NTP led).

10. **Increase funding for TB program**

The TB response in Mozambique is not on track to meet the 2025 milestones or 2035 End-TB targets, more funding for the TB program is needed as additional investment will provide more impact and close the gap to reaching TB strategic targets.

ANNEXES

The Optima mathematical modelling suite was designed to support decision-makers in prioritization, resource allocation and planning to maximise health impact. Optima-HIV was the most widely used component of the Optima modelling suite. A more detailed summary of the model and methods is provided elsewhere.

Optima TB is a mathematical model of TB transmission and disease progression integrated with an economic and program analysis framework. Optima uses TB epidemic modeling techniques and incorporates evidence on biological transmission probabilities, detailed disease progression and population mixing patterns. Optima TB is a compartmental model, which disaggregates populations into different model compartments including susceptible, vaccinated, undiagnosed early or late latent-TB, diagnosed early or late latent-TB, on treatment early or late latent-TB, undiagnosed active TB, diagnosed active TB, on treatment and recovered active-TB populations. In addition, active-TB compartments are further disaggregated by drug resistance type into drug susceptible (DS), multi-drug resistant (MDR) and extensively drug resistant (XDR). Annex 2 summarises the main features of Optima TB.

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ANNEX 1 OPTIMA TB MODEL FEATURES AND KEY DEFINITIONS AT A GLANCE

Disaggregation by smear-status and drug-resistance	• Both smear positive and negative; DS-TB, MDR-TB, XDR-TB
New vs. relapse cases	• The WHO definition for incident TB cases includes both new and relapse cases. In the model, incident TB cases correspond to the following transitions between compartments: • New cases: these are represented by the number of progressions to active TB from early and late latent-TB compartments. 'New' also includes recurring episodes of TB from the recovered compartment following re-infection • Relapse cases: these correspond to all unsuccessful treatments in the model, which include failure, relapse, LTFU and re-treatments
Latent TB	• Multiple compartments for latent TB infection (LTBI) • Cannot skip latent state for disease progression • States include undiagnosed, on treatment, and completed treatment • Accounts for re-infection and latent care-status using a secondary latent TB pathway. Cases previously treated for LTBI, or vaccinated individuals, can transition to the active TB pathway in the case of reinfection
Vaccination, immunity and resistance	• Vaccination explicitly included in model • Patients that spontaneously clear from infection
Treatment	• States for undiagnosed, diagnosed, diagnosed but not on-treatment, on-treatment, and recovered patients for different types of drug-resistance • Failed or defaulted treatment can acquire drug resistance
Treatment outcomes	• Treatment success includes 'cured' and 'treatment completion', as per the WHO • Treatment failure in the model includes 'loss to follow-up' during treatment, 'treatment failure', and 'not evaluated' • Death during TB treatment is not included in treatment failure, but is considered separately
Population structure, key populations and People living with HIV	• Age-structured populations can be user defined • Ability specify additional key populations with defined transition rates to/from general population groups • HIV positive populations represented as separate key population

