THE TUBERCULOSIS EPIDEMIC IN ROMANIA

TB ALLOCATIVE EFFICIENCY MODEL FINDINGS AND RECOMMENDATIONS

2019

WORLD BANK GROUP

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Romania National Institute of Pulmonology authors: Adriana Socaci, Beatrice Mahler-Boca, Domnica Ioana Chiotan, Gilda Popescu, Mihaela Stefan and Nicoleta Cioran

World Bank authors: Clemens Benedikt, Nejma Cheikh, Nicole Fraser and Zara Shubber

Burnett Institute authors: Romesh Abeysuriya, David Kedziora and Rowan Martin-Hughes

University College London authors: Gerard Joseph AbouJaoude, Ibrahim Abubakar, Lara Goscé, Hassan Haghparast-Bidgoli, Tom Palmer and Jolene Skordis-Worrall

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TABLE OF CONTENTS

TABLES

FIGURES

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This study is the result of a collaboration of various institutions and individuals who all made essential contributions to the work presented in this report. Contributors within each organization are listed in alphabetical order.

The core study and analysis and report-writing team comprised of Adriana Socaci, Beatrice Mahler-Boca, Domnica Ioana Chiotan, Gilda Popescu, Mihaela Stefan and Nicoleta Cioran from the Romania National Institute of Pulmonology; "Marius Nasta", Gerard Joseph Abou-Jaoude, Ibrahim Abubakar, Lara Goscé, Hassan Haghparast-Bidgoli, Tom Palmer and Jolene Skordis-Worrall from University College London; Romesh Abeysuriya, David Kedziora and Rowan Martin-Hughes from Burnett Institute; and Clemens Benedikt, Nejma Cheikh, Nicole Fraser, and Zara Shubber from the World Bank.

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ABBREVIATIONS

ACF	Active case finding
BCG	Bacillus Calmette–Guérin
BDQ	Bedaquiline
DR	Drug resistant
DS	Drug susceptible
DOTS	Directly observed treatment, short-course
EU	European Union
HIV	Human immunodeficiency virus
IPT	Isoniazid preventive therapy
LPA	Line probe assay technology
LTBI	Latent tuberculosis infection
MDR	Multi-drug resistant
NSP	National Strategic Plan
NTP	National Tuberculosis Programme
PWID	People who inject drugs
SDG	Sustainable Development Goal
TB	Tuberculosis
TST	Tuberculin skin test
UHC	Universal health coverage
WHO	World Health Organization
XDR	Extensively drug resistant
Xpert	GeneXpert MTB/RIF, detecting DNA sequences specific for M. tuberculosis and rifampicin resistance

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KEY MESSAGES

KEY CHARACTERISTICS OF THE TB EPIDEMIC AND RESPONSE

- **Romania's TB epidemic is on a downward trajectory** and both case detection rates (87%) and treatment success rates for drug-susceptible (DS)-TB (86%) are among the highest in the region
- However, despite significant progress in many aspects of its TB response, Romania continues to experience the largest number of new TB infections in the European Union (approximately 15,000 incident cases in 2016). This amounts to almost a quarter of all new estimated incident cases (23.8%) and deaths (23.4%) in the region.
- There were an estimated **6.3 million latent TB cases** in Romania in 2015, and the delayed activation of latent infections remains a key driver for TB incidence
- Treatment of TB in Romania features lengthy hospitalisation periods (on average approximately 2 months, 6 months and 9 months for DS-, MDR- and XDR-TB respectively), resulting in **high treatment costs**
- **Treatment success rates for drug-resistant (DR) TB cases remain low**, partly due to poor drug availability. Of those starting second-line treatment in 2014 (N=596), the treatment success rate was 44% for MDR-TB cases and 16% for XDR-TB.
- Estimated total TB spending in Romania amounts to approximately **EUR 115 million** for 2018, mainly funded by health insurance funds and government funding through the Ministry of Health

KEY TB ALLOCATIVE EFFICIENCY MODEL FINDINGS AND RECOMMENDATIONS

- If Romania maintains its current TB expenditure and coverage levels, TB incidence should maintain its downward trajectory
- Romania could increase the impact of existing funding by reallocating expenditure across existing and prospective interventions.

To maximise impact, funding should be reallocated as follows:

- Reduce spending on unnecessary hospitalisation for both DS-TB and DR-TB patients, which could free up to 20% of current funding for other uses
- Maintain funding for household contact tracing of all notified TB cases
- Reallocate a proportion of the budget to:
  - Build upon high success rates for DS-TB by increasing funding for DOTS as an alternative to lengthy hospitalisation periods
  - Increase funding for DR-TB treatment by approximately EUR 12 million to improve outcomes, by introducing and financing new DR-TB regimens, including drugs such as Bedaquiline.
  - Increase coverage for enhanced contact tracing in congregate community settings, such as schools and workplaces, to all notified TB cases
  - Spend approximately EUR 8 million to introduce new active case finding programmes in high incidence areas and to target high-risk groups such as homeless people, prisoners and people who inject drugs. This could improve the yearly diagnosis rate by up to 9%.

By 2030, the same budget, allocated differently, could reduce active TB infections by up to 45% and reduce the total number of TB deaths by 40% relative to 2018. In comparison, over the same period, current allocations could reduce both the number of TB infections and the number of TB deaths by 20% only.

Romania's TB epidemic is on a downward trajectory. However...

...Romania still experiences almost a **quarter of all new TB infections** in the European Union

23.8%

Poor treatment outcomes for drug resistant TB continues to be a challenge:

- **6.3M** latent TB cases in 2015
- **±15,000** TB incident cases in 2016
- **€ 115M** TB treatment cost spend in 2018

Romania can increase the impact response to TB by allocating existing expediture:

- reduce spending on unnecessary hospitalization
- maintain funding for household contact tracing of all notified TB cases

Reallocate a proportion of the budget by:

- increase funding for DOTS as an alternative for lengthy hospitalisation periods
- increase funding for Drug Resistant TB treatment
- increase coverage for enhanced contact tracing in congregate community settings
- increase funding for active case finding in high risk areas

Reallocating and optimizing the same budget differently could **reduce active TB infections by up to 45%** and **reduce the total number of TB deaths by 40%** by 2020

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EXECUTIVE SUMMARY

Despite significant progress in many aspects of its TB response, Romania continues to experience the largest number of new TB infections in the European Union, accounting for 23.8% of estimated incident cases in the region (WHO 2018c). Nationally, the TB incidence rate has been on a downward trajectory since 2002 (WHO 2018b). For 2016, the incidence was estimated at 74 per 100 000 population (WHO 2018b), compared with an estimated incidence of around 157 per 100 000 population in 2000 (WHO 2019). While the incidence of multidrug-resistant TB (MDR-TB) is also falling and represents a minority of new cases (around 2.5% ; WHO 2018b), poor treatment outcomes for drug-resistant TB remain a significant challenge.

In 2014, success rates for people receiving second-line treatment for MDR-TB were only 44% (WHO 2018b). Similarly, success rates for people receiving second-line treatment for extensively drug-resistant (XDR) TB were only 16% in 2014 (WHO 2018b). Opportunities exist to significantly improve these outcomes with new treatment regimens including drugs such as Bedaquiline and Linezolid. This report summarises the findings of an allocative efficiency study of the Romanian National TB response, using the Optima TB model.

Optima TB estimates that there were 6.3 million latent TB cases in Romania in 2015 and the delayed activation of so-called 'late-latent' infections remains a key driver for active-TB incidence.

This study aims to inform three key policy questions:

1. What is the epidemic trajectory of TB in Romania?
2. What is the likely impact of meeting national and international care cascade targets on the TB epidemic?
3. How can the TB treatment cascade be improved and resource allocation be optimized?

The key findings from the analyses are detailed below

KEY MESSAGE 1: A large number of latent TB infections sustains the TB epidemic in Romania. Although diagnosis and treatment of active TB have immense benefits for patients, they will have limited impact on TB incidence.

Under current conditions, Optima TB estimates that the incidence of TB will steadily fall from a rate of 82 per 100,000 in 2015 to 65 per 100,000 by 2035. Optima TB estimates that there were 6.3 million latent TB cases in Romania in 2015 and the delayed activation of so-called 'late-latent' infections remains a key driver for active-TB incidence. The prevalence of latent TB cases is increasing in the 65+ population, likely due to the aging of people who have lived through periods of very high TB incidence and may carry latent TB

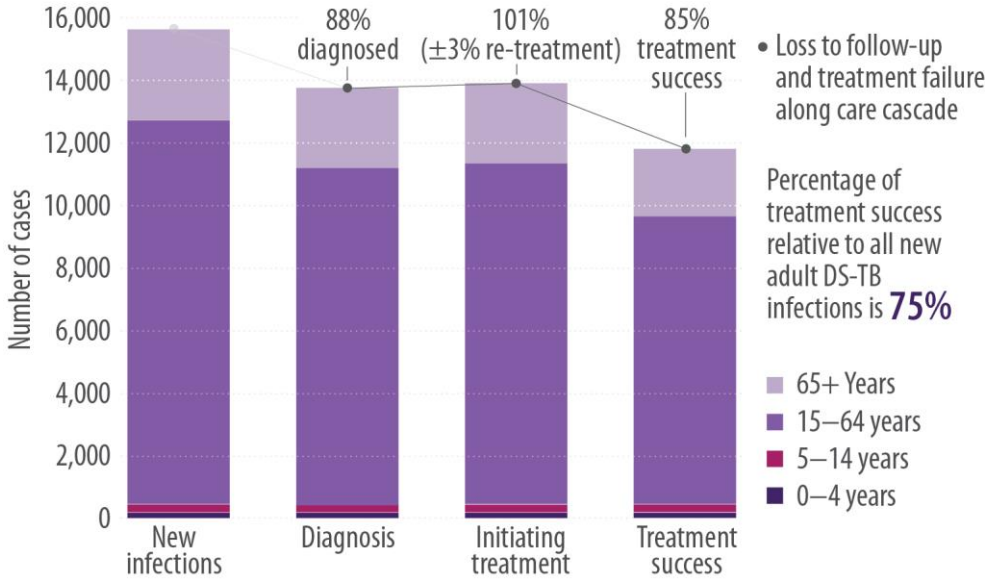
infections for many years. Latent TB prevalence is projected to stabilise around 2020 in this older population, and to be stable or to decrease slightly across all other populations until 2035.

Optimised allocations of TB expenditure are not projected to have a large impact on TB incidence. This is largely because TB incidence is primarily driven by people progressing to active TB from the large pool of latent-TB infections. As the national TB programme is focused on diagnosis and treatment of active TB, the interventions included in our analysis do not affect progression rates from latent-TB to active-TB. Reducing the incidence of TB will likely require broader strategies to address the social determinants of health, such as poverty levels, housing conditions and nutrition, which significantly impact progression to active TB.

Reducing the incidence of TB will likely require broader strategies to address the social determinants of health, such as poverty levels, housing conditions and nutrition, which significantly impact progression to active TB.

Using available health information system (HIS) data, it is estimated that 88% of new DS-TB infections were diagnosed in 2015. Of all diagnosed DS-TB patients, regardless of the year diagnosed, 101% initiated treatment in a given year. This suggests that approximately 3% patients are being retreated for previously diagnosed DS-TB. Of those initiating treatment, 85% attained treatment success. The treatment success rate relative to all new DS-TB infections is estimated at 75% (see ES Figure 1).

Figure ES 1 Modelled care cascade outcomes for people with DS-TB in Romania, under current conditions



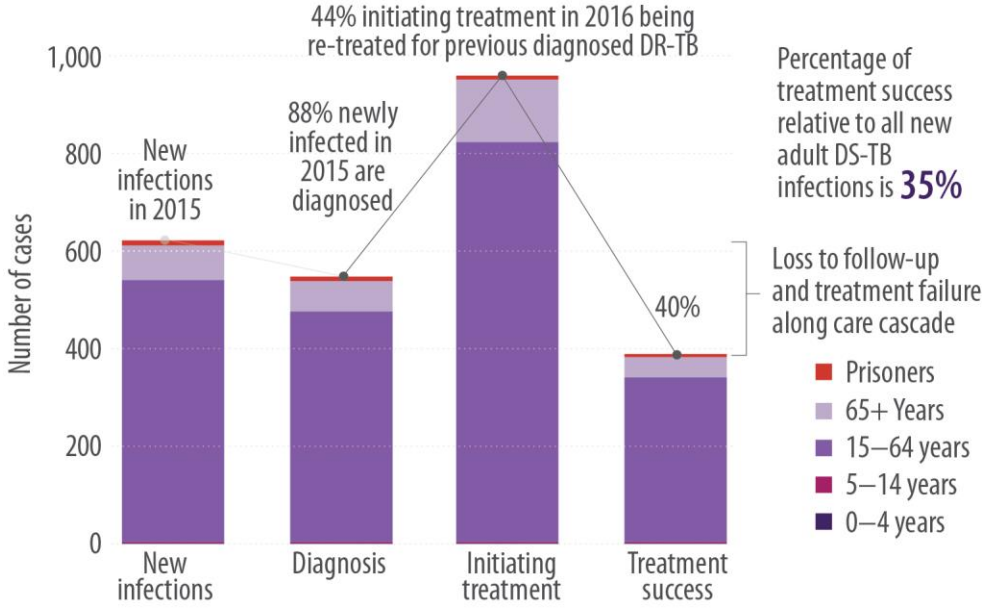
Source: Optima TB model analysis for Romania using 2015 notifications and outcome data.

Note: DS-TB = drug susceptible Tuberculosis; Treatment initiation rate displayed includes previously diagnosed DS-TB cases that did not complete treatment. The treatment initiation rate of newly diagnosed DS-TB cases used to inform the model is 98%.

Using health information systems data, the model projects that 88% of new DR-TB infections were diagnosed in 2015. An estimated 44% of people initiating treatment for DR-TB in a given year are being retreated for previously diagnosed DR-TB. For those initiating treatment, the treatment success rate is 40%. Treatment success relative to all new DR-TB infections is therefore estimated at 35% (see ES Figure 2).

If Romania maintains its current expenditure and coverage levels, TB incidence should maintain its downward trajectory.

Figure ES 2 Modelled care cascade outcomes for people with DR-TB in Romania, under current conditions



Source: Optima TB model analysis for Romania using 2015 notifications data.

Note: The 40% treatment success rate is informed by 2014 cohort outcomes data for MDR-TB and 2012 cohort outcome data for XDR-TB. This was only used in the historical calibration and not to inform future projections after optimization modelling. Treatment initiation rate displayed includes previously diagnosed DS-TB cases that did not complete treatment. The treatment initiation rate of newly diagnosed DR-TB cases used to inform the model is 98%

KEY MESSAGE 2: By meeting national care cascade targets, Romania could reduce the total number of active TB cases by up to 17% by 2035. By meeting national targets for MDR-TB, Romania could achieve a 34% reduction in the total number of MDR-TB infections.

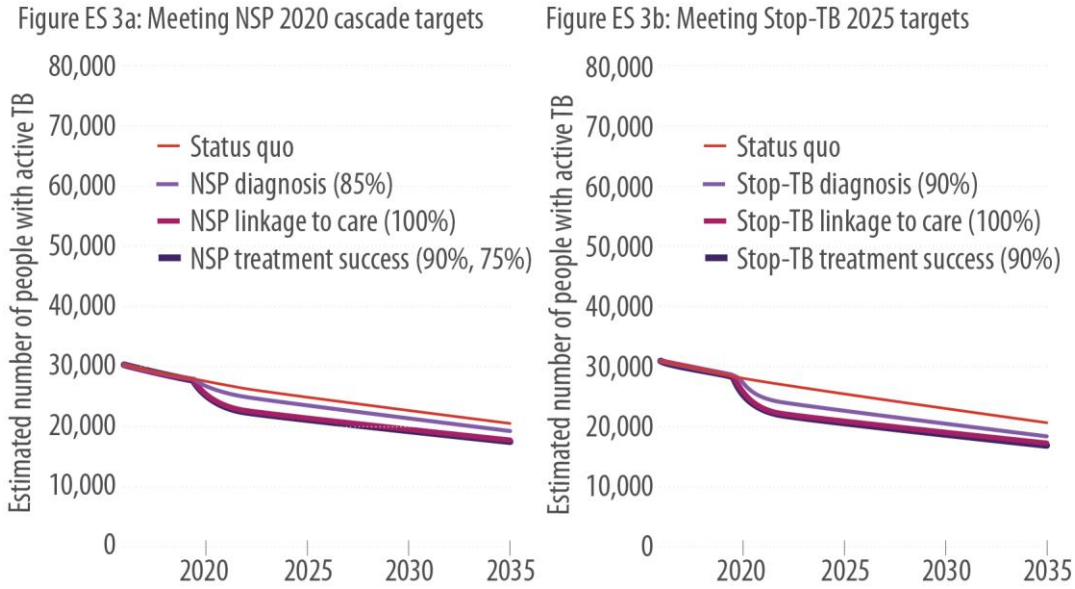
A scenario analysis was conducted to investigate the potential impact of meeting national and international care cascade targets on key TB indicators by 2020 and 2025 respectively. This group of scenarios projects the impact on key TB indicators of reaching 2020 National Strategic Plan (NSP) and 2025 STOP TB care cascade targets for:

- **TB screening and diagnosis:** The NSP aims to diagnose 85% of incident TB cases by 2020 and the STOP-TB targets aim for 90% of incident TB cases to be diagnosed by 2025.
- **TB treatment initiation (linkage to care):** Both the NSP and STOP-TB targets aim for 100% of diagnosed cases to be linked to care
- **TB treatment outcomes:** Both the NSP and STOP-TB targets aim for overall treatment success rates of 90% of TB cases. Additionally, the NSP targets treatment success for 75% of MDR-TB cases. For the purposes of the scenario analysis, this target was also used for XDR-TB.

The results from the scenario analyses of the total number of active-TB infections are shown in Figure ES 3 below. Meeting and sustaining the NSP 2020 care cascade targets in the total population is projected to yield reductions in the total number of active TB cases of up to 17% by 2035. Similarly, meeting and sustaining the STOP-TB 2025 care cascade

targets is projected to yield reductions in the total number of active TB cases of up to 12% by 2035.

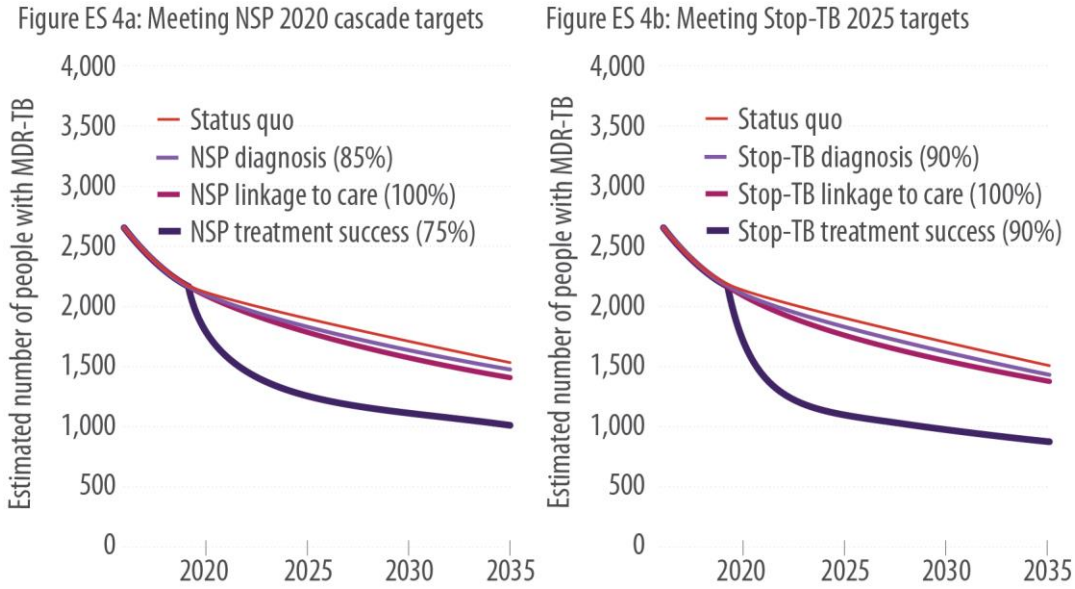
Figure ES 3 Modelled impact on the total number of active-TB infections of meeting care cascade targets for all TB cases (2015–35)



Source: Optima TB model analysis for Romania.

