March 2024 (version 3.0)

Evaluating cost-effective investments to reduce the burden of drug-resistant tuberculosis (TB) in Kyrgyz Republic

Findings from an Optima TB analysis, 2023

Burnet
reach for the many

Acknowledgments

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Suggestion citation

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Abbreviations

ART	Antiretroviral therapy
BCG	Bacillus Calmette-Guérin
Bdq	Bedaquiline
COVID-19	Coronavirus disease caused by the SARS-CoV-2 virus
DR-TB	Drug-resistant tuberculosis
DS-TB	Drug-sensitive tuberculosis
EPTB	Extrapulmonary tuberculosis
HIV	Human immunodeficiency virus
LTBI	Latent tuberculosis infection
MDR-TB	Multidrug resistant tuberculosis
NTP	National TB Programme
PLHIV	People living with HIV
RR-TB	Rifampicin resistant tuberculosis
SN	Smear-negative
SP	Smear-positive
TPT	TB preventive treatment
XDR-TB	Extensively drug-resistant tuberculosis

Contents

Executive summary

BACKGROUND

Estimated tuberculosis (TB) incidence has declined in the Kyrgyz Republic (Kyrgyzstan), from around 154 per 100,000 in 2001 to 105 per 100,000 in 2020, however the country continues to experience a severe TB epidemic. Kyrgyz Republic remains one of the top 30 countries for high burden of Rifampicin resistant (RR) and multi-drug resistant (MDR)-TB. An allocative efficiency analysis was undertaken to estimate the optimal allocation of funding to minimize both drug resistant (DR) TB case and TB-related deaths by 2030.

KEY FINDINGS

Recommendations

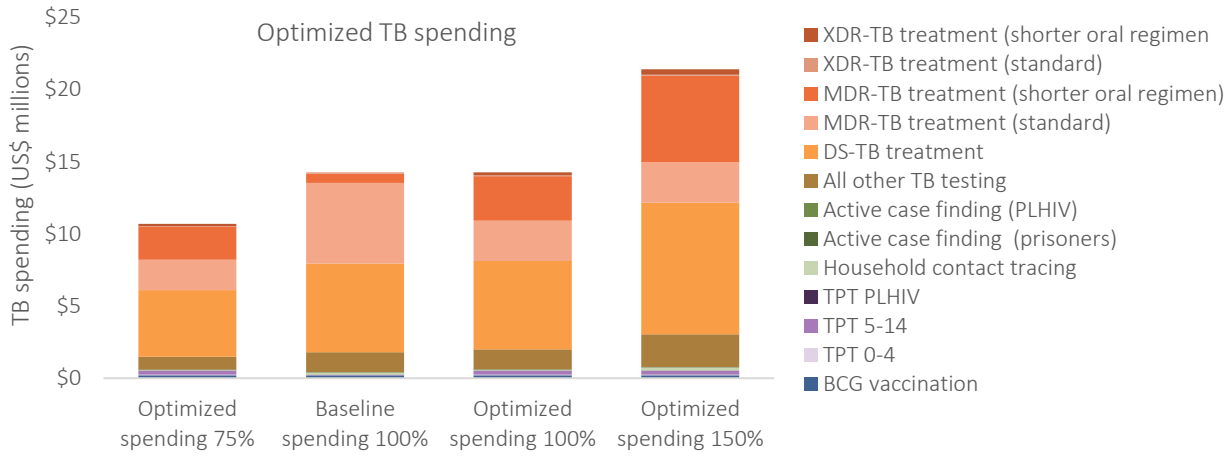
1. **Shorter treatment regimens for drug resistant TB** based on Bedaquiline are more cost-effective, allowing for a larger number of people to be treated for the same amount of spending, as well as better adherence and limiting side-effects for people with TB.
2. **Prioritizing case finding among vulnerable populations** such as people living with HIV could improve diagnosis rates from 46% in 2023 to 50% in 2024.
3. **Expand prevention strategies for children** - including preventive treatment coverage for all children 0 to 14 who are contacts of active TB cases (estimated +3,200), and further increase infant BCG vaccination coverage to reach 100% of children.