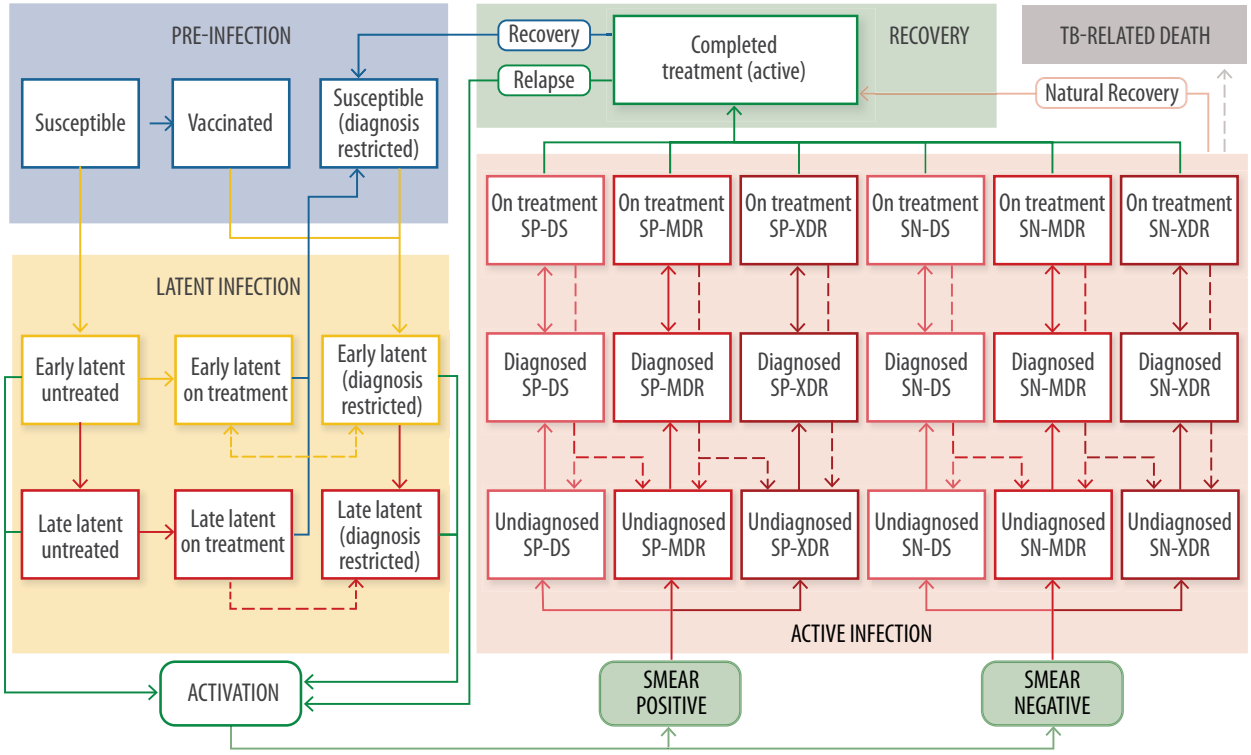
Optima TB is based on a dynamic, population-based TB model (Annex 2). The model uses a linked system of ordinary differential equations to track the movement of people among health states. The overall population is partitioned in two ways: by population group and by TB health state. TB infections occur through the interactions among different populations.

Each compartment in Annex 2 corresponds to a single differential equation in the model, and each rate (Annex 2 arrows) corresponds to a single term in that equation. The analysis interprets empirical estimates for model parameter values in Bayesian terms as previous distributions. The model then

must be calibrated: finding posterior distributions of the model parameter values so that the model generates accurate estimates of notified TB cases, TB incidence, TB prevalence, the number of people on treatment, and any other epidemiological data that are available (such as TB-related deaths). Model calibration and validation normally should be performed in consultation with governments in the countries, in which the model is being applied.

ANNEX 2 TUBERCULOSIS MODEL STRUCTURE

Figure A.2.1 **Schematic diagram of the health state structure of the model**



Source: Prepared based on model structure

Note: Each compartment represents a single population group with the specified health state. Each arrow represents the movement of numbers of individuals between health states. All compartments except for "susceptible" and "vaccinated" represent individuals with either latent or active TB. Death can occur for any compartment, but TB related mortality varies between compartments. SN-DS = smear negative drug susceptible; SP-DS = Smear-positive drug susceptible; SP-MDR =smear positive-multi-drug resistant; SN-MDR =smear negative-multi-drug resistant; SN-XDR = smear negative-extensively drug-resistant; TB = tuberculosis.

TB Resource Optimization and Program Coverage Targets

Optima TB is able to calculate allocations of resources that optimally address one or more TB-related objectives (for example, impact-level targets in a country's TB national strategic plan). Because this model also calculates the coverage levels required to achieve these targets, Optima TB can be used to inform TB strategic planning and the determination of optimal program coverage levels.

The key assumptions influencing resource optimization are the relationships among (1) the cost of TB programs for specific target populations, (2) the resulting coverage levels of targeted populations with these TB programs, and (3) how these coverage levels of TB programs for targeted populations influence screening and treatment outcomes. Such relationships are required to understand how incremental changes in spending (marginal costs) affect TB epidemics.[1]

To perform the optimization, Optima uses a global parameter search algorithm, which is an adaptive stochastic descent algorithm. The algorithm is similar to simulated annealing in that it makes stochastic

1 A traditional approach is to apply unit cost values to inform a linear relationship between money spent and coverage attained. This assumption is reasonable for programs such as an established treatment program that no longer incurs start-up or initiation costs. However, the assumption is less appropriate for diagnostic programs. Most programs typically have initial setup costs, followed by a more effective scale-up with increased funding. However, very high coverage levels have saturation effects because these high levels require increased incremental costs due to the difficulty of diagnosing more people as the yield of diagnostic interventions declines.

downhill steps in parameter space from an initial starting point. However, unlike simulated annealing, the algorithm chooses future step sizes and directions based on the outcome of previous steps. For certain classes of optimization problems, the team has shown that the algorithm can determine optimized solutions with fewer function evaluations than traditional optimization methods, including gradient descent and simulated annealing.