Figure ES 4 presents the impact of meeting and sustaining the NSP 2020 care cascade targets on drug-resistant TB. Simultaneously meeting and sustaining the proposed targets could, by 2035, achieve a 34% reduction in the total number of MDR-TB cases. Similarly, simultaneously meeting and sustaining the STOP-TB 2025 care cascade targets could achieve a 42% reduction in the total number of MDR-TB infections by 2035. Improvement in treatment success is projected to account for the vast majority of this impact.

Figure ES 4 Modelled impact on the total number of active MDR-TB and XDR-TB infections of meeting 2020 NSP care cascade targets for MDR-TB (2015–35)



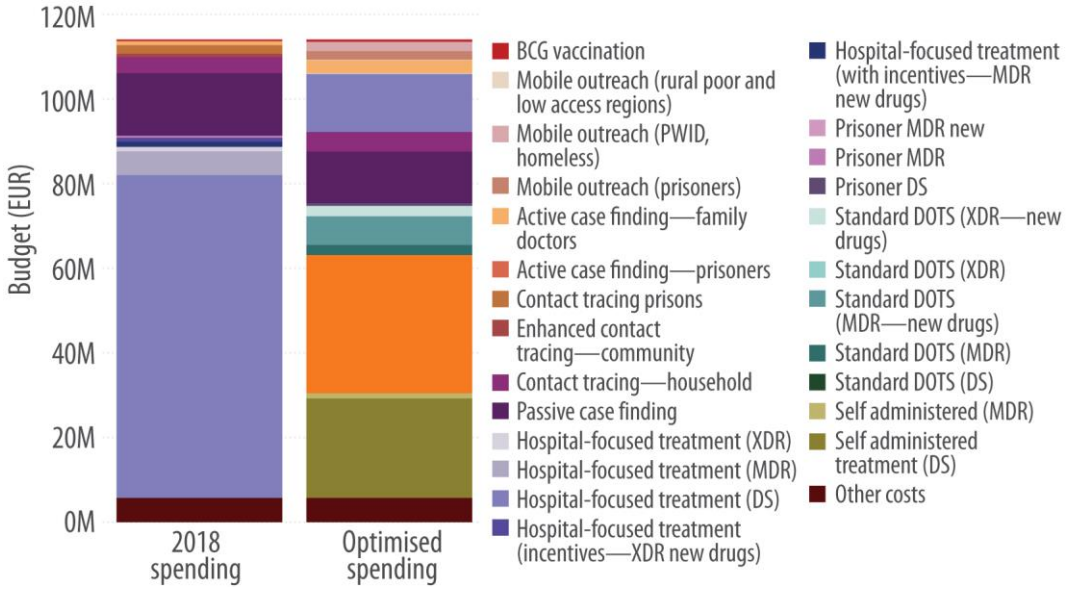
Source: Optima TB model analysis for Romania.

KEY MESSAGE 3: An optimized allocation of resources could result in a 45% reduction in active TB cases and a 40% reduction in TB deaths by 2030.

This analysis estimated that TB expenditure in Romania amounted to approximately EUR 115 million in 2018, comprised mainly of health insurance contributions (49%) and state funding through the Ministry of Health (40%). The analysis then determined the mathematically optimal funding allocations for Romania's National TB Programme (Figure ES 5). The optimal allocation aims to simultaneously minimise the cumulative number of new active-TB infections, the total number of active-TB infections and TB-related mortality between 2018 and 2030. These were modelled as combined optimisation objectives. An optimal allocation of TB funding would increase funding for case finding programmes, reduce hospital-focused treatment and increase funding for DR-TB drug regimens containing new drugs.

The optimal allocation aims to simultaneously minimise the cumulative number of new active-TB infections, the total number of active-TB infections and TB-related mortality between 2018 and 2030.

Figure ES 5 Optimal reallocation of current TB expenditure to simultaneously minimise cumulative TB incidence, prevalence and deaths between 2018 and 2035 in Romania



Source: Optima TB model analysis for Romania

Note: 2018=base year (current allocation); Optimised budget: It was assumed that the budget of EUR 115 million that were available for TB-related programmes in 2018 would remain available on an annual basis up to 2035.

To maximise impact, funding should be reallocated as follows:

- **Reduce spending** on unnecessary hospitalisation for both DS-TB and DR-TB patients, which could free up to 20% of current funding for other uses
- **Maintain funding** for household contact tracing of all notified TB cases
- **Reallocate** a proportion of the budget to:
  - Build upon high success rates for DS-TB by increasing funding for DOTS as an alternative to lengthy hospitalisation periods
  - Increase funding for DR-TB treatment by approximately EUR 12 million to improve outcomes, by introducing and financing new DR-TB regimens, including drugs such as Bedaquiline

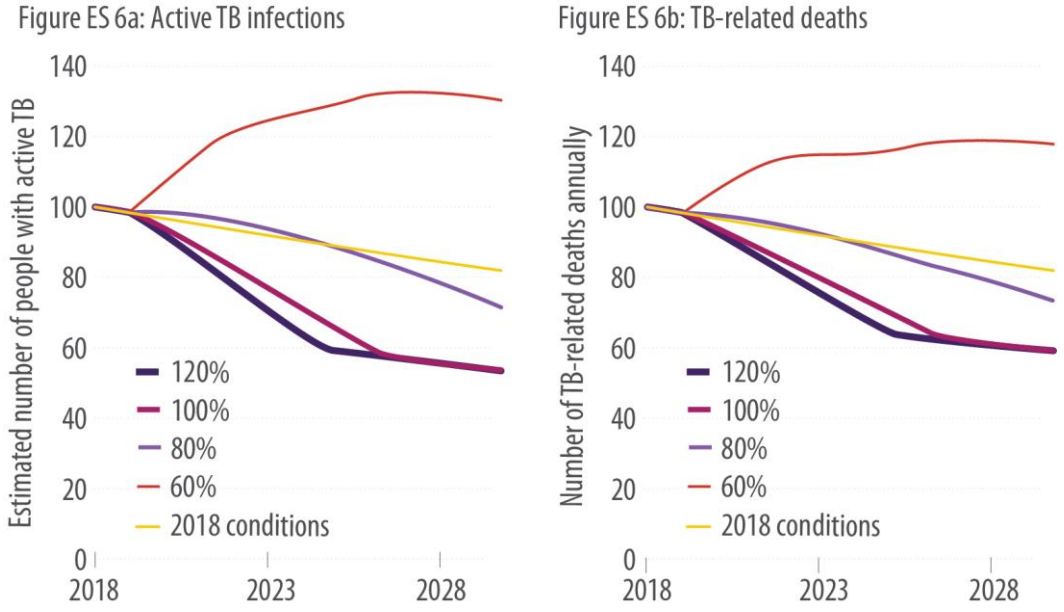
- Increase coverage for enhanced contact tracing in congregate community settings, such as schools and workplaces, to all notified TB cases
- Spend approximately EUR 8 million to introduce new active case finding programmes in high incidence areas and to target high-risk groups such as homeless people, prisoners and people who inject drugs. This could improve the yearly diagnosis rate by up to 9%

KEY MESSAGE 4: In order to make progress in Romania's TB response, it is imperative that current budget level is maintained.

The analysis also explored the optimal investment pattern for **different levels of spending** (Figure ES 6). While the optimised allocation of current expenditure is projected to yield significant gains, there are diminishing marginal returns to spending over 100% of the budget. Reductions in TB spending to 80% of current levels, **if optimally allocated**, could result in a similar epidemic trajectory to those currently observed under baseline conditions in Romania. Reductions in TB spending to 60% of current levels would have a significant negative impact.

Given the context of TB financing in Romania, it is not guaranteed that any savings from reduced hospitalisation would be reallocated to other TB expenditure. Optimisation of current expenditure results in savings of approximately 20% of total expenditure as a result of reduced hospitalisation. Therefore, an optimisation of 80% of current expenditure was conducted to see the impact on conclusions. This would result in active case finding and second-line drugs for XDR TB being prohibitively expensive. As such, to maintain or improve Romania's TB response, it is imperative that current expenditure is maintained and any savings from particular budget lines are reallocated to other aspects of TB diagnosis and care where possible.

ES Figure 1 Modelled impact of optimised allocations on the number of active TB infections and TB-related deaths under different amounts of spending, Romania (2018–30)



Source: Optima TB model analysis for Romania.

Note: 2018=base year (current allocation); Optimised budget: It was assumed that the budget available for TB-related programmes in 2018 would remain available on an annual basis up to 2035; Different expenditure amounts refer to proportions of the 2018 level of spending.

RECOMMENDATIONS

A significant positive health impact could be achieved by sustaining 2018 TB financing of EUR ~115 million and allocating that funding optimally. An optimal funding allocation includes:

1. REDUCED UNNECESSARY HOSPITALISATION FOR BOTH DS-TB AND DR-TB PATIENTS

- Reducing unnecessary hospitalisation, in line with WHO recommendations, will reduce costs without affecting outcomes, provided standard directly observed treatment (DOTS) is in place
- This could free up to 20% of current funding for other uses
- Potential further benefits exist, such as reduced nosocomial transmission and a reduced economic impact on patients

2. BUILD UPON HIGH SUCCESS RATES FOR DS-TB BY USING DOTS AND AMBULATORY TREATMENT

- Using a combination of DOTs and ambulatory treatment after a reduced initial hospitalisation period could reduce the cost of DS-TB treatment by up to EUR 20 million
- Both case detection and treatment success rates for DS-TB in Romania are among the highest in the region
- Improvements in outcomes are possible from increased adherence due to use of DOTs, which could be combined with small financial incentives for patients

3. IMPROVE DR-TB TREATMENT OUTCOMES BY REALLOCATING FUNDS TO INTRODUCE NEW DR-TB REGIMENS, INCLUDING DRUGS SUCH AS BEDAQUILINE

- Increasing funding for DR-TB treatment by approximately EUR 12 million would enable the addition of new drugs, which significantly improve the likelihood of treatment success and reduce the time to smear conversion
- The model estimates that a reallocation of funding from old DR-TB regimens to new treatment regimens for eligible patients could significantly improve treatment success rates

4. MAINTAIN FUNDING FOR HOUSEHOLD CONTACT TRACING

- Current estimated spending should be maintained to identify household members of all notified TB cases, who are at high risk of having active TB
- Earlier identification will improve outcomes and reduce the risk of further transmission

5. INCREASE COVERAGE OF ENHANCED CONTACT TRACING

- Contact tracing beyond the household, in high-risk community settings such as workplaces and schools, can help to improve diagnosis rates and shorten the time to diagnosis

- Currently this is only done for approximately 20% of notified cases but should be expanded to all active TB cases

6. IMPLEMENTATION OF NEW ACTIVE CASE FINDING PROGRAMMES

- Despite a high diagnosis rate for TB, case finding in Romania has been primarily passive
- To further improve the diagnosis rate, active case finding programmes are likely to be an essential part of the TB response
- Approximately EUR 8 million should be spent to introduce new active case finding programmes in high incidence areas and target high-risk groups such as homeless people, prisoners and people who inject drugs
- This could improve the yearly diagnosis rate by up to 9%
- This recognizes that those people whose TB remains undiagnosed are likely to be in vulnerable and hard-to-reach populations
- In addition to allocative efficiency arguments, there is therefore also an equity argument for funding active case finding programmes, as populations targeted by outreach activities will receive care that would otherwise not have been available to them

7. POVERTY REDUCTION AND LATE LATENCY BURDEN

- There are still approximately 6 million people in Romania with late latent TB infections. This is the main driver of active TB incidence
- As the national TB programme is focused on diagnosis and treatment of active TB, the interventions included in our analysis do not affect progression rates from latent TB to active-TB
- Reducing the incidence of TB will likely require broader strategies to address the social determinants of health, such as income, housing or nutrition, which significantly impact progression to active TB

8. COMMUNITY INTERVENTIONS

- Locally based care for TB patients, encompassing economic, psychological and peer support, will help to improve treatment outcomes
- Funding for existing pilots of community interventions should be expanded. Furthermore, locally based education campaigns are likely to facilitate the diagnosis of hard to reach populations. In future, such interventions should be funded by the government as donor-funding in Romania is not guaranteed

THESE CHANGES COULD RESULT IN A 45% REDUCTION IN ACTIVE TB CASES AND A 40% REDUCTION IN TB DEATHS BY 2030.

SECTION 1

INTRODUCTION

1.1 NECESSITY FOR ALLOCATIVE EFFICIENCY IN ROMANIA'S TB RESPONSE

Despite significant progress in many aspects of its TB response, Romania continues to experience the largest number of new TB infections in the European Union, accounting for 23.8% of estimated incident cases in the region (WHO 2018c). Nationally, the TB incidence rate has been on a downward trajectory since 2002(WHO 2018b). For 2016, the incidence was estimated at 74 per 100 000 population (WHO 2018b), compared with an estimated incidence of around 157 per 100 000 population in 2000 (WHO 2019). While the incidence of multidrug-resistant TB (MDR-TB) is also falling and represents a minority of new cases (around 2.5% ; WHO 2018b), poor treatment outcomes for drug-resistant TB remain a significant challenge. In 2014, success rates for people receiving second-line treatment for MDR-TB were only 44% (WHO 2018b). Similarly, success rates for people receiving second-line treatment for extensively drug-resistant (XDR) TB were only 16% in 2014 (WHO 2018b). Opportunities exist to significantly improve these outcomes with new treatment regimens including drugs such as Bedaquiline and Linezolid.

The National Strategic Plan for the Control of Tuberculosis in Romania (NSP, 2015–20) was designed, in part, to address poor outcomes for drug-resistant TB.

The National Strategic Plan for the Control of Tuberculosis in Romania (NSP, 2015–20) was designed, in part, to address poor outcomes for drug-resistant TB. The strategy established eight major objectives:

- Ensure universal access to rapid diagnosis methods for DS-TB and M/XDR-TB by 2020
- Diagnose at least 85% of all estimated DS-TB and MDR-TB cases
- Successfully treat at least 90% of new culture positive TB cases and 85% of all retreatment cases by 2020
- Successfully treat 75% of MDR-TB cases by 2020
- Reduce overall TB mortality rate to 4.3 per 100 000 population by 2020
- No affected families facing catastrophic costs due to tuberculosis
- Decrease case notification rate of all forms of TB – bacteriologically confirmed plus clinically diagnosed, new and previously treated cases—from 73 per 100,000 population in 2013 to less than 50 cases per 100 000 population by 2020
- Improve health system capacity to control TB

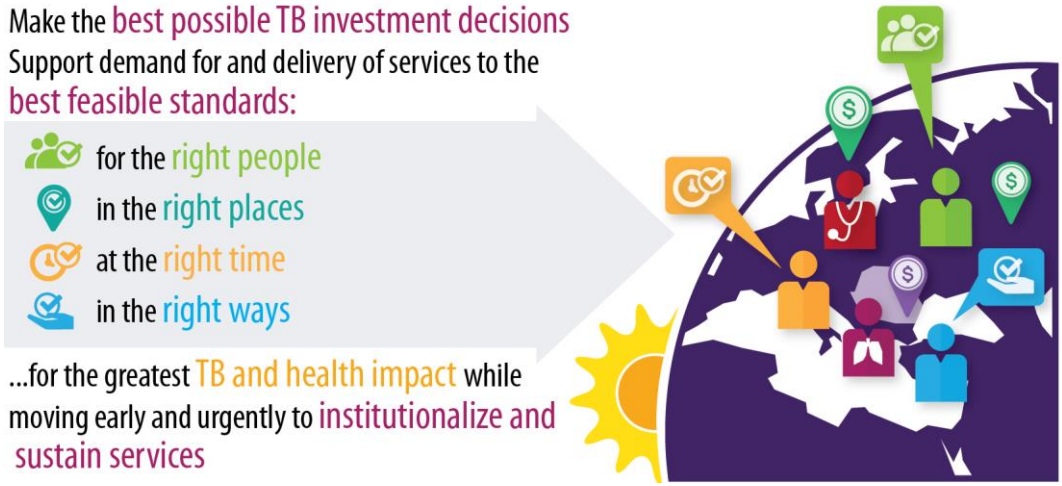
The NSP also aims to improve TB detection in high-risk populations, such as prisoners, through active case finding. Current diagnosis of TB in Romania is primarily through passive case finding, with vulnerable populations less likely to be diagnosed and diagnosis likely to occur at a later stage of disease. As the NSP aims to achieve substantial reductions in TB incidence and mortality by 2020, an efficient, effective, targeted TB response is needed.

By considering both disease burden and defined objectives, an optimal allocation distributes budgets in the most efficient way across interventions, using evidence on intervention costs and effectiveness.

Importantly, the NSP 2015–20 promotes a vision of eliminating tuberculosis as a public health problem in Romania by 2050. This requires targeted, evidence-based interventions to improve the quality of TB care and prevention. One of the three 'pillars' on which the NSP is based is 'Innovative Research and Evidence-based Strategies', recognising the need for collaborative research which provides evidence for decision-making. In order to meet the strategic TB targets, and to maximise what can be achieved with available TB resources, it is therefore important to assess the best funding allocations across the different TB interventions. By considering both disease burden and defined objectives, an optimal allocation distributes budgets in the most efficient way across interventions, using evidence on intervention costs and effectiveness.

Allocative efficiency analyses ask the following question: 'how can available financial resources be optimally allocated to achieve a set of stated objectives?' The concept is summarised in Figure 1.1, which highlights the importance of delivering the right services to the correct target groups, at the right time and in the right places, to maximise the impact of TB investments.

Figure 1.1 Allocative efficiency in the TB response



Source: World Bank.

The World Bank supports countries in their efforts to achieve Universal Health Coverage (UHC) through a range of strategies relating to health sector reform, health financing as well as analytical support to enhance efficiency and effectiveness of health service delivery. As part of its wider support, the World Bank—in collaboration with other partners—has supported disease-specific allocative efficiency studies in more than 40 countries. Initially, the focus of allocative efficiency studies was on HIV responses. The focus has now expanded towards TB, nutrition, malaria, non-communicable diseases (NCDs) and health service prioritisation.

There is wide consensus that better outcomes could be achieved in many settings with a given amount of TB funding; or that given outcomes could be achieved with less TB funding if resources are distributed optimally or if resources are used in the most efficient ways. Mathematical modelling is one way to determine optimised TB resource allocation.

An allocative efficiency study of Romania's TB response, using the Optima TB model, was conducted to support Romania in its decision-making on strategic TB investments during the current NSP period and up to 2030.