Baseline

The model estimates there were 8,000 new and relapse cases of TB in 2022, of which an estimated 31% were drug resistant. In 2021 an estimated US$14.2 million was spent on direct TB prevention, screening and treatment programs, of which 88% was spent on treatment.

Optimization of current spending

With the same total resources for TB as estimated in 2021, reallocating spending from standard treatment to shorter oral regimens for MDR and XDR as well as increasing funding for preventive treatment for children 0-14 and BCG vaccination could avert 470 (1%) new TB infections and 25 (1%) TB-related deaths from 2024 to 2030 compared with if baseline spending were continued.



The number of active DR-TB cases is projected to reduce by 14% (-920) by 2030 under status-quo conditions, increasing to a 22% reduction (-1,416) with an optimized 50% increase in TB spending.

TB targets

National TB targets of TB incidence below 95 per 100,000 people and mortality below 3.5 per 100,000 people could be within reach if additional resources are allocated optimally. However, reaching End TB targets may remain out of reach with the current set of interventions. Additional targeted active case finding in other groups at higher risk combined with reductions in the social determinants of TB, and improved collection of strategic information to support program planning and monitoring may be necessary to achieve further reductions in TB incidence.

1 Background

Although overall estimated tuberculosis (TB) incidence has declined in the Kyrgyz Republic (Kyrgyzstan), from around 154 per 100,000 in 2001 to 105 per 100,000 in 2020, the country continues to experience a severe TB epidemic (1). Disruptions due to COVID-19 and pandemic response measures may have slowed progress (2, 3), and both incidence and TB-related mortality have increased since 2020.

Further, Kyrgyz Republic remains one of the top 30 countries for high burden of Rifampicin resistant (RR) and multi-drug resistant (MDR)-TB (2). In 2021, 27% of new cases and 59% of previously treated cases had RR/MDR-TB (1). Key and vulnerable populations identified to be most-at-risk of TB or with poorer TB outcomes in Kyrgyz Republic include migrant workers, people with chronic disease, people living with HIV, prisoners, people with drug or alcohol dependency and people living in poverty (1, 4). People living with HIV have doubled from 2013 to 2019, increasing the number of people living with HIV/TB comorbidity.

Access to modern rapid molecular methods for testing have improved TB diagnosis in Kyrgyz Republic, and rapid diagnostics were used among 83% of people newly diagnosed with TB in 2021 (1). However, there are regional disparities in the availability of these methods (3). Overall treatment success for TB is 82% in Kyrgyz Republic, and 72% among MDR-TB cases (1). Treatment side effects and stigma contribute to relatively high loss-to-follow-up among those on treatment for DR-TB, estimated at 14%-19% in 2019 (3). In 2021 only 15% of individuals were being treated with World Health Organization (WHO)-recommended shorter treatment regimens. Expansion of better-tolerated, all-oral short treatment regimens and psychosocial support services may support further advances in treatment outcomes.

The TB response in Kyrgyz Republic remains funded through both domestic (60%) and international (40%) sources, including the Global Fund (5). In October 2022, the National Parliament called for the Ministry of Health to implement the "Program of the Cabinet of Ministers of the Kyrgyz Republic Tuberculosis - VI for 2022-2026", calling for a reduction in stigma and discrimination of those with TB, thereby ensuring a people-oriented and integrated care system. The national targets for 2026 were set to reduce incidence to 95 per 100,000 people and mortality below 3.5 per 100,000 people (6).

Prior Optima TB analysis

Kyrgyz Republic conducted an Optima TB analysis in 2019-20. Three key priorities identified in the analysis to jointly minimize incidence of TB, prevalence of active TB and TB-related deaths were to: (1) reduce unnecessary hospitalization; (2) improve diagnosis through active case finding programs for groups at higher risk of TB; and (3) increase preventive treatment children aged 0-4 years identified as household contacts of active TB cases. In 2021, the established model was used to assess the impacts of COVID-19-related disruptions on TB services in Kyrgyz Republic. A 32% reduction in TB detection was estimated to be primarily due to reduced demand for TB services (6). At the same time, the analysis found that the pandemic accelerated outpatient treatment, improved rapid reporting of data, and that there had been an increase in number of contacts screened per TB notification (1.4 in 2019 to 1.6 in 2020), suggesting an adoption of most of the recommendations of the 2020 Optima TB analysis.