Uncertainty Analyses

Optima uses a Markov chain Monte Carlo algorithm for performing automatic calibration and for computing uncertainties in the model fit to epidemiological data. With this algorithm, the model is run many times (typically, 1,000–10,000) to generate a range of epidemic projections. Their differences represent uncertainty in the expected epidemiological trajectories. The most important assumptions in the optimization analysis are associated with the cost-coverage and coverage-outcome curves.[2]

2 All available historical spending data and achieved outcomes of spending, data from comparable settings, experience, and extensive discussion with stakeholders in the country of application can be used to inform these ranges. All logistic curves within these ranges then are allowable and are incorporated in Optima uncertainty analyses. These cost-coverage and coverage-outcome curves thus are reconciled with the epidemiological, and biological data in a Bayesian optimal way, thereby enabling the calculation of unified uncertainty estimates.

ANNEX 3 POPULATION SIZES

Population name	Value	Year	Source or Assumption
0–14 years old	13,410,016	2017	UN Population Division; UNAIDS
15+ years old	14,258,818	2017	
15+ years old HIV+	2,000,000	2017	

ANNEX 4 BIRTHS AND BACKGROUND (NON-TB) MORTALITY

Population name	Value	Year	Source or Assumption
Annual number of births	1,122,995	2016	Provided by country
Annual non-TB death rate, 0–14 years old	0.72%	2017	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.[3]
Annual non-TB death rate, 15+ years old	0.53%	2017	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, 15+ years old HIV+	1.24%	2017	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.

Note: TB = tuberculosis.

3 All available historical spending data and achieved outcomes of spending, data from comparable settings, experience, and extensive discussion with stakeholders in the country of application can be used to inform these ranges. All logistic curves within these ranges then are allowable and are incorporated in Optima uncertainty analyses. These cost-coverage and coverage-outcome curves thus are reconciled with the epidemiological, and biological data in a Bayesian optimal way, thereby enabling the calculation of unified uncertainty estimates.

ANNEX 5 TB EPIDEMIOLOGICAL PARAMETERS

Full Name	Population	Latest year or default value	Source or Assumption
Vaccination Rate	Annual number of births	98.7%	Provided by country
Early Latency Departure Rate	All populations	0.2001	Houben et al. 2016 (appendix of TIME model) - 0.1%/year reactivation rate (0.01–0.25).
Late Latency Departure Rate*	All populations	0.003	Andrews et al. 2012 - risk of progression to active.
Probability of Early-Active vs. Early-Late LTBI Progression*	All populations	0.177	Andrews et al. 2012 - risk of progression to active.
Infection Vulnerability Factor (Vaccinated vs. Susceptible)	All populations	0.5	Mantgani et al., 2013 (protective efficacy of BCG found to range from 0-80%). A value of 0.5 was used for populations aged 0–14, and no protection (i.e., 1) was used for all populations older than 14 years old.
Infection vulnerability factor (relative population susceptibility)	All populations	1.0	A value of '1' is the default, but this is likely to be significantly higher in vulnerable populations such people living with HIV. Values between 1–11 were used in calibrations
Smear positive (SP) TB Infectiousness*	All populations	1.0	A value of '1' is the default
Smear negative (SN) TB Infectiousness (Compared to SP-TB)	All populations	0.22	Behr et al.1999
Active Infection Rate (Active Recovered)*	All populations	0.02	This value is representative of a global average
Smear positive TB natural recovery rate	All populations	0.03	Tiemersma et al. 2011
Smear negative TB natural recovery rate	All populations	0.16	Tiemersma et al. 2011
Smear positive untreated-TB death rate	All populations	0.12	Tiemersma et al. 2011
Smear negative untreated-TB death rate	All populations	0.02	Tiemersma et al. 2011

Source:

Note: * = Parameters with the least confidence/available literature, and chosen across different studies to be adjusted to calibrate the model. Not all of these apply to the calibration process in Mozambique; Notified cases disaggregated by age and resistance-type were provided by the country; BCG = Bacille Calmette-Guerin; TB = tuberculosis; LTBI = latent TB infection.