1.2 SPENDING AND TREATMENT FOR TB IN ROMANIA

TB Expenditure Summary

TB services in Romania are funded through four main streams: (1) the National Insurance house, which covers in-patient hospital care (accounting for approximately 54% of all TB expenditure in 2015); (2) the Ministry of Health, which covers ambulatory care and other services, including TB dispensaries (31%); (3) the National TB programme (NTP), covering drugs, diagnostics and other supplies, which is funded by a combination of government and donor funds (7%); and (4) other international funding, primarily from the Global Fund (3%) and Norway (5%), covering various projects including DR-TB treatment with newer drug regimens. Based on data provided by the individual funding sources, it is estimated that total spending on TB in 2015 amounted to approximately EUR 85 million in Romania.

Table 1.1 Romania: TB expenditure by source of financing (2015)

FUNDING SOURCE	2015 SPENDING (EUR)	% SHARE
Global Fund	2,802,586	3%
Health insurance fund	45,636,138	54%
Ministry of Health	26,433,409	31%
Ministry of Health – National Tuberculosis Programme	6,341,684	7%
Norway	3,905,556	5%
Grand Total	**85,119,373**	**–**

Source: Based on data provided for the individual funding sources.

For the purpose of the analyses in this report, the budget for 2018 was estimated based on the 2015 budget, with adjustment for known increases in spending. Firstly, Ministry of Health expenditure increased from approximately EUR 26 million in 2015 to approximately EUR 40 million in 2017. Additionally, in mid-2018 dispensary staff received a 50% salary increase, which was also accounted for in the 2018 budget estimate. This will further increase the Ministry of Health's expenditure to approximately EUR 56 million, resulting in a total estimated TB expenditure of approximately EUR 115 million, which will be used as current spending for the purposes of this analysis. This increased demand for TB spending is likely to be challenging for the health system, and reinforces the necessity for allocative efficiency.

In addition to the total expenditure reported above, a detailed breakdown of expenditure on drugs, diagnostics and other supplies was provided by the National Tuberculosis Programme. Hospital TB expenditure by county was also provided. All of these sources

facilitated the estimation of programme costs for inclusion in the analysis in this report (see Table 3.8).

Diagnosis of TB in Romania

The diagnosis of TB has been predominantly through passive case-finding in Romania, meaning that TB is only diagnosed after a person seeks healthcare. Passive case-finding generally results in diagnosis at a later stage of disease than diagnosis through active case-finding. Active case finding in Romania has thus far been limited to tracing contacts of people with diagnosed TB, screening health workers and screening prisoners upon entry and exit. Due to a lack of funding, Romania did not have rapid diagnostic methods until 2015, when new technologies were financed by external donors.

New active case-finding modalities are now being introduced in Romania. Mobile outreach vans are being piloted to target high-risk populations, with the aim of ensuring early diagnosis and treatment for people who are typically hard to reach. This recognises that ambulatory TB care may be inaccessible and ineffective for many people in Romania. Targeted populations include the homeless and people who inject drugs (currently 1 van), prisoners (1 van), and low-access rural areas (2 vans). These projects are funded from external sources, and the NTP in Romania has previously stated that active case finding is not cost effective (NTP 2013).

New active case-finding modalities are now being introduced in Romania. Mobile outreach vans are being piloted to target high-risk populations, with the aim of ensuring early diagnosis and treatment for people who are typically hard to reach.

A potential further form of intensified case-finding identified as being of interest for this analysis is training family doctors in high-risk areas to screen people who are attending for non-TB related health conditions. A more proactive approach to TB diagnosis at this level could facilitate more diagnoses at an earlier stage of disease.

Treatment of TB in Romania

Treatment of TB in Romania is primarily hospital-based, typically involving extended periods of hospitalisation of 9 weeks for DS-TB and up to 39 weeks for DR-TB. Current hospital funding in Romania continues to incentivise lengthier hospitalisation. The United Nations Human Rights Council Special Rapporteur on Extreme Poverty and Human Rights found that in Romania "recent expenditures have favoured hospital funding, at the expense of urgently needed improvements in primary, community, and preventative care arrangements"(Alston 2015). Reducing unnecessary hospitalisation, in line with WHO recommendations (de Colombani et al. 2015), can reduce costs without affecting treatment outcomes. Reduced hospitalisation is also likely to reduce nosocomial transmission, as TB patients share the hospital environment with other non-TB patients. There are also likely wider non-TB impacts. For example, it may reduce the negative impact of treatment on patient employment and income.

Provision of treatment for DR-TB has been inconsistent in Romania. Approximately 20% of DR-TB patients have had treatment funded by the Global Fund, while the remaining DR-TB patients are funded domestically. The latter group have faced unavailability of the full range of second-line medications recommended by WHO, resulting in very poor treatment outcomes. This is due to longstanding issues with both reimbursement and procurement of TB drugs in Romania (Romanian Health Observatory 2017). In 2018, legislative changes in Romania were accepted that should improve the availability of second-line drugs, including Bedaquiline, for patients funded by domestic sources. This could vastly improve treatment outcomes for DR-TB.

A proven strategy to improve TB treatment adherence is Directly Observed Therapy (DOTS), whereby people are monitored to ensure they adhere to treatment and are provided with other support (Karumbi and Garner 2015). DOTS has been implemented inconsistently in Romania. Further, since 2009 family doctors have not been paid for TB monitoring and treatment, leaving many patients with inadequate support for self-administered treatment. Improving the provision of DOTS in line with WHO guidelines could improve adherence in Romania.

A proven strategy to improve TB treatment adherence is Directly Observed Therapy (DOTS), whereby people are monitored to ensure they adhere to treatment and are provided with other support.

Incentives to adhere to treatment may also be effective in improving outcomes. Using funding from the Global Fund, patients in six counties have been receiving small financial incentives of 50 lei per month for DS-TB and 80 lei per month for DR-TB. While some uncertainty about the effectiveness of these programmes remains, the impact of these incentives appears promising (Hoorn et al. 2016) and they could form part of a package to improve treatment adherence.

Finally, Romania has started to implement innovative community-based programs to improve treatment outcomes (see next section). These programs require multidisciplinary teams to address the different factors causing poor adherence, and assess the level of support required by people on treatment. Pilots in six counties include psychological counselling and peer support components. Unfortunately, due to data unavailability, it was not possible to include these programmes in the analysis in this report. However, these programmes may assist in improving future TB treatment in Romania.

This page is for collation purposes.

SECTION 2

STUDY 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 Appendix A (Technical summary of Optima TB) and Appendix B (Data inputs into the model).

2.1 ALLOCATIVE EFFICIENCY QUESTIONS ADDRESSED

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

Q1: What is the epidemic trajectory of TB in Romania?

- What are the future estimated 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:
  - By selected age groups (0–4, 5–14, 15–64 and 65+ years)?
  - By resistance type?
  - For prisoners?

Q2: What is the likely impact on the TB epidemic of meeting national and international care cascade targets (see Table 2.2)?

Q3: How can the TB treatment cascade be improved and resource allocation optimized?

- What are the main breakpoints in the tuberculosis treatment cascades for drug susceptible TB, MDR-TB and XDR-TB?
- What are the key interventions for addressing break points in the cascade and what is the evidence for their effectiveness?
- Which steps of the cascade should be prioritized in resource allocation and programming?

2.2 METHODOLOGY

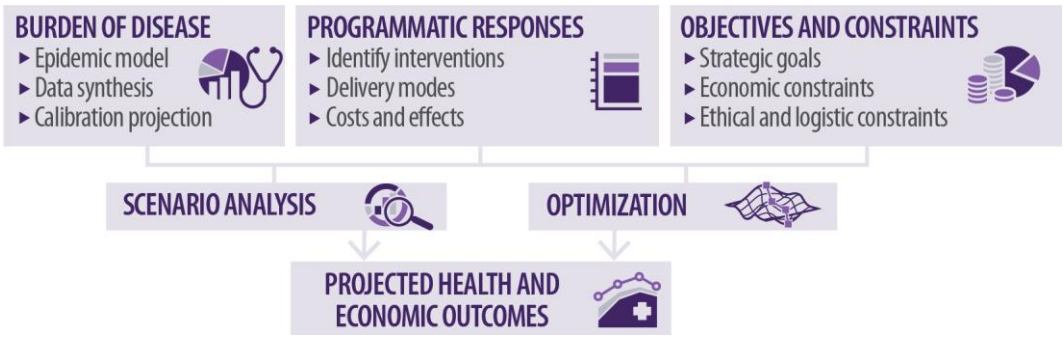
Collaboration and Stakeholder Involvement

The analysis was a collaboration between the Government of Romania, the Marius Nasta Institute, 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, programme, and costing 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 the 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 programme 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.

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 Appendix A.

In the absence of a national TB prevalence survey, Optima TB was calibrated primarily based on data on TB case notifications in consultation with national TB experts. 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 incidence and prevalence.

To assess how incremental changes in spending affect TB epidemics and determine an optimised 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 on overall epidemic indicators. Furthermore, by using a mathematical optimisation algorithm, Optima TB is able to determine an optimised allocation of funding across different TB interventions. Additional details of the Optima TB model and the Romania application are included in Appendices A and B.

By using a mathematical optimisation algorithm, Optima TB is able to determine an optimised allocation of funding across different TB interventions.

Analytical Framework

Model parameters are summarised in Table 2.1 and detailed in Appendix B. For context on the TB programmes listed below, see Section XX. All prospective treatment programme, denoted by an asterisk in Table 2, include small financial incentives to improve patient adherence.

Table 2.1 Model parameterisation

CATEGORY	PARAMETERIZATION IN THE OPTIMA MODEL	DESCRIPTION/ ASSUMPTIONS
Populations defined in the model	General Population (0–4 years)	Male and Female Children aged 0–4
	General Population (5–14)	Male and Female Young Population aged 5–14
	General Population (15–64)	Male and Female Adult Population aged 15–64
	General Population (65+)	Male and Female Elderly Population aged 65+
	Prisoners	Male and Female prisoners
Programme expenditure areas defined in the model and included in optimisation analysis	Hospital Focused Modality	Current treatment delivery for DS/MDR/XDR-TB implemented in Romania, with a given number of hospitalisation days by resistance-type
	Ambulatory Delivery Modality*	WHO recommended outpatient service delivery, with a reduced number of days hospitalized. Hospital based only during the intensive phase of a given regimen or until smear conversion
	Directly Observed Treatment (DOTS)*	Standardized short-course anti-TB treatment given under direct and supportive observation

Table 2.1 continued

Table 2.1 Model parameterisation (continued)

CATEGORY	PARAMETERIZATION IN THE OPTIMA MODEL	DESCRIPTION/ ASSUMPTIONS
	Old MDR and XDR Regimens	These include the standardised MDR-TB and XDR-TB drug regimens without Bedaquiline or delamanid
	New MDR and XDR Regimens*	These include the standardised MDR-TB and XDR-TB drug regimen, with the addition of Bedaquiline or delamanid
	BCG Vaccination	Vaccination with Bacillus Calmette-Guérin targeting the 0–4 population
	Passive Case Finding across all Populations	Diagnosis package for people who present to the health facility with symptoms; includes a Chest X-ray, Xpert, Sputum Smear Microscopy and Culture testing
	Household Contact Tracing of TB cases	Investigation and follow-up treatment with IPT preventative therapy for suspected LTBI for household contacts of TB cases
Programme expenditure areas defined in the model and included in optimisation analysis	Community Contact Tracing of TB cases	Investigation and follow-up treatment with IPT preventative therapy for suspected LTBI for community contacts of TB cases
	Prison Contact Tracing	Investigation and follow-up treatment with IPT preventative therapy for suspected LTBI for prison contacts of TB cases
	Active Case Finding – family doctors	Active case-finding by symptom screening of people attending family doctors for unrelated reasons
	Active case finding – prisoners	Active case-finding by targeted screening of prisoners with chest X-rays and Xpert
	Mobile outreach – prisoners	Active case-finding in mobile outreach vans by targeted screening of prisoners with chest X-rays and Xpert
	Mobile outreach – homeless and PWID	Active case-finding in mobile outreach vans by targeted screening of homeless and PWID with chest X-rays and Xpert
	Mobile outreach – rural poor and low access regions	Active case-finding in mobile outreach vans by targeted screening in rural poor and low access regions with chest X-rays and Xpert

Table 2.1 continued

Table 2.1 Model parameterisation (continued)

CATEGORY	PARAMETERIZATION IN THE OPTIMA MODEL	DESCRIPTION/ ASSUMPTIONS
Programme expenditure areas defined in the model and included in optimisation analysis	The components of TB spending that were not included in the optimisation analysis:	Some programme areas have not been optimised 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
Expenditure areas not optimised	Isoniazid Preventive Therapy (IPT)	Cost of IPT for non-active TB cases identified through contact-tracing.
	Tuberculin Skin Test	Cost of conducting TST test to diagnose LTBI
	Quantiferon	Cost of conducting Quantiferon test to diagnose LTBI
	2000	Year of model initiation, start year for data entry
Years and time horizons	2015	Base year
	2020	Timeframe National Strategic Plan on TB
	2025	Milestone year for End TB Strategy and target year for achievement of Stop TB partnership targets
	2030	Target year for achievement of SDG targets
	2035	Target year for End TB Strategy
Baseline scenario funding	**As per authors' expenditure analysis**	Total spending on TB in 2018 as per this study's expenditure analysis (estimated approximately EUR 115 million)

Costs of all treatment programmes listed above were estimated using a 'bottom-up' approach, based on average daily costs from hospital data. An average cost per ambulatory interaction was also derived and applied to both screening programmes 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 Appendix A, while unit costs are shown in Appendix B.

Strategic TB targets used in the Analysis

The NSP 2015–20 and global 2025 STOP TB targets both aim to improve diagnosis rates, treatment initiation rates and treatment success rates. The targets used in the modelling analyses are shown in Table 2.2.

Table 2.2 National and international TB care cascade targets

IMPACT OF IMPROVED CARE CASCADE	CURRENT CONDITIONS (2015)	NSP TARGET (2020)	STOP TB TARGET (2025)
DS-TB care			
Diagnosis	78.7%	85%	90%
Treatment initiation	97.7%	100%	100%
Treatment success	84.6%	90%	90%
MDR-TB care			
Diagnosis	78.7%	85%	90%
Treatment initiation	97.7%	100%	100%
Treatment success	44%	75%	90%
XDR-TB care			
Diagnosis	67.9%	85%	90%
Treatment initiation	97.7%	100%	100%
Treatment success	16%	75%	90%

Sources: WHO Romania TB country profile; Romania National Strategic Plan 2015–20; STOP-TB.

Limitations of the analysis

As with any mathematical modelling analysis it is necessary to make assumptions about data that are not routinely collected, 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. For example, a study in South Africa (Andrews et al. 2012) concluded that undiagnosed TB prevalence was the parameter with the greatest influence on cost-effectiveness. As no TB prevalence survey data were available for Romania at the time of these analyses, routine data on TB notifications formed the basis for estimating disease burden. WHO estimates of total 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 under estimated in populations with lower diagnosis rates.
- **TB in key populations:** Prisoners, people who inject drugs and homeless people were identified as key populations for TB modelling analyses. However, sufficient data were available only for prisoners, so this was the only key population included in the optimisation analyses (see Table 2.1 for all sub-populations initially defined in this analysis).
- **TB expenditure:** Although some assessment of TB expenditure has been done, data were generally not available for 2018 expenditure. Sources also reported TB spending in very broad expenditure areas only, while this analysis looks at discrete TB interventions. Unit costs for interventions are therefore subject to some uncertainty as they were calculated using a bottom-up approach, based on expenditure from different funding sources.

- **Cost-outcome relationships:** In the version of the Optima TB model used for this analysis, cost-outcome relationships were assumed to be linear. Future applications of Optima TB using the updated model will benefit from the inclusion of non-linear Cost-Coverage-Outcome Curves to capture diminishing marginal returns to screening programs.
- **Implementation efficiency:** The analysis included considerations of implementation efficiency in a limited way only, as it 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 optimisation.
- **Sensitivity analysis:** Given the broad range of questions addressed in this analysis, the large range of data inputs required by the model and the multiple uncertainties, a formal sensitivity analysis was not attempted.
- **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.

This page is for collation purposes.

SECTION 3

RESULTS

This section outlines the projected epidemic trajectory for DS-, MDR- and XDR-TB infections across different sub-populations in Romania.

3.1 WHAT IS THE EPIDEMIC TRAJECTORY OF TB IN ROMANIA?

Estimates for the 2015 base year of the Romania analysis

Given that 2015 was used as the base year for the scenario 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 2015.

Table 3.1 Model estimates of number and prevalence of active TB infections by sub-population (2015)

POPULATION	ACTIVE TB CASES	ACTIVE DS-TB CASES	ACTIVE MDR-TB CASES	ACTIVE XDR-TB CASES	ACTIVE TB PREVALENCE
0–4 years	218	216	2	0	0.02%
5–14 years	422	419	2	1	0.03%
15–64 years	12,879	12,443	394	42	0.15%
65+ years	2,248	2,199	43	6	0.13%
Prisoners	211	209	2	0	1.08%
Total	**15,978**	**15,486**	**443**	**48**	**0.13%**

Source: Optima TB model output, based on data extracted from Romania's TB surveillance system and demographic data from national population census surveys.

Table 3.2 Model estimates of active TB incidence, latent infections and TB-related deaths, by sub-population (2015)

POPULATION	INCIDENCE PER 100K	LATENT TB CASES	TB-RELATED DEATHS PER YEAR	OVERALL DEATH RATE (%)
0–4 years	24	7,518	12	0.20%
5–14 years	21	125,422	38	0.02%
15–64 years	93	4,963,850	2,313	0.72%
65+ years	64	1,166,440	476	5.08%
Prisoners	793	14,888	19	0.72%
Total	**78**	**6,278,118**	**2,859**	**1.37%**

Source: Optima TB model output, based on data extracted from Romania's TB surveillance system and demographic data from national population census surveys.

Past trends in Romania's TB epidemic

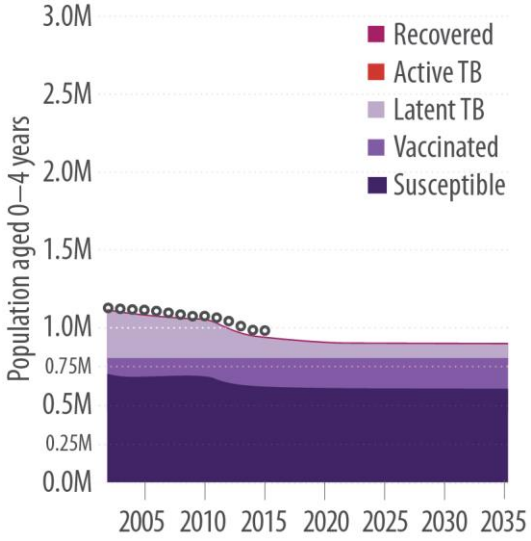
Historical TB notifications data for Romania were used as a benchmark to calibrate the model and assess past epidemic trends. Notification data for recent years suggest that Romania's TB epidemic is declining and the percentage of drug-resistant cases notified remains fairly constant:

- 19,202 notified TB cases in 2011, of which 3.2% were DR
- 16,689 notified TB cases in 2013, of which 4.0% were DR
- 15,183 notified TB cases in 2015, of which 3.9% were DR

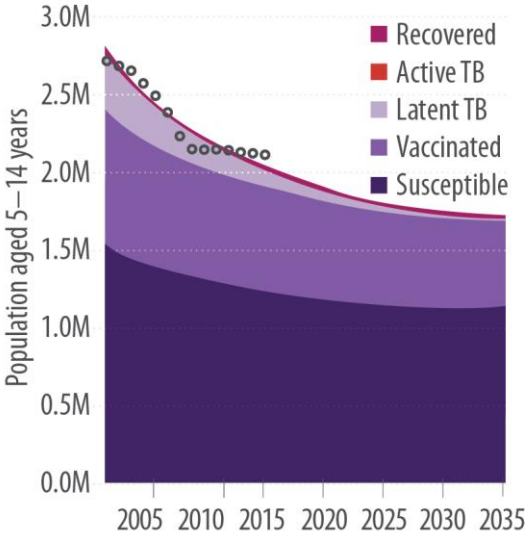
Past epidemic trends for the period 2002 to 2015 show significant differences across sub-populations included in the analysis. Results are presented for children aged 0–4 and 5–14 (Figure 3.1), adults aged 15–64 and 65 and above (Figure 3.2) and prisoners (Figure 3.3).