Study objectives

This Optima TB analysis aims to assess the cost-effectiveness of current and future programs for TB prevention, case finding and treatment and thereby estimate the most efficient allocation of resources for Kyrgyz Republic to minimize drug-resistant TB cases and TB-related deaths by 2030. Specifically, this analysis will:

1. Assess the cost-effectiveness of current and future programs for TB prevention, case finding and treatment;
2. Evaluate opportunities to improve the cost-effectiveness of TB screening, diagnosis, prevention and treatment programs to minimize the number of active MDR-TB cases by 2030; and
3. Assess how TB prevention, screening and treatment interventions should be prioritized as part of the End TB strategy to achieve 2030 targets.

2 Methodology

OVERVIEW OF OPTIMA TB MODEL

To carry out the analyses, the team used the Optima TB model, a mathematical optimization model applied to assess the optimal allocation of available resources across TB programs to maximize impact. Details of the Optima TB model and model parameters are included in Appendix A. Optima TB is a deterministic, compartmental model that partitions the population by age group and risk, TB health state (for example, susceptible, vaccinated, latent TB, active TB), diagnosis, and drug resistant types, and tracks people's movement among health states. The model incorporates evidence on biological transmission probabilities, detailed infection progression and population mixing patterns. A detailed illustration of the compartmental model structure is included in Figure A1.

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

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

COLLABORATION AND STAKEHOLDER INVOLVEMENT

The analysis was a collaboration between the National TB Programme (NTP) Kyrgyz Republic, Burnet Institute and the Global Fund. National collaborators defined the scope of the analysis, collated national epidemiological, program and cost data, and reviewed and validated all input data, model calibration and cost-coverage-outcome relations.

POPULATIONS AND TB PROGRAM AREAS

Populations considered in this analysis were:

- Children 0-4 years
- Children 5-14 years
- Adults 15-64 years
- Adults 65+ years
- Prisoners 15+ years

Based on available data, the following TB programs were considered in the analysis:

Table 1. TB programs included in the Optima TB Kyrgyz Republic analysis, 2023

Prevention	TB preventive treatment (TPT) for contacts:	0-4 years
		5-14 years
	TPT for PLHIV	
	BCG vaccination	
Diagnosis	Household contact tracing	
	Active case finding among prisoner populations	

	Active case finding among PLHIV
	All other TB testing
Treatment	DS-TB treatment
	MDR-TB treatment (standard)
	MDR-TB treatment (shorter oral regimens)
	XDR-TB treatment (standard)
	XDR-TB treatment (shorter oral regimens)

Notes: BCG, Bacillus Calmette-Guerin; DS, drug susceptible; MDR, multi-drug resistant; TB, tuberculosis; XDR, extensively drug-resistant

SCOPE OF ANALYSIS

Study partners identified a range of scenarios for inclusion in the analysis based on national priorities, policy questions and available data (Table 2). Each scenario assumes that changes in intervention coverage occur in 2024 and are sustained until 2030.

Table 2. Scenarios included in the Optima TB Kyrgyz Republic analysis, 2023

Scenario	Description
Baseline scenario	Continued spending and fixed allocation of US$14,250,383 (100% of TB prevention, screening and treatment spending) maintained over 2024-2030
Optimized spending 100%	Continued spending of US$14,250,383 (100%) with allocation optimized to reduce TB incidence and TB-related deaths by 2030.
Reduced/increased spending (50%, 75%, 125%, 150%, 200%) optimized	Considers if available resources for TB programs were reduced or increased. Percentages are relative to the most recent targeted TB spending.
Reaching national TB targets	Assesses progress to reach (1) national 2026 TB targets of incidence below 95 per 100,000 people and mortality below 3.5 per 100,000 people, and (2) End TB milestones for 80% reduction in TB incidence and 90% reduction in TB-related deaths from 2015 to 2030, through interventions supporting rapid diagnosis and treatment by: scaling up active case finding and preventive treatment for all contacts, reducing time to diagnosis and time to treatment initiation, and reducing social determinants leading to TB activation.