ANNEX 6 NUMBER OF NOTIFIED PULMONARY TB CASES BY AGE AND DRUG RESISTANCE TYPE (2017)

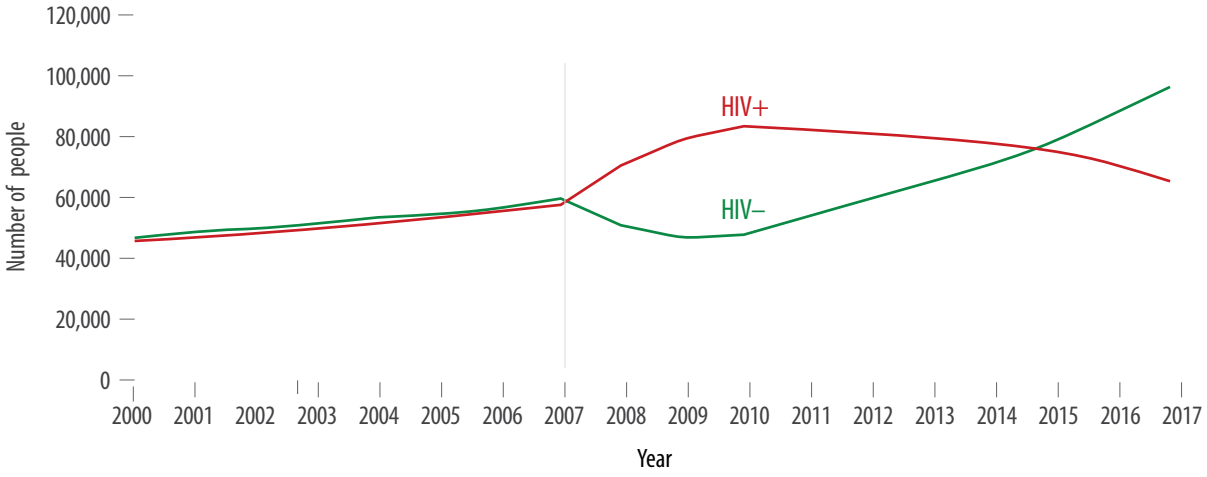
Population	Number of notified DS-TB cases	Number of notified MDR-TB cases	Number of notified XDR-TB cases	Total number of notified cases
0–14 years old	10,398	36	1	**10,435**
15+ years old	40,625	551	18	**41,194**
15+ years old HIV+	27,642	375	12	**28,029**

Notes: DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

ANNEX 7 CALIBRATION METHODOLOGY UNCERTAINTIES IN DISAGGREGATING TUBERCULOSIS INCIDENCE BY HIV STATUS

- Mozambique NTP did not have notifications data disaggregated by HIV status
- It was therefore necessary to use WHO data to estimate the proportion of TB patients in Mozambique who are also HIV-positive
- As there appear to be some inconsistencies in WHO data for earlier years, values before 2010 were not used in the model calibration
- Instead, a baseline value of 61% (IHME estimate for 2001) was used, and a linear increase each year until 2010 (63.6% WHO) was assumed

Figure A.7.1 Uncertainties in disaggregating tuberculosis incidence by HIV status



ANNEX 8 EPIDEMIOLOGICAL ASSUMPTIONS

Epidemiological parameter	Assumption
Smear-Status	Smear status results for DS-TB were based on notifications data for 2001-2017 reported by the Mozambique National Tuberculosis program
Treatment Outcomes	Based on those reported by the WHO. These are disaggregated by resistance type and HIV-status but not by agein the absence of population-specific data.
Active TB incidence	Used the WHO active TB incidence estimates, and assumed that pulmonary notified cases are a best indicator of the specific burden within population groups. These were used to disaggregate the WHO estimate into sub-population pulmonary TB incidence.
Active/Latent-TB Prevalence	Used Houben and Dodd (2016) latent-TB prevalence estimates as a basis for initialization estimates and comparison with model outputs. Although WHO estimates for active TB prevalence were also used in the same way, these do not appear to be reliable as they report estimated prevalence equal to estimated incidence for the most recent year in which estimates are available (2014). There is considerable uncertainty in actual prevalence of active TB in Mozambique until the results of the prevalence survey that is currently underway are available.