Figure 3.1 Modelled demographic trends in Romania for children aged 0-4 and 5-14 (2000-2015)

3.1a Cross-section of 0–4 year population



3.1b Cross-section of 5–14 year population



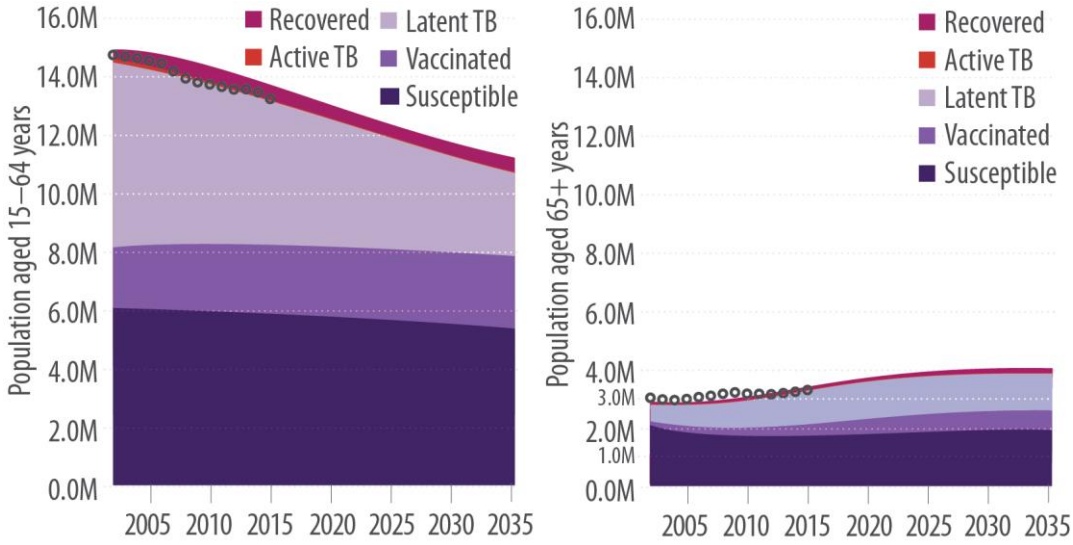
Source: Calibrated Optima TB model Romania.

The following key observations can be made:

- **Children:** The number of children aged 0–4 and 5–14 years has been decreasing steadily in Romania between 2002 and 2015. Children are vaccinated at birth in Romania (97.6% in 2014). The size of the vaccinated compartment in Figure 3.1 is based on the assumption of 50% efficacy of vaccination at birth (Mangtani et al. 2014).
- **Adults:** Romania has an ageing population. The 15–64 population is projected to decrease in size in Romania. The 65+ population is projected to increase in size, with life expectancy at birth in Romania increasing from 71 in 2000 to 75 in 2016 (UNDESA 2017).
- **Prisoners:** The size of the prisoner population has decreased significantly in Romania from 48,267 in 2000, to 27,455 in 2016 (World Prison Brief 2017). Due to the high incidence of TB, and given living conditions in prisons, it was assumed that a higher proportion (70%) of prisoners have latent TB compared to the general adult population (approximately 40%).

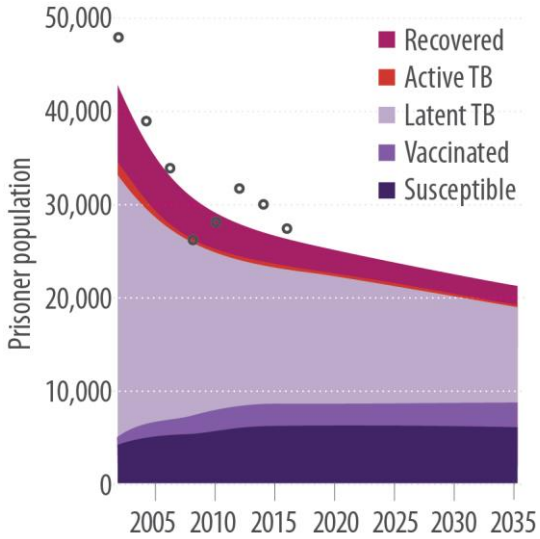
Figure 3.2 Modelled demographic trends in Romania for adults aged 15–64 and 65+ (2000–15)

3.2a Cross-section of 15–64 year population 3.2b Cross-section of 65+ year population



Source: Calibrated Optima TB model Romania.

Figure 3.3 Modelled demographic trends in Romania for prisoners (2000–15)



Source: Calibrated Optima TB model Romania.

Long-term projected incidence trends in Romania's TB epidemic

Epidemic projections into the future are highly dependent on the assumptions regarding intervention coverage and resource availability. Long-term projections for TB incidence rates, assuming TB intervention coverage and outcome conditions as per 2015, are shown below in Table 3.3 for 2020 and 2035. Given constant conditions, the projected incidence rates per 100 000 were on a further downward trajectory, decreasing by an average of approximately 1% per year between 2015 and 2035. The incidence of TB in both child populations remains far lower than in the adult population. While TB incidence has fallen rapidly in the prisoner population, the incidence rate remains approximately nine times greater than in the general population.

Table 3.3 Modelled TB incidence per 100,000 in Romania, by sub-population (2015, 2020 and 2035)

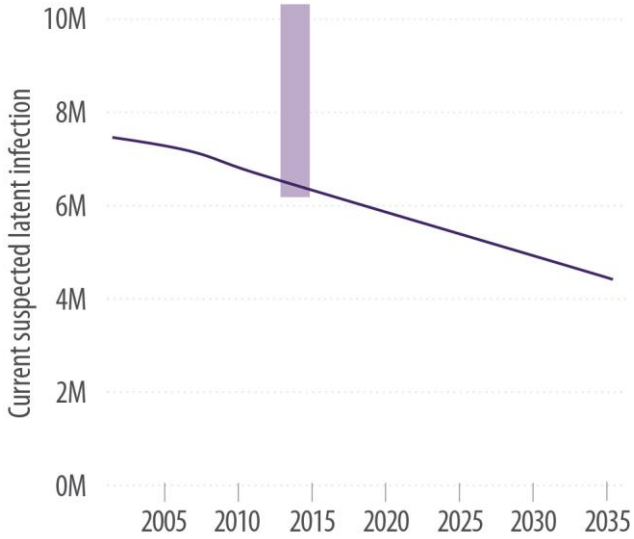
SUB-POPULATION	TB INCIDENCE RATE 2015	TB INCIDENCE RATE 2020	TB INCIDENCE RATE 2035
0–4 years	14	10	7
5–14 years	18	13	5
15–64 years	94	89	72
65+ years	84	86	80
Prisoners	816	769	688
Total	**82**	**78**	**65**

Source: Optima TB model analysis for Romania.

Temporal trends in latent TB infections

The actual prevalence of latent TB in Romania is unknown. Optima TB, based on observed active TB infections in Romania, estimated 6.3 million latent TB cases in Romania for 2015 (Figure 3.4). This is consistent with published national estimates of between 6.1 and 10.5 million latent TB cases in Romania in 2014, with a best estimate of 8.9 million (Houben and Dodd 2016). Latent TB infections represent the reservoir sustaining the TB epidemic; a large pool of people with latent infections will continue to sustain TB incidence through progression to active TB despite advances in active TB treatment. Given national targets and the global drive to eliminate TB, there is an increasing interest to better address latent TB infections (WHO 2018a).

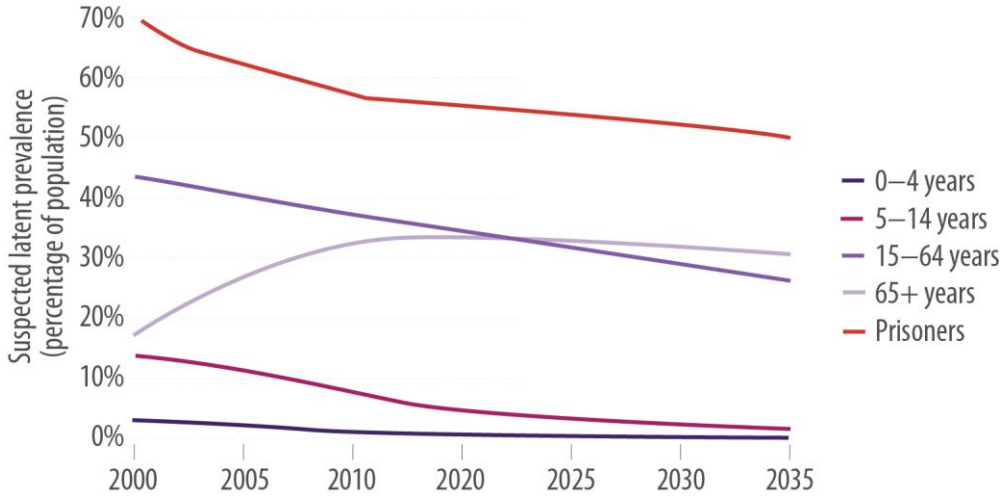
Figure 3.4 Model-derived total latent TB infections in Romania (2000–35)



Source: Calibrated Optima TB model for Romania. Shaded area represents range of estimate from Houben and Dodd (2016).

Figure 3.5 shows long-term latency trends in each sub-population under base case assumptions. While Optima TB predicts latent TB prevalence to be stable or decreasing across all other populations, the prevalence and number of latent TB cases is increasing in the 65+ population as the population size increases. This is due to aging of the adult population who have lived through periods of very high TB incidence in Romania and appears to stabilize around 2020.

Figure 3.5 Modelled prevalence of latent TB infections in Romania by sub-population (2000–35)



Source: Calibrated Optima TB model for Romania

3.2 WHAT IS THE LIKELY IMPACT OF MEETING NATIONAL AND INTERNATIONAL CARE CASCADE TARGETS ON THE TB EPIDEMIC?

A scenario analysis was performed to understand the impact of meeting national and international care cascade targets, by 2020 and 2025 respectively, 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 measured. For example, in the 2020 target scenario, coverage targets are achieved by 2020 and the impact of achieving and sustaining 2020 coverage levels is tracked up to 2035.

Testing and treatment scenarios to meet 2020 NSP and 2025 STOP-TB targets

This group of scenarios models the impact of meeting 2020 NSP and 2025 STOP TB targets separately for:

- TB screening/testing
- TB treatment initiation (linkage to care)
- TB treatment outcomes

These effects are then considered simultaneously to assess what impact on key TB indicators can be obtained by meeting 2020 NSP and 2025 STOP TB targets.

Improved TB screening/testing

What is the impact of reaching 2020 and 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 (2015)*	NSP 2020 TARGETS	STOP-TB 2025 TARGETS
Case detection for DS-TB	78.7%	85%	90%
Case detection for MDR-TB	78.7%	85%	90%
Case detection for XDR-TB	78.7%	85%	90%

Sources: Romania National Strategic Plan 2015-2020; WHO Romania TB country profile; STOP-TB
Note: *The model's "diagnosis rate" was calculated using notified as a proportion of total prevalence and not incidence. Case detection rate was assumed the same for DS-TB and DR-TB due to lack of data.

Improved treatment initiation (better linkage to care)

What is the impact of reaching 2020 and 2025 targets for treatment initiation? Table 3.5 lists the parameters varied in the model to determine the effect of linkage to TB care using treatment initiation targets as proxy.

Table 3.5 Scenario parameters: Improved treatment initiation (for linkage to care)

IMPROVING TREATMENT INITIATION AND AVERTING PRE-TREATMENT LOSS TO FOLLOW UP	CURRENT CONDITIONS (2015)	NSP 2020 TARGETS	STOP-TB 2025 TARGETS
Treatment initiation for DS TB regimens	97.7%	100%	100%
Treatment initiation for MDR TB regimens	97.7%	100%	100%
Treatment initiation for XDR TB regimens	97.7%	100%	100%

Sources: Romania National Strategic Plan 2015–20; WHO Romania TB country profile; STOP TB.

Improved treatment outcomes

What is the impact of reaching 2020 and 2025 targets for treatment outcomes? Table 3.6 displays the various targets related to improved treatment outcomes in the TB care cascade. Although the NSP does not explicitly establish a target for XDR-TB, for the purposes of the scenario analysis the target for MDR-TB was also applied to XDR-TB.

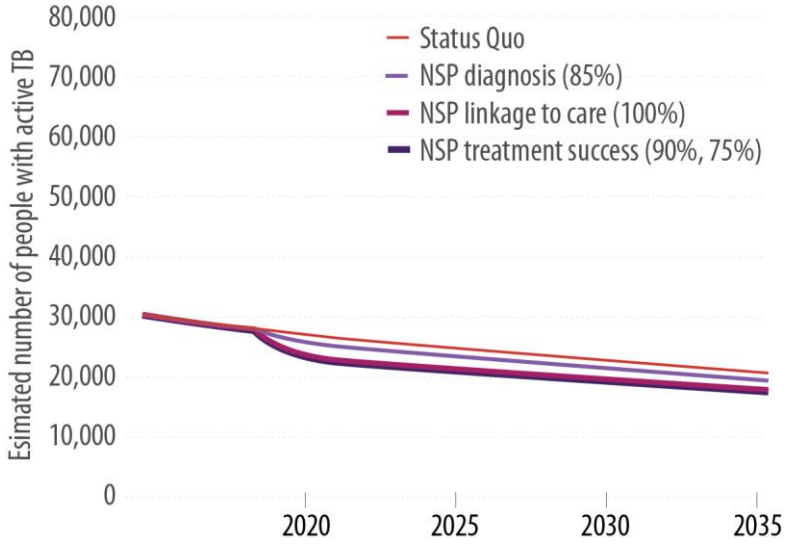
Table 3.6 Scenario parameters: Improved treatment outcomes

IMPROVED TREATMENT OUTCOMES	CURRENT CONDITIONS (2015)	NSP 2020 TARGETS	STOP-TB 2025 TARGETS
Treatment success rates for DS-TB regimens	85%	90%	90%
Treatment success rates for MDR-TB regimens	44%	75%	90%
Treatment success rates for XDR-TB regimens	16%	75%	90%

Source: WHO (2018). Romania National Strategic Plan 2015–20; WHO Romania TB country profile; STOP-TB.

Figure 3.6 presents the impact of meeting and sustaining the NSP care cascade targets on all active TB prevalence in the total population. This is projected to yield significant reductions in the total number of active TB cases, of up to 17%. Improvements in linkage to care yield the greatest reductions of 8%, followed by increased testing and higher rates of treatment success.

Figure 3.6 Modelled impact of meeting NSP TB care cascade targets on the number of people with active TB (2015–35)

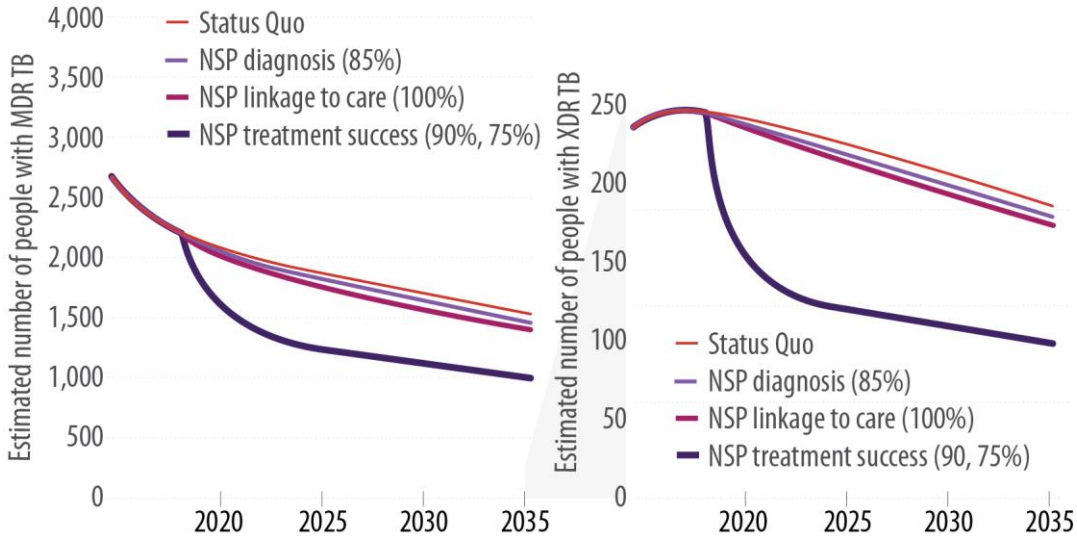


Source: Optima TB model analysis for Romania

Figure 3.7 presents the impact of meeting and sustaining the NSP care cascade targets for drug-resistant TB. Simultaneously meeting and sustaining the proposed targets can, by 2035, achieve a 34% reduction in the total number of MDR-TB cases and a 47% reduction in the total number of XDR-TB infections. Improvement in treatment success is projected to account for the vast majority of this impact for both MDR-TB and XDR-TB cases.

Figure 3.7 Modelled impact of meeting NSP TB care cascade targets on the number of people with DR-TB (2015–35)

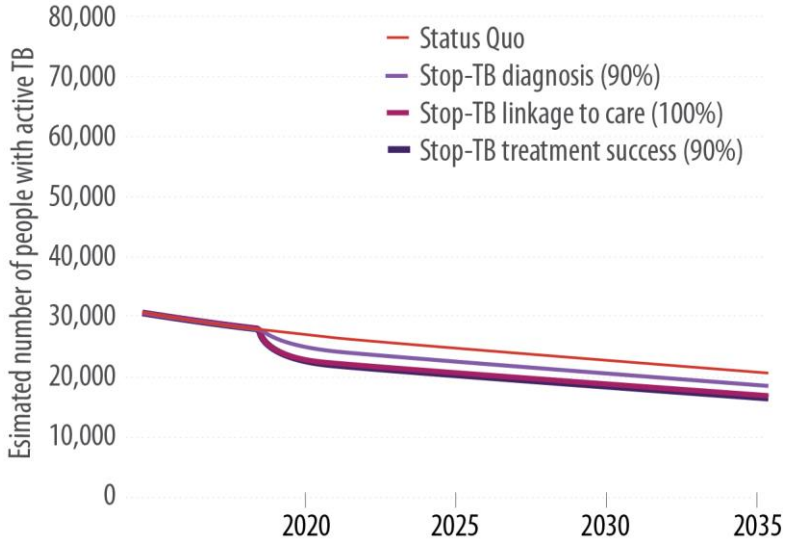
3.7a Modelled number of people with MDR-TB 3.7b Modelled number of people with XDR-TB



Source: Optima TB model analysis for Romania.