MODELLING SPECIFICATIONS

Model inputs

An updated Optima TB model for Kyrgyz Republic was developed and recalibrated using previously collated data from the two analyses conducted in 2020 and 2021, and supplied with additional epidemiological and programmatic data available until 2022. Epidemiological, program and cost data (Table 3) were collated by the study team and collaborators using an adapted Excel-based Optima TB data entry spreadsheet. Other model inputs and parameters are described in Appendix B. This analysis was limited to pulmonary TB only. Pulmonary TB is estimated to account for 78%

of TB incidence (1), aligned with 80% of TB notifications in National TB Programme data in the first three quarters of 2022.

Table 3. Main sources of data used in the Optima TB Kyrgyz Republic model, 2023

Data type	Source
Epidemiologic data	Demographic data for population size, birth rate estimates and all-cause mortality from UN World Population Division (7); prison population estimates followed national data used for Optima HIV modelling (8); pulmonary TB notifications, TB-related deaths supplied by National TB Programme, 2015-2022.
Program coverage data	Coverage of BCG vaccination at birth in 2016 and positive yield by testing modality supplied by National TB Programme, 2018, and assumed to remain constant. Number of people screened by testing modality, treatment outcomes by strain and number of TPT initiations supplied by the National TB Programme 2018-2021 plus the first three quarters of 2022. Treatment initiations were inferred from notification data in 2021 and the most recent available proportional coverage data for screening and testing modalities in 2018, both supplied by the National TB Programme.
Cost data	Cost per person diagnosed and annual cost per treatment initiation aligned with the most recent data reported in the Optima TB analysis in 2020 (9).

Model calibration

In consultation with national TB experts, Optima TB was calibrated to available epidemiologic data on TB case notifications and WHO estimated TB incidence (Global TB Programme 2022 estimates). The model was calibrated to closely match 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 indicators including TB incidence and prevalence (Appendix C).

Optimization objectives

Allocations were optimized to evenly prioritize progress by 2030 on proportionally reducing each of the prevalence of DS-TB, MDR-TB and XDR-TB and reducing the number of TB-related deaths. Based on the estimated baseline conditions of 2022, this resulted in model weightings of 1, 2, and 30 for reductions in the active number of DS-TB, MDR-TB, and XDR-TB cases respectively, and 25 per TB-related death averted.

Optimization constraints

Changes in funding to achieve optimized allocations did not consider reallocation of care costs between hospitalized and ambulatory treatment modalities. Spending was constrained to not reduce current coverage of preventive treatment for people living with HIV.

3 Findings

EPIDEMIOLOGICAL SITUATION

TB incidence

In 2022, Optima TB modelling estimates 7,964 incident pulmonary TB cases modelled in Kyrgyz Republic, including both new and relapse cases (Table 4, Figure 1). Consistent with WHO-reported trends for all forms of TB, estimated pulmonary TB incidence in Kyrgyz Republic has overall significantly declined since the early 2000s. However, this trend was reversed in 2021, most likely due COVID-19 related disruptions. Initially, tuberculosis patients could not receive their daily dose of drugs and doctors could not convene to discuss drug resistant cases (10).

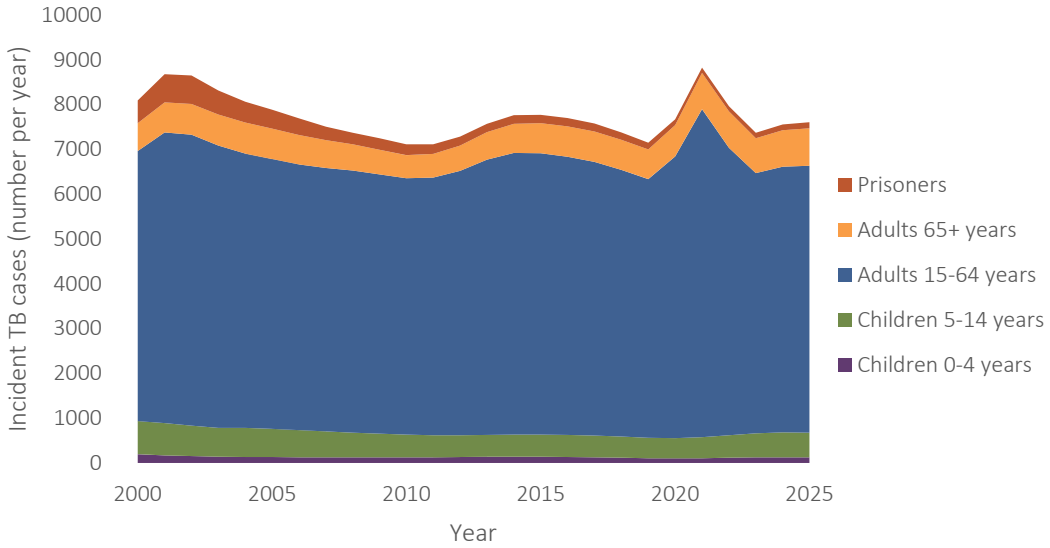
Table 4. Modelled estimates of TB incidence, number of prevalent active TB infections, latent infections, and TB-related deaths by sub-population, 2022