ANNEX 9 PROGRAMMATIC DATA: SCREENING AND DIAGNOSTICS

Intervention	Unit cost/ person screened (USD), 2017	Number of screens, 2017	Total estimated spending (EUR)	Yield	Source or assumption
Outpatient screening (excluding PLHIV)	3.58	525,525	8,916,890	4.00%	Shapiro et al., 2013
PLHIV outpatient screening	1.07	8,298,182	1,880,392	0.45%	Kranzer, 2010; Kranzer, 2012
Active case finding (health workers)	2.84	13,399	38,030	2.95%	Local data
Active case finding (contact tracing)	14.57	113,776	1,657,168	5.88%	Shapiro et al., 2013
Active case finding (community outreach)	12.01	741,867	8,910,671	1.85%	NTP desk review
Active case finding (miners)	12.47	20,237	252,400	2.50%	Shapiro et al., 2013
Active case finding (prisons)	10.00	12,327	123,221	6.29%	Shapiro et al., 2013

Note: All unit costs were derived by the authors of this report using data provided by country colleagues; PLHIV = people living with HIV.

ANNEX 10 SENSITIVITY OF SCREENING /TESTING METHODS

Screening or testing method	Sensitivity	Source or assumption
Full symptom screen	84%	Van't Hoog et al., 2013
Sputum Smear microscopy	61%	Van't Hoog et al., 2013
Xpert MTB/RIF	89%	Van't Hoog et al., 2013
Clinical diagnosis	24%	Van't Hoog et al., 2013

ANNEX 11 TB TREATMENT INTERVENTIONS: TARGET GROUPS, UNIT COSTS, VOLUME, TOTAL SPEND AND OUTCOME

Treatment program	Unit cost/ course of treatment (USD)	Patients covered, 2017	Source or assumption	Total estimated spending (USD)	Treatment success	Source or assumption
Ambulatory DS treatment	86.53	77,091	Number of notified cases	6,670,684	88.0%	Current treatment outcomes
Ambulatory MDR treatment (long course)	2,563.00	884	Number of notified cases. NTP data on regimen coverage.	2,266,387	69.3%	WHO Review of the evidence on Bedaquiline, 2016
Ambulatory MDR treatment (short course)	794.00	59	Number of notified cases. NTP data on regimen coverage.	46,586	69.3%	WHO Review of the evidence on Bedaquiline, 2016
Ambulatory XDR treatment	8,021.00	51	Number of notified cases. NTP data on regimen coverage.	409,093	66.4%	Pym et al., 2016; WHO report on Bedaquiline, 2016

Note: DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

ANNEX 12 COMPONENT COSTS OF TB TREATMENT REGIMENS (USD)

Treatment programs	Drug regimen cost*	Inpatient costs*	Outpatient costs*	Monitoring costs*	Patient support costs*	Total unit cost*
Ambulatory-focused DS treatment	22.57	0.00	48.30	15.66	0.00	86.53
Ambulatory-focused MDR treatment (long course)	3,154.94	46.90	68.19	150.39	72.41	3,492.84
Ambulatory-focused MDR treatment (short course)	1,250.75	46.90	52.56	150.39	72.41	1,573.02
Ambulatory-focused XDR treatment	12,846.95	54.57	73.87	150.39	72.41	13,198.19

Note: * = all costs in USD; DS = drug susceptible; HR = human resources; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

ANNEX 13 COST OF MDR-TB REGIMEN (SHORT COURSE)

MDR short-course regimen	Cost (USD)
Bedaquiline	528.60
Clofazimine	304.91
Cycloserine	140.35
Levofloxacin	35.40
Linezolid	241.50
Total	**1,250.75**

Note: MDR = multi-drug resistant.

ANNEX 14 COST OF MDR-TB REGIMEN (LONG COURSE)

MDR long-course regimen	Cost (USD)
Bedaquiline	1,120.82
Clofazimine	677.58
Cycloserine	311.88
Levofloxacin	78.66
Linezolid	966.00
Total	**3,154.94**

Note: MDR = multi-drug resistant.