Figure 3.8 presents the impact of meeting and sustaining the STOP-TB care cascade targets on all active TB prevalence in the total population. Meeting and sustaining the proposed care cascade targets is projected to yield significant reductions in the total number of active TB infections, of up to 12%. Improvements in linkage to care yield the greatest reductions of 6%, followed by increased testing and higher rates of treatment success.

Figure 3.8 Modelled impact of meeting STOP-TB care cascade targets on the number of people with active TB (2015–35)

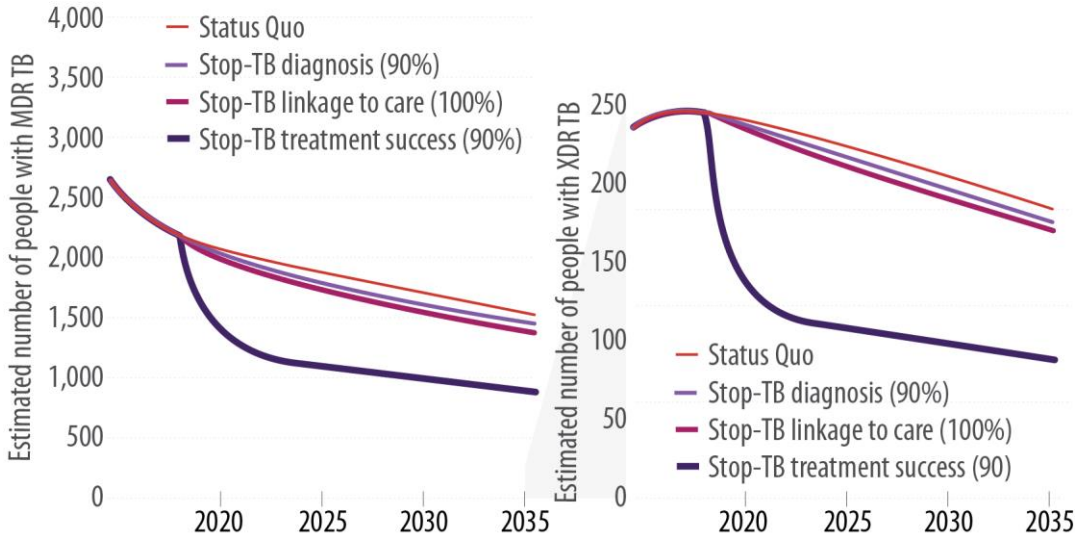


Source: Optima TB model analysis for Romania

Figure 3.9 presents the impact of meeting and sustaining the STOP-TB care cascade targets for drug-resistant TB. Simultaneously meeting and sustaining the proposed targets can, by 2035, achieve a 42% reduction in the total number of MDR-TB infections and a 53% reduction in the total number of XDR-TB. Improvement in treatment success is projected to account for the vast majority of this impact for both MDR-TB and XDR-TB cases.

Figure 3.9 Modelled impact of meeting STOP-TB treatment outcome targets on the number of people with DR-TB (2015–35)

3.9a Modelled number of people with MDR-TB 3.9b Modelled number of people with XDR-TB



Source: Optima TB model analysis for Romania

3.3 HOW CAN THE TB TREATMENT CASCADE BE IMPROVED AND RESOURCE ALLOCATION BE OPTIMIZED?

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 maximise health outcomes. The results were generated by Optima TB's optimisation algorithm described briefly earlier in this report and in more detail in Appendix A.

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

The scope of this section is to explore whether greater reductions in key indicators can be achieved by optimally re-allocating TB spending.

In general, optimised allocations of resources are only optimal relative to a specific set of objectives and within a given time frame. In other words, an optimal allocation to minimise TB incidence may differ from an optimal allocation to minimise TB prevalence or deaths. In order to reflect the different dimensions of the TB response, the optimisation analysis was performed for a combination of five objectives with different weighting:

- Minimise the incidence of TB (weight=1)
- Minimise the prevalence of DS-TB (weight=1)
- Minimise the prevalence of MDR-TB (weight=2)
- Minimise the prevalence of XDR-TB (weight=4)
- Minimise TB-related deaths (weight=5)

An important addition to mathematical optimisation analyses is the definition of constraints. Key reasons for constraining analyses include the following:

- Constraints to the magnitude of reallocations can reflect the challenges involved in implementing the scale-up of interventions, considering limitations in the health sector capacity to increase service delivery over a short time period
- Adding constraints around treatment regimens can capture non-universal eligibility for a regimen
- There may be funding mechanisms and donor-based programme targeting policies which require constraining certain expenditure categories

In consultation with the study team and participating experts, minimum and maximum funding amounts for specific interventions were defined (Table 10) to match constraints on intervention funding.

Table 3.7 Constraints in the optimization analysis

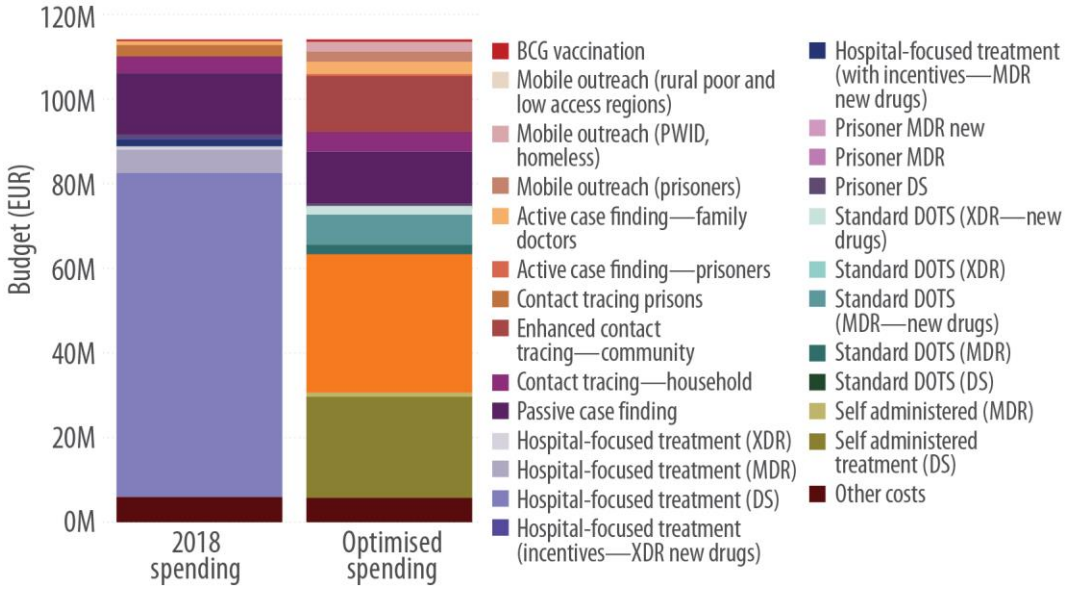
	MINIMUM COVERAGE (%)	MAXIMUM COVERAGE (%)
BCG Vaccination	100% of newborns	–
Directly observed treatment (DOTS)	40% of all treatment cases	–
Regimens including new MDR drugs	50% of all treatment cases	–
Regimens including new XDR drugs	50% of all treatment cases	–

3.4 OPTIMISED ALLOCATION OF EXPENDITURE TO MINIMISE INCIDENCE, PREVALENCE AND DEATHS

Figure 3.10 and Table 3.8 show the overall optimised allocation of expenditure to minimise TB incidence, prevalence and deaths. In this analysis it was assumed that the same EUR 115 million that were available for TB-related interventions in 2018 would remain available each year up to 2035. The optimised budget allocation differs from current allocations in several areas, the main changes being:

- **Reduced hospitalization of patients** – Patient to be treated for a shorter period in the inpatient setting, with the majority of the treatment being delivered in the outpatient setting.
- **Improved case finding** – Enhanced contact tracing in congregate settings, training family doctors in high incidence settings and mobile outreach for people who inject drugs, homeless and prisoners.
- **Improved treatment regimens for better treatment outcomes** – New drug regimens for DR-TB, containing drugs such as Bedaquiline.

Figure 3.10 Optimal reallocation of current TB expenditure to simultaneously minimise cumulative TB incidence, prevalence and deaths between 2018 and 2035 in Romania



Source: Optima TB model analysis for Romania.

Note: 2018=base year (current allocation); Optimised budget: It was assumed that the budget of EUR 115 million that were available for TB-related programmes in 2018 would remain available on an annual basis up to 2035.

Table 3.8 Current and optimal allocations of 2018 TB spending, by intervention (in million EUR)

INTERVENTION	CURRENT (2018) SPENDING (MILLION EUR)	OPTIMISED SPENDING (MILLION EUR)	DIFFERENCE (MILLION EUR)	% OF OPTIMISED BUDGET
BCG vaccination	0.270	0.270	0.000	0.002
Passive Case Finding	15.100	12.741	-2.359	0.111
Contact tracing - household	3.970	3.971	0.001	0.035
Enhanced contact tracing - community	2.730	13.493	10.763	0.118
Contact tracing prisons	0.056	0.056	0.000	0.000
Active case finding – prisoners	0.409	0.409	0.000	0.004
Active case finding - family doctors	0.000	2.908	2.908	0.025
Mobile outreach (prisoners)	0.000	2.478	2.478	0.022
Mobile outreach (PWID, homeless)	0.000	2.573	2.573	0.022
Mobile outreach (rural poor/ low access regions)	0.000	0.000	0.000	0.000
Hospital focused treatment (DS)	77.100	0.000	-77.100	0.000
Hospital focused treatment (MDR)	5.450	0.000	-5.450	0.000
Hospital focused treatment (XDR)	0.916	0.000	-0.916	0.000
Hospital focused treatment (with incentives - DS)	0.000	0.000	0.000	0.000
Hospital focused treatment (with incentives - MDR)	0.000	0.000	0.000	0.000
Hospital focused treatment (with incentives - MDR new drugs)	1.440	0.000	-1.440	0.000
Hospital focused treatment (incentives - XDR)	0.000	0.000	0.000	0.000
Hospital focused treatment (incentives - XDR new drugs)	0.321	0.000	-0.321	0.000
Ambulatory treatment (DS)	0.000	23.700	23.700	0.207
Ambulatory treatment (MDR)	0.000	0.820	0.820	0.007
Standard DOTS (DS)	0.000	33.200	33.200	0.290
Standard DOTS (MDR)	0.000	2.040	2.040	0.018
Standard DOTS (MDR - new drugs)	0.000	7.150	7.150	0.062

Table 3.8 continued...

Table 3.8 Current and optimal allocations of 2018 TB spending, by intervention (in million EUR) (continued)

INTERVENTION	CURRENT (2018) SPENDING (MILLION EUR)	OPTIMISED SPENDING (MILLION EUR)	DIFFERENCE (MILLION EUR)	% OF OPTIMISED BUDGET
Standard DOTS (XDR)	0.000	0.000	0.000	0.000
Standard DOTS (XDR - new drugs)	0.000	1.910	1.910	0.017
Prisoner DS	0.902	0.902	0.000	0.008
Prisoner MDR	0.021	0.015	-0.006	0.000
Prisoner MDR new	0.000	0.008	0.008	0.000
Other costs	5.940	5.940	0.000	0.052
Total screening/diagnosis	**22.497**	**38.899**	–	–
Total treatment	**86.210**	**69.744**	–	–
Total fixed costs	**6.223**	**6.223**	–	–

Source: Optima TB model analysis for Romani.

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 TB programmes. An optimised allocation of resources would increase funding for screening interventions by 74% (Table 3.8). Screening and diagnosis would then consume about 34% of total TB spending. This increase in spending on screening and diagnosis is possible due to the savings in treatment costs for DS-TB as a result of reduced hospitalization.

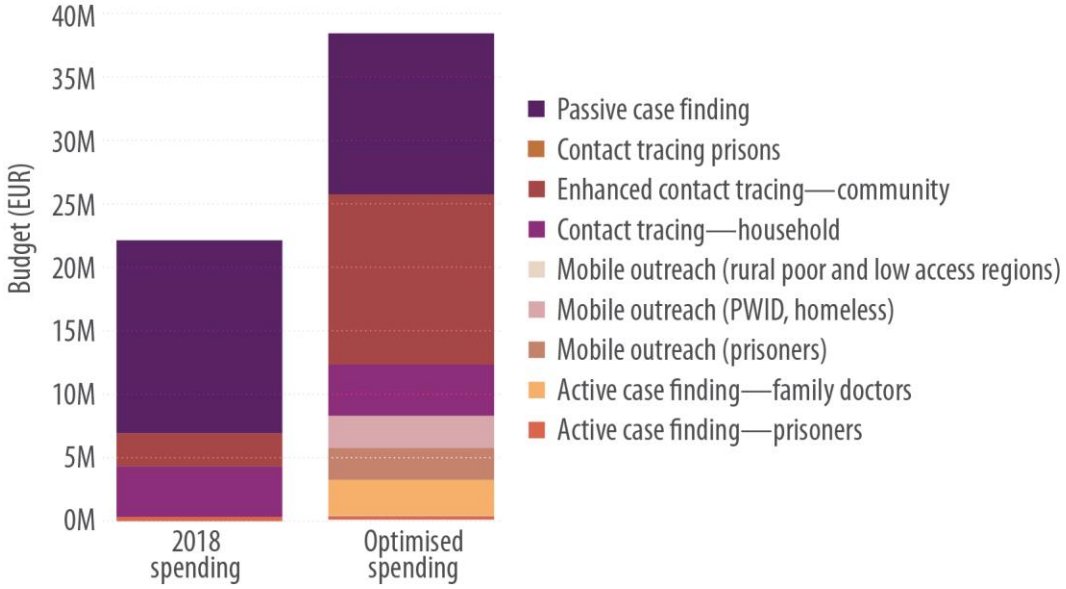
Figure 3.11 shows current and optimised allocation of EUR 38.9 million for screening/ diagnostic interventions. The optimal allocation would entail:

- Sustaining household contact tracing for all TB cases
- Extending community contact tracing to all TB cases, by tracing contacts in congregate settings such as schools and workplaces
- Training family doctors in high incidence areas to screen patients attending for incidental reasons
- Mobile outreach targeting high-risk groups including people who inject drugs, homeless and prisoners

Compared to current expenditure, there is a significant increase in active case finding programmes in an optimal allocation. Despite a high diagnosis rate for TB, case finding in Romania has been primarily passive. To further improve the diagnosis rate, active case finding programmes are likely to be an essential part of the TB response. This recognizes that those people whose TB remains undiagnosed are likely to be in vulnerable and hard-to-reach populations. In addition to allocative efficiency arguments, there is also an equity argument for funding active case finding programmes, as it means that populations targeted by outreach activities would receive care that would otherwise not be available to them.

Considering that the actual prevalence and incidence of TB and the size of the undiagnosed population are not known, strategies to increase case finding should be continuously monitored and carefully evaluated. This is required in order to assess whether the yield of newly identified cases is commensurate to investments.

Figure 3.11 Optimal reallocation of current TB screening and diagnosis expenditure to simultaneously minimise cumulative TB incidence, prevalence and deaths between 2018 and 2035 in Romania



Source: Optima TB model analysis for Romania.

Note: 2018=base year (current allocation); Optimised budget: It was assumed that the budget of EUR 115 million that were available for TB-related programmes in 2018 would remain available on an annual basis up to 2035.

Shifts within treatment interventions

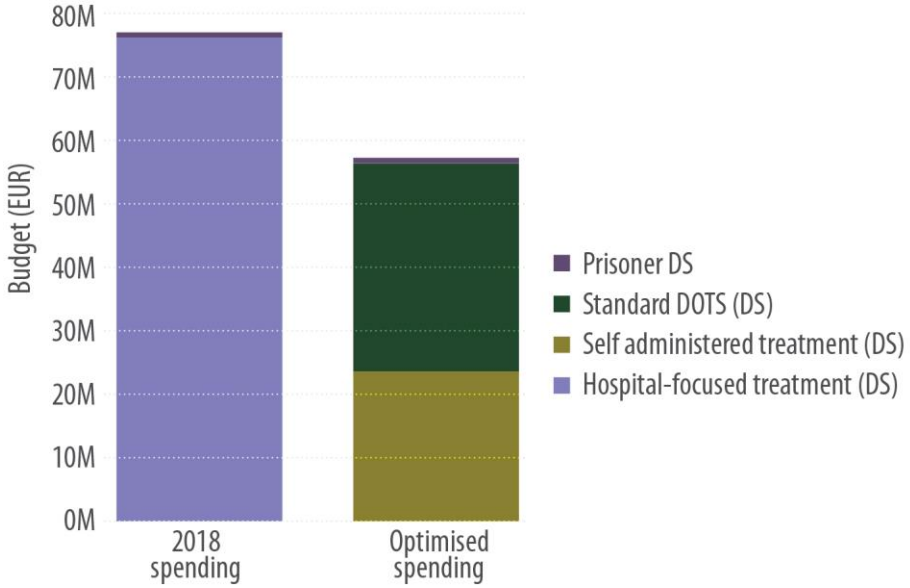
In an optimised intervention mix, TB treatment would receive less funding and would absorb approximately 60% of total TB spending in Romania compared with the current 75%. MDR-TB and XDR-TB treatments would receive EUR 10.0 million and EUR 1.9 million respectively, an increase in their current spending allocation.

Optimisation across treatment interventions (Figure 3.11) suggests changes in annual funding, particularly to reduce hospitalization for both DS-TB and DR-TB. This reduces the total cost of DS-TB treatment from approximately EUR 78.0 million to EUR 57.8 million, enabling the increased use of new MDR- and XDR-TB drugs, in addition to the introduction of active case finding programmes. The expensive and unnecessary hospitalization of TB patients in Romania has already been acknowledged (de Colombani et al. 2015), and reducing this will have a significant impact on costs without reducing the efficacy of treatment regimens. There are also likely to be wider benefits from such a change, including reduced nosocomial transmission and reduced negative economic impacts on patients.

The expensive and unnecessary hospitalization of TB patients in Romania has already been acknowledged and reducing this will have a significant impact on costs without reducing the efficacy of treatment regimens.

These shifts in allocation take into account the constraints established for certain regimens, in particular the eligibility for new DR-TB drug regimens (Table 3.9).

Figure 3.12 Current (2018) and optimised allocations of resources for DS-TB treatment to minimise TB incidence, prevalence and deaths in Romania

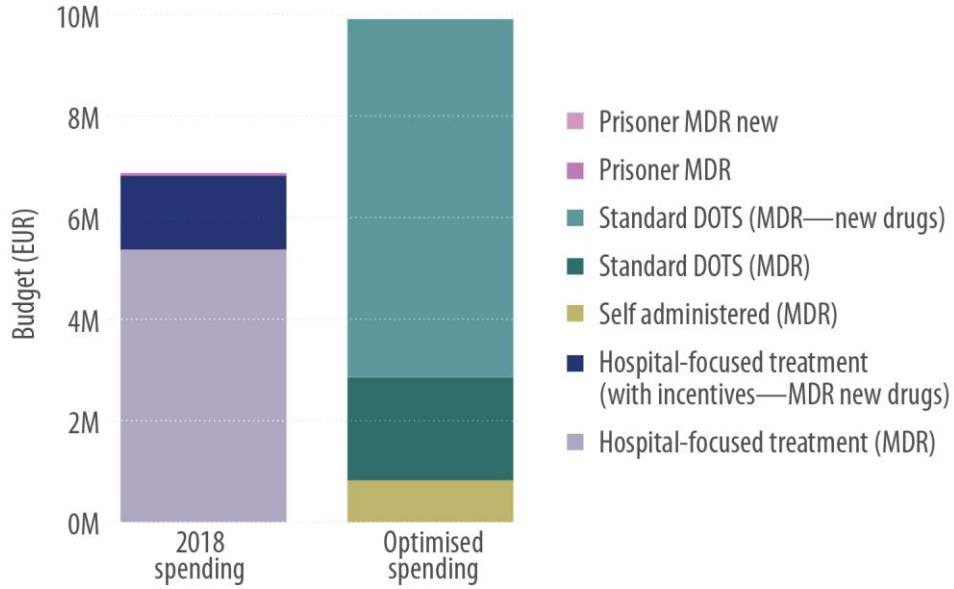


Source: Optima TB model analysis for Romania.