	Incident TB			Prevalent TB		
	New and relapse cases[1]	Incidence per 100,000 population	DR-TB cases (% of all new and relapse cases)	Total active TB	Latent TB prevalence	TB-related deaths
0-4 years	117	15	27 (23%)	268	0.6%	11
5-14 years	500	34	113 (23%)	1,498	2.4%	44
15-64 years	6,423	157	2,064 (32%)	20,316	16.3%	486
65+ years	810	256	208 (26%)	1,949	22.6%	64
Prisoners	116	1830	48 (41%)	319	83.2%	5
Total	7,966	119	2,461 (31%)	24,351	11.7%	610

Source: Optima TB Kyrgyz Republic model output, 2023

The majority of new cases of pulmonary TB continue to be among adults aged 15-64. However, relative to population size prisoners have the highest incidence of TB in Kyrgyz Republic, with estimated 1,830 new cases per 100,000 population in 2022. Children aged 0-4 years have the lowest estimated incidence. The BCG vaccination coverage is estimated to be 97% at birth, with a reported 123,086 vaccinated out of 127,518 eligible in 2022. Prior to COVID-19-related disruptions in 2021, adults aged 65+ have been the only population group with increasing TB incidence, increasing from 234 per 100,000 in 2010 to 256 per 100,000 in 2022 in Optima TB modelling. This is attributed to a high number of late-latent infections acquired during periods of higher TB-burden.

Figure 1. Incident (new and relapse) pulmonary TB cases by population group, 2000–2025

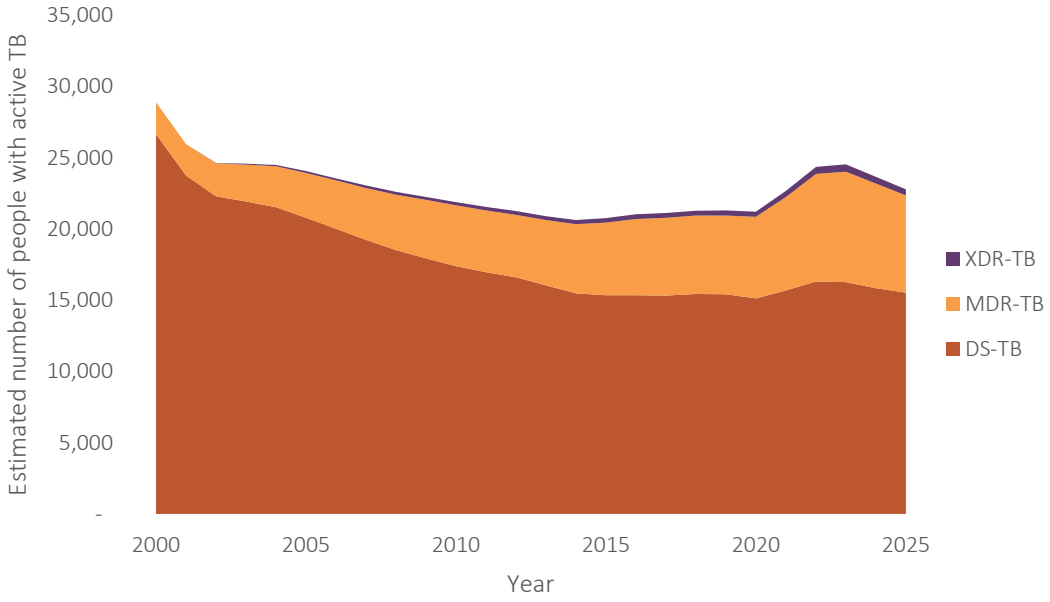


Source: Optima TB Kyrgyz Republic model output, 2023.