ANNEX 15 COST OF XDR-TB REGIMEN

XDR regimen	Cost (USD)
Bedaquiline	1,120.82
Clofazimine	1,626.19
Delamanid	8,379.36
Cycloserine	561.38
Linezolid	1,159.20
Total	**12,846.95**

Note: XDR = extensively drug-resistant

ANNEX 16 CONSTRAINTS FOR PROGRAM FUNDING

The following minimum and maximum funding amounts for specific programs were included to match constraints on program funding

	Minimum coverage (%)	Maximum coverage (%)
BCG Vaccination	98.7% of newborns	–
Preventive treatment (contacts of active TB - under 5)	100% of all identified contacts of active TB aged 5 and under	–
Treatment for DR-TB cases	100% of diagnosed DR-TB cases to receive treatment for DR-TB	–

Note: BCG = Bacille Calmette-Guerin; TB = tuberculosis; DR = drug resistant.

ANNEX 17 NUMBER OF NOTIFIED PULMONARY TB INFECTIONS PER POPULATION GROUP (2017)

Population	DS-TB	MDR-TB	XDR-TB	Total notified
0–14 years	10,398	36	1	10,435
15+ years	40,625	551	18	41,194
15+years HIV+	27,642	375	12	28,029
Total	**78,665**	**962**	**31**	**79,658**

Note: DS = drug susceptible; TB = tuberculosis; MDR = multi-drug resistant; XDR = extensively drug-resistant.

ANNEX 18 MODELLED TB INCIDENCE PER 100K BY POPULATION GROUP

Population	2017	2022	2035
0–14 years	144	164	127
15+ years	519	534	406
15+years HIV+	2,752	1,783	545
Total	**495**	**447**	**303**

ANNEX 19 MODELLED LATENT INFECTION AND DEATHS (2017)

Population	Number of latent TB cases	Annual number of TB-related deaths per year
0–14 years	1,108,440	1,863
15+ years	8,180,868	18,412
15+years HIV+	1,203,562	30,094
Total	**10,492,870**	**50,369**

Note: TB = tuberculosis.

ANNEX 20 DEFINING NEW AND RELAPSE CASES IN THE MODEL

The WHO definition for incident TB cases includes both new and relapse cases

In the model, incident TB cases correspond to the following transitions between compartments:

- **New cases:** these are represented by the number of progressions to active TB from early and late latent-TB compartments. 'New' also includes recurring episodes of TB from the recovered compartment following re-infection
- **Relapse cases:** these correspond to all unsuccessful treatments in the model, which include failure, relapse, LTFU and re-treatments

ANNEX 21 DEFINING TREATMENT OUTCOMES IN THE MODEL

- **Treatment success** includes 'cured' and 'treatment completion', as per the WHO definition
- **Death during TB treatment** is not included in treatment failure, but is considered separately
- **Treatment failure** and **'loss to follow-up'** during treatment are included as separate outcomes in the model

ANNEX 22 OPTIMAL ALLOCATION OF MOZAMBIQUE'S TB EXPENDITURE – SCREENING (100% OF CURRENT SPENDING)

Program Name	2017 Spending (USD)	Optimized spending (USD)	Change
Outpatient screening (excluding PLHIV)	8.917	17.833	8.916
PLHIV outpatient screening	1.880	3.746	1.865
Active case finding (health workers)	0.038	0.128	0.090
Active case finding (miners)	0.252	0.191	-0.062
Active case finding (contact tracing)	1.657	3.554	1.896
Active case finding (community outreach)	8.911	2.093	-6.818
Active case finding (prisons)	0.123	0.720	0.597
Total Screening	**21.779**	**28.264**	

Note: PLHIV = people living with HIV.

ANNEX 23 OPTIMAL ALLOCATION OF MOZAMBIQUE'S TB EXPENDITURE – TREATMENT AND PREVENTION (100% OF CURRENT SPENDING)

Program Name	2017 Spending (USD)	Optimized spending (USD)	Change
Preventive TB treatment (contacts of active TB - under 5)	1.540	2.456	0.916
Preventive TB treatment (PLHIV)	12.026	0.000	-12.026
Ambulatory-focused DS treatment	6.671	9.851	3.181
Ambulatory-focused MDR treatment (long course)	2.266	3.607	1.341
Ambulatory-focused MDR treatment (short course)	0.248	0.040	-0.208
Ambulatory-focused XDR treatment (short course)	0.409	0.682	0.272
Total treatment and prevention	**24.067**	**17.542**	

Note: DS = drug susceptible; TB = tuberculosis; MDR = multi-drug resistant; PLHIV = people living with HIV; USD = United states dollar; XDR = extensively drug-resistant.

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