In anticipation of revised WHO guidelines for the use of Bedaquiline, a constraint was used such that a minimum of 50% of DR-TB patients receive the new drug regimens. While this should significantly improve outcomes for DR-TB, the increased cost of these regimens is likely to be a burden on the TB response in Romania. The future pricing of these drugs should be monitored due to the potential impact on cost-effectiveness

Figure 3.13 shows an optimal allocation of spending for MDR-TB. Coverage of new drugs is at the minimum level as per the constraints used (50%). The remaining 50% of patients receive older drug regimens and of these, around 62% receive DOTS.

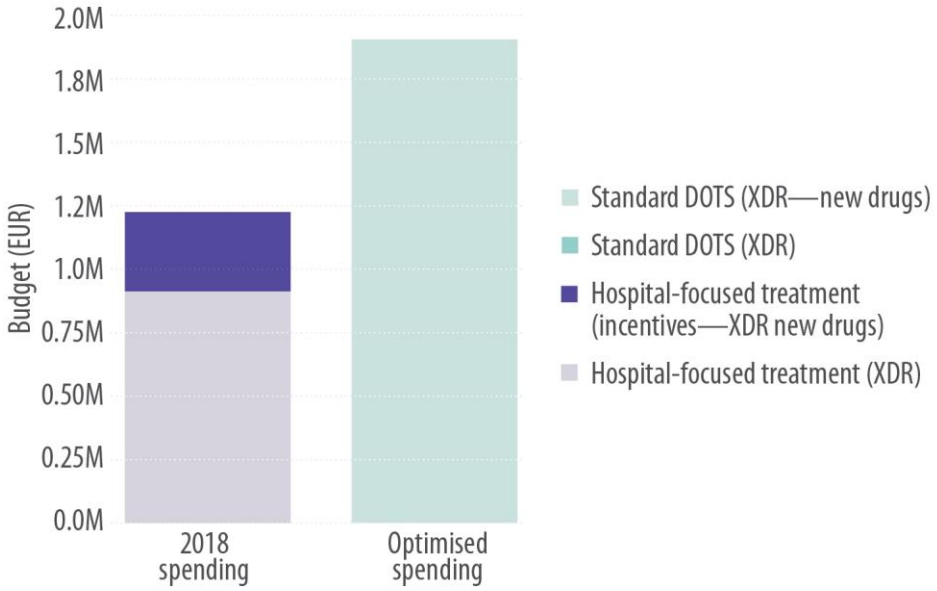
Figure 3.13 Current (2018) and optimised allocations of resources for MDR-TB treatment to minimise TB incidence, prevalence and deaths in Romania



Source: Optima TB model analysis for Romania.

Figure 3.14 shows an optimal allocation for XDR-TB. In contrast to MDR-TB, in an optimal allocation, all patients receive new drug regimens. This reflects the extremely poor outcomes on the older drug regimens observed for XDR-TB in Romania currently.

Figure 3.14 Current (2018) and optimised allocations of resources for XDR-TB treatment to minimise TB incidence, prevalence and deaths in Romania

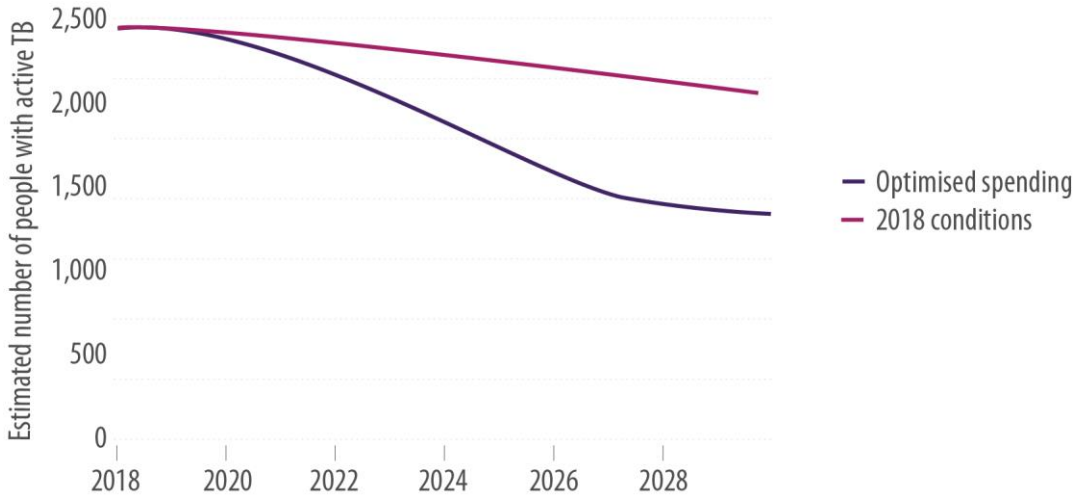


Source: Optima TB model analysis for Romania.

Improved outcomes with optimised allocations

As shown in Figures 3.15–3.18, an optimised allocation of resources could have a substantial impact on key TB indicators. By 2030, an optimised allocation of spending could reduce the number of active TB cases by 45% relative to 2018 (Figure 3.15). Under current conditions, relative to 2018, the projected reduction in TB cases could be as much as 20%.

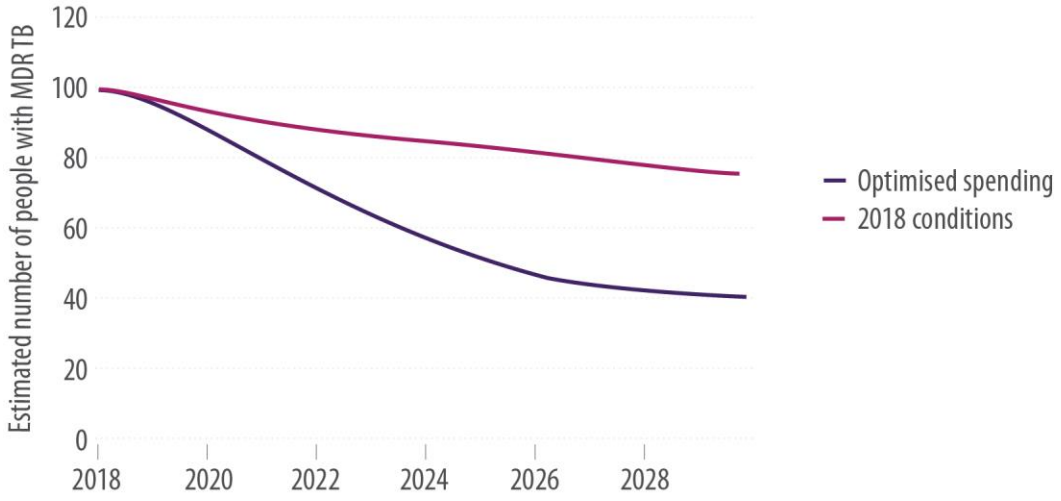
Figure 3.15 Estimated number of people with active TB under current and optimised allocations, Romania



Source: Optima TB model analysis for Romania.
Note: Total annual expenditure is assumed constant at EUR 115 million until 2035.

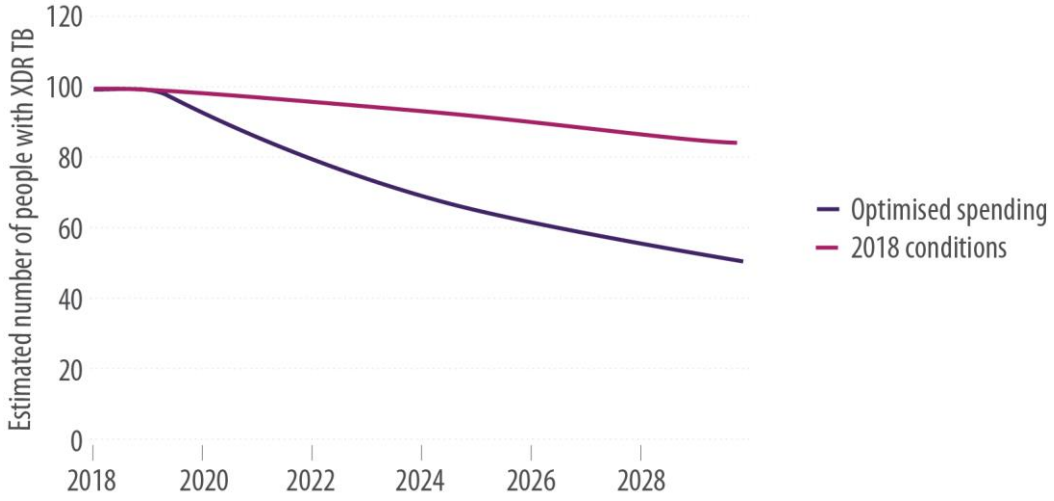
For MDR-TB (Figure 3.16) and XDR-TB (Figure 3.17) an optimal allocation could result in a reduction in the number of active TB infections of 60% and 50% respectively, relative to 2018. This compares with a 15% reduction under current conditions. This difference reflects the significant gains in treatment outcomes from the introduction of new drug regimens.

Figure 3.16 Estimated number of people with MDR-TB under current and optimised allocations, Romania



Source: Optima TB model analysis for Romania.
Note: Annual expenditure is assumed constant at EUR 115 million until 2035.

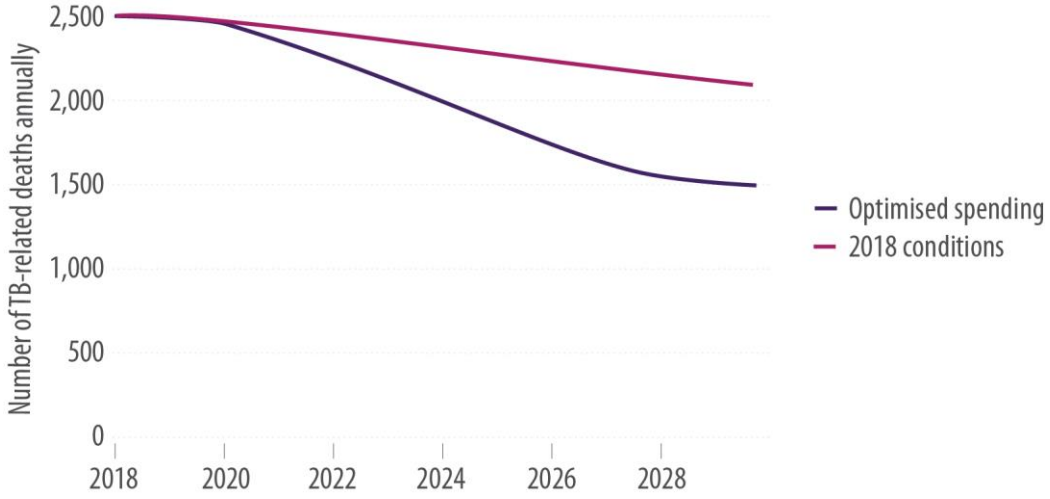
Figure 3.17 Estimated number of people with XDR-TB under current and optimised allocations, Romania



Source: Optima TB model analysis for Romania.
Note: Total annual expenditure is assumed constant at EUR 115 million until 2035.

An optimized allocation of funding could also, by 2030, reduce the number of deaths relative to 2018 by around 40% (Figure 3.18). Current conditions suggest a decline of around 20% in the same period.

Figure 3.18 Estimated number of TB-related deaths under current and optimised allocations, Romania



Source: Optima TB model analysis for Romania
Note: Total annual expenditure is assumed constant at EUR 115 million until 2035

Optimised allocation of resources to improve TB care cascades

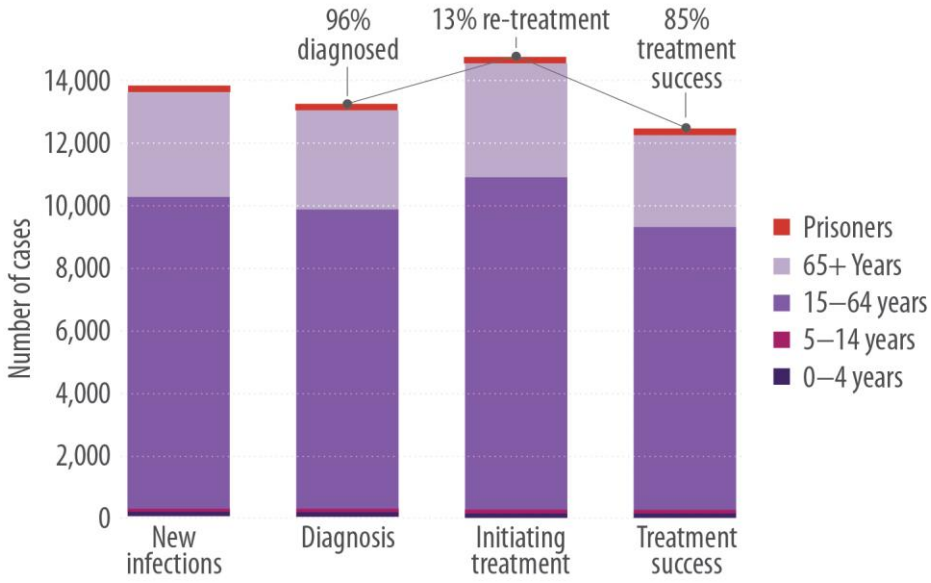
The impact of the optimised allocation along the TB care cascade is shown below. It is worth noting that the precise figures are not directly comparable with the more familiar cohort-based outcome indicators that are widely used to measure success in the TB response. As Optima is a compartmental model, these are annual probabilities that only give a proportional outcome in conjunction with all the other annual probabilities flowing out of the compartment. Nevertheless, they are useful in displaying improvements resulting from an optimised allocation, as it is clearly demonstrated that more people are attaining treatment success.

Figure 3.19 shows the modelled number of DS-TB cases by stage of care cascade in 2025. An optimised allocation of the 2018 budget is projected to yield a diagnosis rate of 96%. This results in a treatment success relative to all new DS-TB infections of 82%, compared to 75% under current conditions.

Figure 3.20 shows the modelled number of DR-TB cases by stage of care cascade in 2025. As before, an optimised allocation of the 2018 budget is projected to yield a diagnosis rate of 96%. This results in a treatment success relative to all new DS-TB infections of 47%, compared to 35% under current conditions.

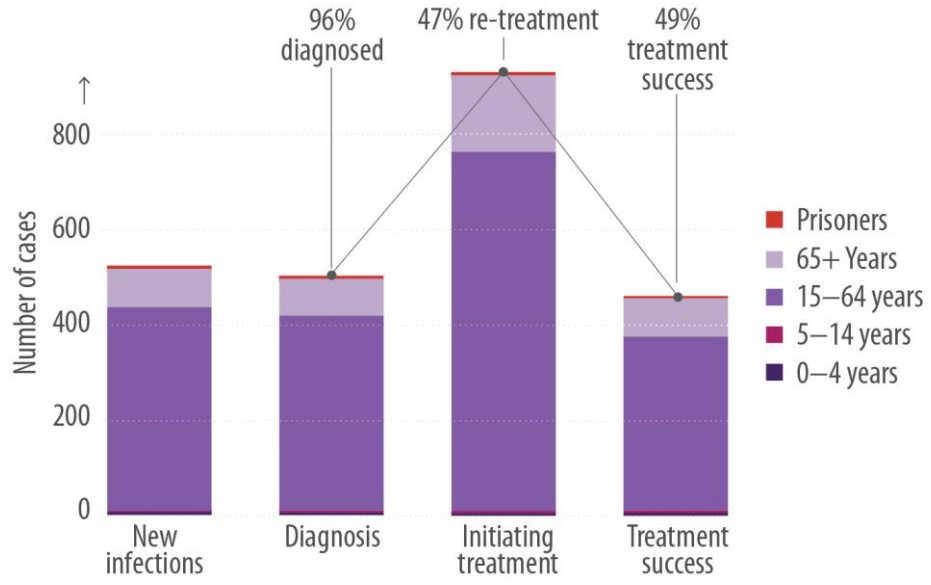
An optimised allocation of the 2018 budget is projected to yield a diagnosis rate of 96%. This results in a treatment success relative to all new DS-TB infections of 82%, compared to 75% under current conditions.

Figure 3.19 Care cascade outcomes (2025) for DS-TB cases with an optimised allocation of current spending Romania



Source: Populated Optima TB model for Romania.

Figure 3.20 Care cascade outcomes (2025) for DR-TB cases with and optimised allocation of current spending, Romania



Source: Populated Optima TB model for Romania.

Optimised allocations under different amounts of spending and their impact

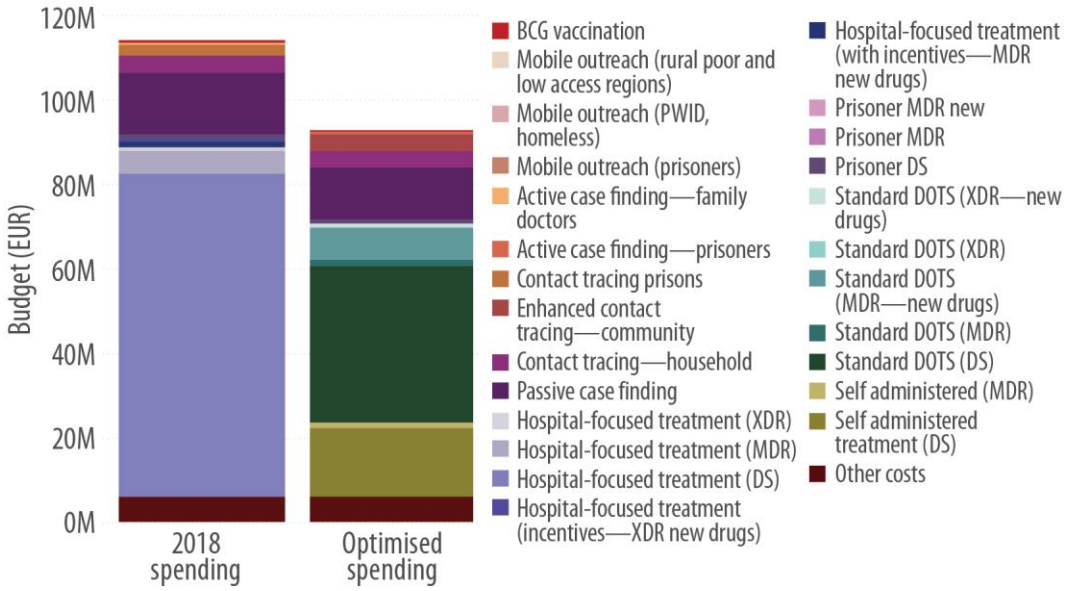
While savings from reduced hospitalisation were reallocated to other TB expenditure in the optimisation above, in reality these funds may not necessarily be spent on TB. As hospitals are funded through the national insurance house, savings may be reallocated elsewhere in the hospital budget. Given this possibility, it is necessary to review the optimised allocations in the absence of this saving. Optimisation of current expenditure results in savings of approximately 20% of total expenditure as a result of reduced

hospitalisation. Therefore, an optimisation of 80% of current expenditure was conducted to see the impact on conclusions.

Figure 3.21 shows the allocation pattern with 80% of current expenditure. While patterns in treatment allocations remain broadly similar, there are differences in the optimal allocation of expenditure on screening and diagnosis programmes. Rather than being used for all cases, enhanced contact tracing is used in approximately 30% of notified cases. Funding is also no longer allocated to active case finding programmes. Such programmes are therefore only likely to form a substantial part of an optimal TB response if the savings gained from reduced hospitalisation of TB patients can be retained within the TB budget or if other funds can be allocated to the TB response to maintain the current funding levels.

There is also reduced expenditure on XDR-TB, and an associated reduction in the impact on the prevalence of XDR-TB. This is due to new drug regimens being prohibitively expensive under this level of funding, and highlights that maintaining any savings from reduced hospitalisation within the TB response is imperative to continue progress against XDR-TB.

Figure 3.21 Optimal reallocation of 80% of current TB expenditure to simultaneously minimise cumulative TB incidence, prevalence and deaths between 2018 and 2035 in Romania

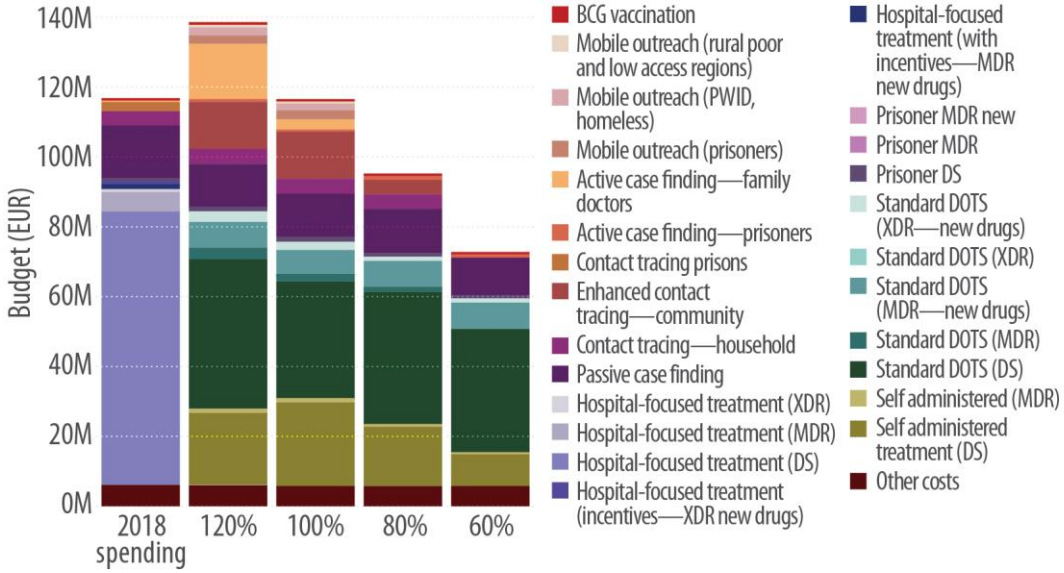


Source: Optima TB model analysis for Romania.
Note: 2018=base year (current allocation).

Optimised budget: It was assumed that the budget of EUR 115 million that were available for TB-related programmes in 2018 would remain available on an annual basis up to 2035. Different expenditure amounts refer to proportions of the 2018 level of spending.

Figure 3.22 shows the optimal allocation at different spending levels. The pattern of optimised treatment expenditure remains consistent across spending levels, with a shift towards a combination of ambulatory treatment and DOTS, and towards improved drug regimens including new drugs for DR-TB. Screening programmes are expanded as the budget increases. First, funding for enhanced contact tracing is expanded. As the budget increases further, new active case finding programmes, such as mobile outreach, are funded.

Figure 3.22 Optimal reallocation of different amounts of TB expenditure to simultaneously minimize cumulative TB incidence, prevalence and deaths between 2018 and 2035 in Romania

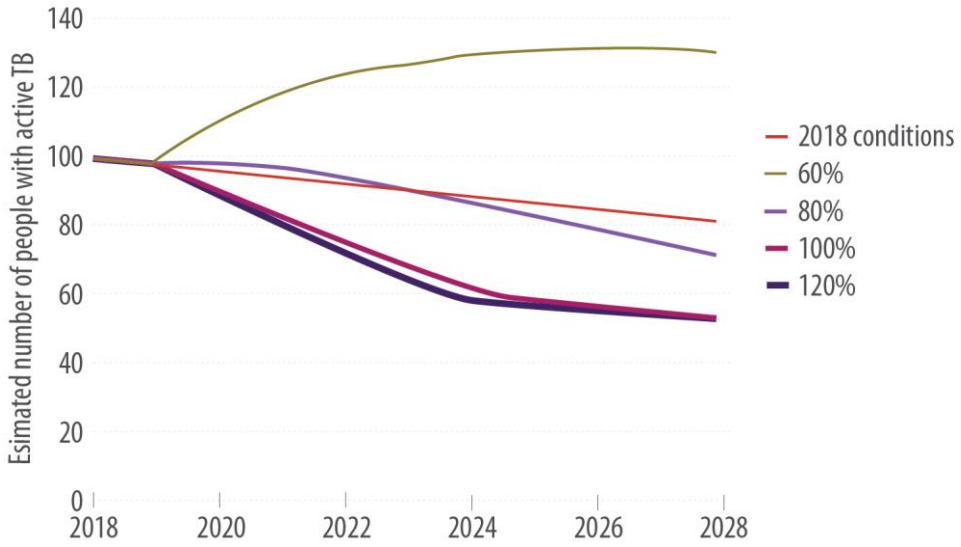


Source: Optima TB model analysis for Romania

Note: 2018=base year (current allocation)

Figure 3.23 and Figure 3.24 show the impact of the optimal allocation on the number of active TB cases and the number of TB-related deaths. While the optimised allocation of current expenditure is projected to yield significant gains, there are diminishing marginal returns to spending to spending over 100% of the budget. Reductions in TB expenditure to 80% of current levels, if optimally allocated, would result in a similar epidemic trajectory to currently observed conditions in Romania. Reductions in TB expenditure to 60% of current levels would have a significant negative impact. In order to make progress in the TB response, it is therefore imperative that current expenditure is maintained and optimally allocated.

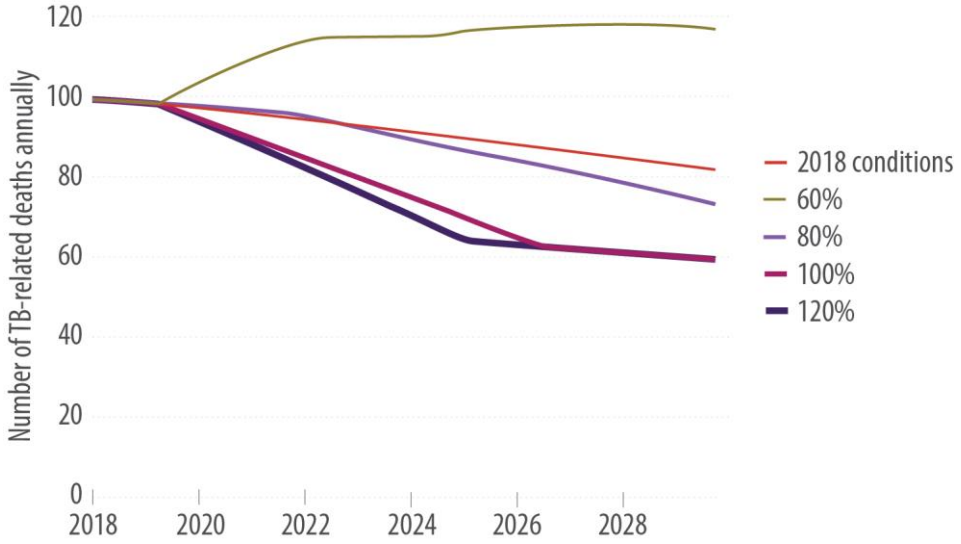
Figure 3.23 Modelled impact of optimised allocations on the number of active TB infections under different amounts of spending, Romania (2018–30)



Source: Optima TB model analysis for Romania.

Note: 2018=base year (current allocation); Optimised budget: It was assumed that the budget available for TB-related programmes in 2018 would remain available on an annual basis up to 2035. Different expenditure amounts refer to proportions of the 2018 level of spending.

Figure 3.24 Modelled impact of optimised allocations on annual TB-related deaths under different amounts of spending, Romania (2018–30)



Source: Optima TB model analysis for Romania.

Note: 2018=base year (current allocation); Optimised budget: It was assumed that the budget available for TB-related programmes in 2018 would remain available on an annual basis up to 2035. Different expenditure amounts refer to proportions of the 2018 level of spending.

Other possible ways to optimise the TB response, not analysed in the model

The analyses presented previously do not include all possible ways to optimize the TB response. A number of other areas could be considered when strengthening the TB response. For example:

- **Community interventions** - an area in which investment is already taking place but for which insufficient data was available to include in our analysis. Locally based care for TB patients, encompassing economic, psychological and peer support, can help improve treatment outcomes. Furthermore, locally based education campaigns are likely to facilitate the diagnosis of hard to reach populations. In future, such interventions should be funded by the government as donor-funding in Romania is not guaranteed.
- **Poverty reduction** – Optimised allocations of TB expenditure are not projected to have a large impact on TB incidence. This is largely because TB incidence is primarily driven by people progressing to active TB from the large pool of latent-TB infections. As the national TB programme is focused on diagnosis and treatment of active TB, the interventions included in our analysis do not affect progression rates from latent-TB to active-TB. Reducing the incidence of TB will likely require broader strategies to address the social determinants of health, such as income, housing or nutrition, which significantly impact progression to active TB.

This page is for collation purposes.

SECTION 4

CONCLUSIONS

4.1 SHIFTING FUNDING TOWARDS OPTIMAL ALLOCATION

The scenarios analysed highlight significant opportunities to reduce TB deaths and avert infections by meeting national and international TB care cascade targets, particularly those targets aiming to improve treatment outcomes for DR-TB cases. The improved treatment outcomes resulting from a transition to new treatment regimens, including drugs such as Bedaquiline, are also noted.

The scenarios analysed highlight significant opportunities to reduce TB deaths and avert infections by meeting national and international TB care cascade targets, particularly those targets aiming to improve treatment outcomes for DR-TB cases.

Other opportunities to improve testing and treatment include:

- TB testing programmes:
  - Contact tracing remains important and funding should be sustained
  - Enhanced contact tracing in congregate community settings, such as schools and workplaces, should be expanded
  - Active case finding programmes targeting vulnerable and hard-to-reach populations such people who inject drugs and homeless should be introduced
- TB treatment programmes:
  - Reducing hospitalization periods for both DS- and DR-TB would result in significant cost savings. This will offset the cost of introducing new and expensive drug regimens for DR-TB.

4.2 GAINING IMPACT THROUGH RE-ALLOCATIONS

The same budget **allocated differently** could, by 2030:

- Reduce the number of active TB infections by up to 45%
- Reduce the number of MDR-TB infections by up to 60%
- Reduce the number of XDR-TB infections by up to 50%
- Reduce the total number of TB deaths by up to 40%

While an optimal allocation of the 2018 budget could result in Romania meeting national and international targets for diagnosis rates (improvement from 88% to 96% by 2025), it is unlikely that targets for treatment outcomes will be met without improvements in

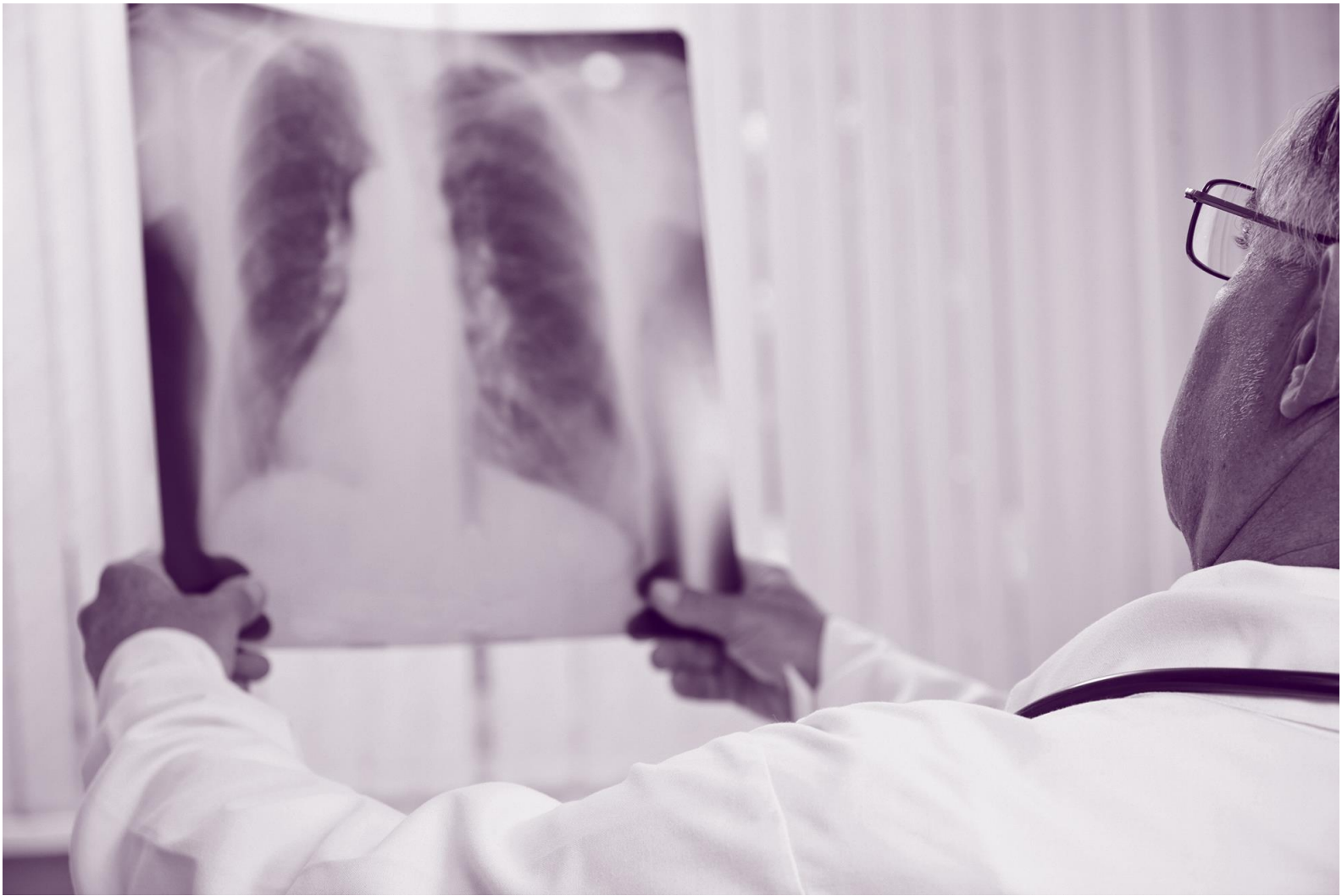
factors not included in this model, even if funding was increased above its current level (see diminishing returns to the allocation of 120% of current spending in Figures 3.23 and 3.24).

4.3 TB ANALYTICS FOR DECISION-MAKING

In the course of implementing the allocative efficiency analysis, several intermediate analytic products had value for stakeholders:

- TB expenditure breakdown by intervention (summarised in Figure 3.10 and Table 3.8)
- Unit cost estimates (presented in Tables B 6.3, B 6.5–6.7)

The Optima TB parameterisation draws on an extensive published literature. The study team compared assumptions and values with individual studies where appropriate. The Romania analysis has helped to further develop and refine the Optima TB model. Like all modelling tools, there are always additional improvements to be made, so the decision support models can provide is continuously enhanced for its policy-relevance.



SECTION 5

RECOMMENDATIONS

A significant positive health impact could be achieved by sustaining 2018 TB financing of EUR ~115 million and allocating that funding optimally. An optimal funding allocation includes:

1. REDUCED UNNECESSARY HOSPITALISATION FOR BOTH DS-TB AND DR-TB PATIENTS

- Reducing unnecessary hospitalisation, in line with WHO recommendations, will reduce costs without affecting outcomes, provided standard directly observed treatment (DOTS) is in place
- This could free up to 20% of current funding for other uses
- Potential further benefits exist, such as reduced nosocomial transmission and a reduced economic impact on patients

2. BUILD UPON HIGH SUCCESS RATES FOR DS-TB BY USING DOTS AND AMBULATORY TREATMENT

- Using a combination of DOTs and ambulatory treatment after a reduced initial hospitalisation period could reduce the cost of DS-TB treatment by up to EUR 20 million
- Both case detection and treatment success rates for DS-TB in Romania are among the highest in the region
- Improvements in outcomes are possible from increased adherence due to use of DOTs, which could be combined with small financial incentives for patients

3. IMPROVE DR-TB TREATMENT OUTCOMES BY REALLOCATING FUNDS TO INTRODUCE NEW DR-TB REGIMENS, INCLUDING DRUGS SUCH AS BEDAQUILINE

- Increasing funding for DR-TB treatment by approximately EUR 12 million would enable the addition of new drugs, which significantly improve the likelihood of treatment success and reduce the time to smear conversion
- The model estimates that a reallocation of funding from old DR-TB regimens to new treatment regimens for eligible patients, could significantly improve treatment success rates

4. MAINTAIN FUNDING FOR HOUSEHOLD CONTACT TRACING

- Current estimated spending should be maintained to identify household members of all notified TB cases, who are at high risk of having active TB
- Earlier identification will improve outcomes and reduce the risk of further transmission

5. INCREASE COVERAGE OF ENHANCED CONTACT TRACING

- Contact tracing beyond the household, in high-risk community settings such as workplaces and schools, can help to improve diagnosis rates and shorten the time to diagnosis
- Currently this is only done for approximately 20% of notified cases but should be expanded to all active TB cases

6. IMPLEMENTATION OF NEW ACTIVE CASE FINDING PROGRAMMES

- Despite a high diagnosis rate for TB, case finding in Romania has been primarily passive
- To further improve the diagnosis rate, active case finding programmes are likely to be an essential part of the TB response
- Approximately EUR 8 million should be spent to introduce new active case finding programmes in high incidence areas and target high-risk groups such as homeless people, prisoners and people who inject drugs
- This could improve the yearly diagnosis rate by up to 9%.
- This recognizes that those people whose TB remains undiagnosed are likely to be in vulnerable and hard-to-reach populations
- In addition to allocative efficiency arguments, there is therefore also an equity argument for funding active case finding programmes, as it means that populations targeted by outreach activities would receive care that would otherwise not be available to them

7. POVERTY REDUCTION AND LATE LATENCY BURDEN

- There are still approximately 6 million people in Romania with late latent TB infections. This is the main driver of active TB incidence
- As the national TB programme is focused on diagnosis and treatment of active TB, the interventions included in our analysis do not affect progression rates from latent TB to active-TB
- Reducing the incidence of TB will likely require broader strategies to address the social determinants of health, such as income, housing or nutrition, which significantly impact progression to active TB

8. COMMUNITY INTERVENTIONS

- Locally based care for TB patients, encompassing economic, psychological and peer support, will help to improve treatment outcomes

- Funding for existing pilots of community interventions should be expanded. Furthermore, locally based education campaigns are likely to facilitate the diagnosis of hard to reach populations. In future, such interventions should be funded by the government as donor-funding in Romania is not guaranteed

These changes could result in a 45% reduction in active TB cases and a 40% reduction in TB deaths by 2030.

This page is for collation purposes.

SECTION 6

APPENDICES

APPENDIX A. TECHNICAL SUMMARY OF OPTIMA TB

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 programme 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). Box 2 summarises the main features of Optima TB.

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

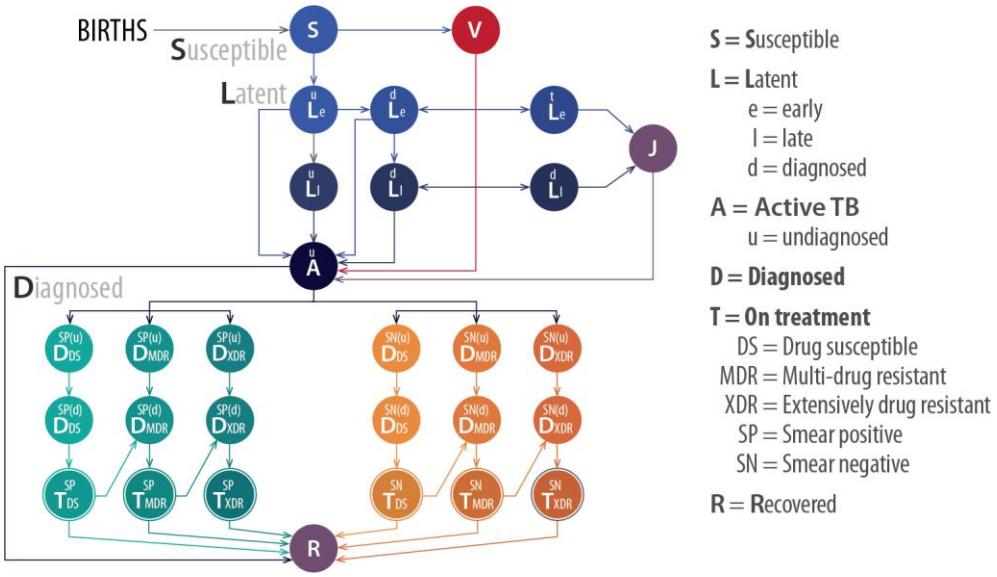
Population structure, key populations and People living with HIV

- 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 (Figure 33). 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 (Figure A 6.1, disks) corresponds to a single differential equation in the model, and each rate (Figure A 6.1, 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.

Figure A 6.1 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.

TB RESOURCE OPTIMISATION AND PROGRAMME 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 programme coverage levels.

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

To perform the optimisation, 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 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 optimisation problems, the team has shown that the algorithm can determine optimised solutions with fewer function evaluations than traditional optimisation 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 optimisation analysis are associated with the cost-coverage and coverage-outcome curves.

APPENDIX B. MODEL DATA INPUTS

DEMOGRAPHIC INPUTS

Table B 6.1 Population sizes

POPULATION NAME	VALUE	YEAR	SOURCE OR ASSUMPTION
General population, 0–4 years old	955,770	2015	Provided by country
General population, 5–14 years old	2,117,899	2015	Provided by country
General population, 15–64 years old	13,338,581	2015	Provided by country
General population, 65+ years old	3,407,447	2015	Provided by country
Prisoners, 15–64 years old	27,455	2015	World Prison Brief

Table B 6.2 Births and background (non-TB) mortality

POPULATION NAME	VALUE	YEAR	SOURCE OR ASSUMPTION
Annual number of births	193,103	2014	Romanian Statistical Yearbook 2016, National Institute for Statistics
Annual non-TB death rate, 0–4 years old	0.20%	2015	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, 5–14 years old	0.02%	2015	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, 15–64 years old	0.72%	2015	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, 65+ years old	5.08%	2015	Insitute for Health Metrics and Evaluation, Global Burden of Disease study 2016.
Annual non-TB death rate, Prisoners	0.72%	2015	In the absence of data to inform this, assumed equal to the 15–64 population non-TB death rate

TB EPIDEMIOLOGICAL PARAMETERS

Table B 6.3 TB epidemiological parameters

FULL NAME	POPULATION	LATEST YEAR OR DEFAULT VALUE	SOURCE OR ASSUMPTION
Vaccination Rate	Annual number of births	97.6%	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. The values used in calibration were either 0.00185 or 0.0037, with the higher values used for the PLHIV populations
Probability of Early-Active vs. Early-Late LTBI Progression*	All populations	0.177	Andrews et al. 2012 - risk of progression to active. The values used in calibration were either 0.177 or 0.354, with the higher value used for the PLHIV populations
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.
Smear positive (SP) TB Infectiousness*	All populations	1	Values between 1 - 30 in calibrations were used (highest being prisoners and lowest 5–14 years old)
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

Table B 6.3 continued

Table B 6.3 TB epidemiological parameters (continued)

FULL NAME	POPULATION	LATEST YEAR OR DEFAULT VALUE	SOURCE OR ASSUMPTION
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

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 Romania. The underlying epidemiological parameters adjusted when calibrating for Romania, were: "Late Latency Departure Rate"; "Probability of Early-Active vs. Early-Late LTBI Progression"; "Smear positive (SP) TB Infectiousness"; "Active Infection Rate (Active Recovered)"; "Late Latency Departure Rate"

NOTIFICATION DATA

Notified cases disaggregated by age and resistance-type were provided by the country.

Table B 6.4 Number of notified cases by age and drug resistance type (2015)

POPULATION	NUMBER OF NOTIFIED DS-TB CASES	NUMBER OF NOTIFIED MDR-TB CASES	NUMBER OF NOTIFIED XDR-TB CASES	TOTAL NUMBER OF NOTIFIED CASES
General population, 0–4 years	216	2	0	218
General population, 5–14 years	435	2	0	437
General population, 15–64 years	11,628	484	61	12,173
General population, 65+ years	2,146	32	8	2,186
Prisoners	166	3	0	169

DIAGNOSIS-TREATMENT OUTCOMES

Table B 6.5 Diagnosis Rate by population age and type

PARAMETER	0–4 YEARS	5–14 YEARS	15–64 YEARS	65+ YEARS	PRISONERS	LATEST YEAR AVAILABLE	SOURCE / ASSUMPTION
DS Proportion smear positive	0.591	0.591	0.591	0.591	0.385	2014	GLC mission reports
MDR Proportion smear positive	0.796	0.796	0.796	0.796	0.796	2014	Data provided by country
XDR Proportion smear positive	0.906	0.906	0.906	0.906	0.906	2014	Data provided by country
DS Diagnosis Rate*	0.787	0.787	0.787	0.787	0.787	2014	Based on notified cases, incidence, and prevalence
DS Treatment Uptake Rate	0.977	0.977	0.977	0.977	1.0	2014	WHO
DS Treatment Abandonment Rate	0.058	0.058	0.163	0.163	0.077	2014	WHO EURO Surveillance Reports
DS Treatment Success Rate	0.950	0.950	0.916	0.916	0.941	2014	WHO EURO Surveillance Reports
MDR Diagnosis Rate*	0.787	0.787	0.787	0.787	0.515		Assumed same as DS-TB due to lack of data in the general population
MDR Treatment Uptake Rate	0.977	0.977	0.977	0.977	1.0	2014	Assumed same as DS-TB due to lack of data in the general population
MDR Treatment Abandonment Rate	0.272	0.272	0.272	0.272	0.272	2014	WHO EURO Surveillance Reports
MDR Treatment Success Rate	0.518	0.294	0.252	0.197	0.204	2014	WHO EURO Surveillance Reports and country data

Table B 6.5 continued

Table B 6.5 Diagnosis Rate by population age and type (continued)

PARAMETER	0–4 YEARS	5–14 YEARS	15–64 YEARS	65+ YEARS	PRISONERS	LATEST YEAR AVAILABLE	SOURCE / ASSUMPTION
XDR Diagnosis Rate*	0.787	0.787	0.787	0.787		2014	Assumed same as DS-TB due to lack of data in the general population
XDR Treatment Uptake Rate	0.977	0.977	0.977	0.977	1	2014	Assumed same as DS-TB due to lack of data in the general population
XDR Treatment Abandonment Rate	0.272	0.272	0.272	0.272	0.272	2014	WHO EURO Surveillance Reports
XDR Treatment Success Rate	0.079	0.079	0.079	0.079	0.079	2014	WHO EURO Surveillance Reports

Note: *The model "diagnosis rate" is the annual transition of people from the undiagnosed compartments to the diagnosed compartments. It is calculated taking into consideration the number of notified cases, estimated incidence and prevalence. All diagnosis-treatment outcomes were assumed to be the same for smear positive and smear negative TB due to lack of data.

PROGRAMMATIC DATA: SCREENING AND DIAGNOSTICS

Table B 6.6 Screening interventions: Target groups, unit costs, volume, total spend and yield

INTERVENTION	TARGET POPULATION	UNIT COST (EUR), 2018	NUMBER OF SCREENS, 2016	SOURCE OR ASSUMPTION	TOTAL ESTIMATED SPENDING (EUR)	YIELD	SOURCE OR ASSUMPTION	INITIAL SCREENING AND TESTS RECEIVED
Passive Case Finding	General population	42.23	344,123	Annual number of symptom screens carried out informed by NTP data	15,059,191	4.57%	Calculated based on NTP data	Symptom screening with X-ray, followed by Gene Xpert
Contact tracing - household	General population	59.61	52,148	Assumed that all notified cases lead to household contact tracing of 4 contacts on average based on TP advice	3,970,792	2.5%	Shapiro et al., 2013	Symptom screening with X-ray, followed by Gene Xpert
Enhanced contact tracing - community	General population	55.02	39,111	Assumed that 20% of notified cases lead to enhanced contact tracing of 15 contacts on average based on NTP advice	2,731,430	1.18%	Shapiro et al., 2013	Symptom screening with X-ray, followed by Gene Xpert
Contact tracing prisons	Prisoners	58.36	750	Assumed 5 contacts traced per notified case in prisons.	56,171	2.5%	Shapiro et al., 2013	Symptom screening with X-ray, followed by Gene Xpert
Active case finding - prisoners	Prisoners	53.36	7,073	All prisoners are screened on entry and exit	408,740	0.65%	Shapiro et al., 2013	Symptom screening with X-ray, followed by Gene Xpert

Table B 6.6 continued

Table B 6.6 Screening interventions: Target groups, unit costs, volume, total spend and yield (continued)

INTERVENTION	TARGET POPULATION	UNIT COST (EUR), 2018	NUMBER OF SCREENS, 2016	SOURCE OR ASSUMPTION	TOTAL ESTIMATED SPENDING (EUR)	YIELD	SOURCE OR ASSUMPTION	INITIAL SCREENING AND TESTS RECEIVED
Active case finding - family doctors	General population	30.71	0	Not currently implemented	–	0.13%	Shapiro et al., 2013	Symptom screening with X-ray, followed by Gene Xpert
Mobile outreach (prisoners)	Prisoners	103.36	0	Not currently implemented	–	0.65%	Shapiro et al., 2013	Gene Xpert
Mobile outreach (PWID, homeless)	General population (PWID and homeless are not defined as separate populations)	97.79	0	Not currently implemented	–	0.75%	Shapiro et al., 2013	Gene Xpert
Mobile outreach (rural poor and low access regions)	General population (rural poor are not defined as separate populations)	79.91	0	Not currently implemented	–	0.17%	Shapiro et al., 2013	Gene Xpert

Note: All unit costs were derived by the authors of this report using budget data provided by country colleagues.

Table B 6.7 Sensitivity of screening /testing methods

SCREENING OR TESTING METHOD	SENSITIVITY	SOURCE OR ASSUMPTION
Full symptom screen and X-ray	0.9%	Van't Hoog et al., 2013
Gene Xpert	0.92%	Van't Hoog et al., 2013

PROGRAMMATIC DATA: TB TREATMENT

Table B 6.8 Treatment interventions: Target groups, unit costs, volume, total spend and outcome

TREATMENT PROGRAMME	UNIT COST/ COURSE OF TREATMENT (EUR)	PATIENTS COVERED, 2016	SOURCE OR ASSUMPTION	TOTAL ESTIMATED ANNUAL SPENDING (EUR)	TREATMENT SUCCESS	ADHERENCE TO TREATMENT	SOURCE OR ASSUMPTION
Hospital focused treatment (DS)	5,895	13,081	Number of notified cases	77,117,997	0.85	0.92	Current treatment outcomes
Hospital focused treatment (MDR)	20,792	351	Number of notified cases, disaggregated using % coverage of GLC cohort of patients	5,448,343	0.44	0.54	Current treatment outcomes
Hospital focused treatment (XDR)	31,979	88	Number of notified cases, disaggregated using % coverage of GLC cohort of patients	1,427,264	0.16	0.26	Current treatment outcomes
Hospital focused treatment (with incentives -DS)	6,024	–	Not currently implemented	–	0.87	0.92	Lutge et al., 2015

Table B 6.8 continued

Table B 6.8 Treatment interventions: Target groups, unit costs, volume, total spend and outcome (continued)

TREATMENT PROGRAMME	UNIT COST/ COURSE OF TREATMENT (EUR)	PATIENTS COVERED, 2016	SOURCE OR ASSUMPTION	TOTAL ESTIMATED ANNUAL SPENDING (EUR)	TREATMENT SUCCESS	ADHERENCE TO TREATMENT	SOURCE OR ASSUMPTION
Hospital focused treatment (with incentives -MDR)	20,999	–	Not currently implemented	–	0.45	0.55	Lutge et al., 2015
Hospital focused treatment (with incentives -MDR new drugs)	22,023	45	Number of notified cases, disaggregated using % coverage of GLC cohort of patients	916,173	0.75	0.85	Diacon et al, 2014; Lutge et al., 2015
Hospital focused treatment (with incentives -XDR)	32,187	–	Not currently implemented	–	0.17	0.27	Lutge et al., 2015
Hospital focused treatment (with incentives -XDR new drugs)	46,231	11	Number of notified cases, disaggregated using % coverage of GLC cohort of patients	320,918	0.66	0.76	Diacon et al, 2014; Lutge et al., 2015
Ambulatory treatment (DS)	2,889	–	Not currently implemented	–	0.87	0.92	Lutge et al., 2015
Ambulatory treatment (MDR)	12,328	–	Not currently implemented	–	0.45	0.55	Lutge et al., 2015

Table B 6.8 Treatment interventions: Target groups, unit costs, volume, total spend and outcome (continued)

TREATMENT PROGRAMME	UNIT COST/ COURSE OF TREATMENT (EUR)	PATIENTS COVERED, 2016	SOURCE OR ASSUMPTION	TOTAL ESTIMATED ANNUAL SPENDING (EUR)	TREATMENT SUCCESS	ADHERENCE TO TREATMENT	SOURCE OR ASSUMPTION
Standard DOTs (DS)	6,044	–	Not currently implemented	–	0.92	0.92	Karumbi and Garner, 2015
Standard DOTs (MDR)	20,131	–	Not currently implemented	–	0.48	0.58	Karumbi and Garner, 2015
Standard DOTs (MDR – new drugs)	46,080	–	Not currently implemented	–	0.79	0.89	Diacon et al, 2014; Karumbi and Garner, 2015
Standard DOTs (XDR)	24,844	–	Not currently implemented	–	0.17	0.27	Karumbi and Garner, 2015
Standard DOTs (XDR – new drugs)	51,740	–	Not currently implemented	–	0.66	0.76	Diacon et al, 2014; Karumbi and Garner, 2015
Prisoner DS	5,895	161	Number of notified cases	901,600	0.94	1.00	Current treatment outcomes
Prisoner MDR	20,668	3	Number of notified cases	21,240	0.26	0.54	Current treatment outcomes
Prisoner MDR new	46,168	–	Not currently implemented	–	0.73	0.83	Diacon et al, 2014

Note: All programme costs were estimated by micro-costing using local data. When estimating treatment effectiveness, a quality factor of 0.8 was applied to account for the likely loss of impact between trial and real-world implementation (see DCP3 impact working paper number 21).

Table B 6.9 Component costs of TB treatment regimens (EUR)

REGIMEN	INPATIENT COSTS	OUTPATIENT COSTS	DRUG COSTS	OTHER COSTS	TOTAL TREATMENT COST	DIAGNOSIS AND MONITORING COSTS	TOTAL TREATMENT COST WITH DIAGNOSIS
Hospital focused treatment (DS)	3,329	1,249	80	53	4,711	1,184	5,895
Hospital focused treatment (MDR)	8,892	2,814	4,500	124	16,330	4,462	20,792
Hospital focused treatment (XDR)	13,338	2,834	11,000	124	27,296	4,683	31,979
Hospital focused treatment (with incentives -DS)	3,329	1,249	80	181	4,840	1,184	6,024
Hospital focused treatment (with incentives -MDR)	8,892	2,814	4,500	331	16,537	4,462	20,999
Hospital focused treatment (with incentives -MDR new drugs)	8,892	2,814	5,600	255	17,561	4,462	22,023
Hospital focused treatment (with incentives -XDR)	13,338	2,834	11,000	332	27,504	4,683	32,187
Hospital focused treatment (with incentives -XDR new drugs)	13,338	2,834	25,000	376	41,548	4,683	46,231
Ambulatory treatment (DS)	1,037	351	80	238	1,706	1,184	2,889
Ambulatory treatment (MDR)	1,482	867	5,000	517	7,866	4,462	12,328
Standard DOTs (DS)	1,037	3,505	80	238	4,860	1,184	6,044
Standard DOTs (MDR)	1,482	8,671	5,000	517	15,669	4,462	20,131
Standard DOTs (MDR – new drugs)	2,964	8,160	30,000	493	41,617	4,462	46,080
Standard DOTs (XDR)	5,928	8,714	5,000	519	20,161	4,683	24,844

Table B 6.9 continued

Table B 6.9 Component costs of TB treatment regimens (EUR) (continued)

REGIMEN	INPATIENT COSTS	OUTPATIENT COSTS	DRUG COSTS	OTHER COSTS	TOTAL TREATMENT COST	DIAGNOSIS AND MONITORING COSTS	TOTAL TREATMENT COST WITH DIAGNOSIS
Standard DOTs (XDR – new drugs)	8,892	7,693	30,000	472	47,057	4,683	51,740
Prisoner DS	3,329	1,249	80	53	4,711	1,184	5,895
Prisoner MDR	8,892	2,814	4,500	–	16,206	4,462	20,668
Prisoner MDR new	8,892	2,814	30,000	–	41,706	4,462	46,168

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COST DATA

In addition to the cost data shown above, the following unit costs were used.

Table B 6.10 Summary table of unit costs for TB prevention and diagnosis

DIAGNOSIS & PREVENTIVE INTERVENTIONS	UNIT COST (EUR)
Passive Case Finding	55.51
Contact tracing - household	72.89
Enhanced contact tracing - community	68.31
Contact tracing prisons	71.64
Active case finding - prisoners	66.64
Active case finding - family doctors	43.99
Mobile outreach (prisoners)	116.64
Mobile outreach (PWID, homeless)	111.07
Mobile outreach (rural poor and low access regions)	92.99
GeneXpert testing	119.80

Note: All costs estimated based on local data.

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