Prevalent TB

In 2022, there were a cumulative 24,351 active pulmonary TB cases in Kyrgyz Republic based on Optima modelled estimates, of which an estimated 33% were DR-TB (Table 4). The proportion of people with active TB with drug resistant TB has increased over time, from an estimated 21% in 2010 to a high of 34% in 2023 (Figure 2).

Figure 2. Trends in the estimated number of people with active TB by drug resistance type, 2000–2025



Source: Optima TB Kyrgyz Republic model output, 2023.
Notes: DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; XDR, extensively drug-resistant.

TB notification and case detection

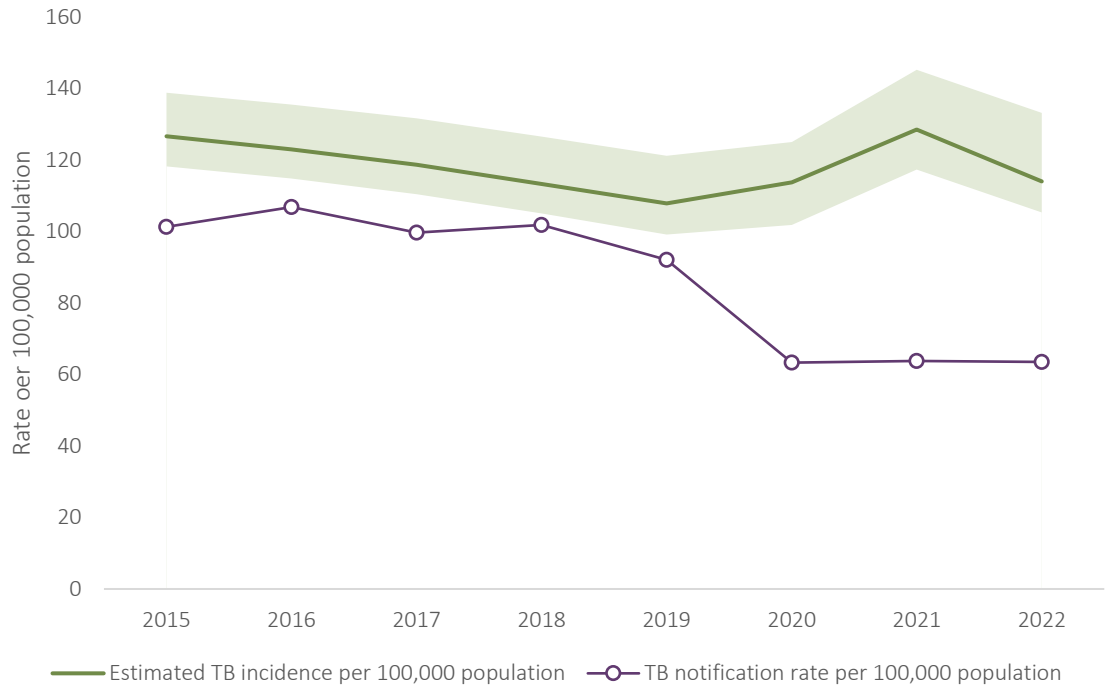
In 2022, there were a total of 4,247 new and relapse pulmonary TB notifications in Kyrgyz Republic (64 per 100,000 population), of which 78% were among the 15-64 sub-population group. The

estimated case detection rate (the proportion of estimated new and relapse TB cases that are detected in a given year(11)) ranged from 0.29 among prisoners to 0.74 among adults aged 65+ years.

Since 2020, the gap in case detection has increased due to COVID-19-related disruptions and impacts. Decreased screening activities and delays in care-seeking led to a reduction in TB notification rate, while TB incidence has subsequently increased (Figure 3).

As of the most recently available data from the third quarter of 2022, the number of TB notifications per 100,000 population had remained close to static from the 2020 and 2021 rates, suggesting that diagnosis and care-seeking remains disrupted.

Figure 3. Estimated pulmonary TB incidence rate and notification rate per 100,000 population, 2015–2022

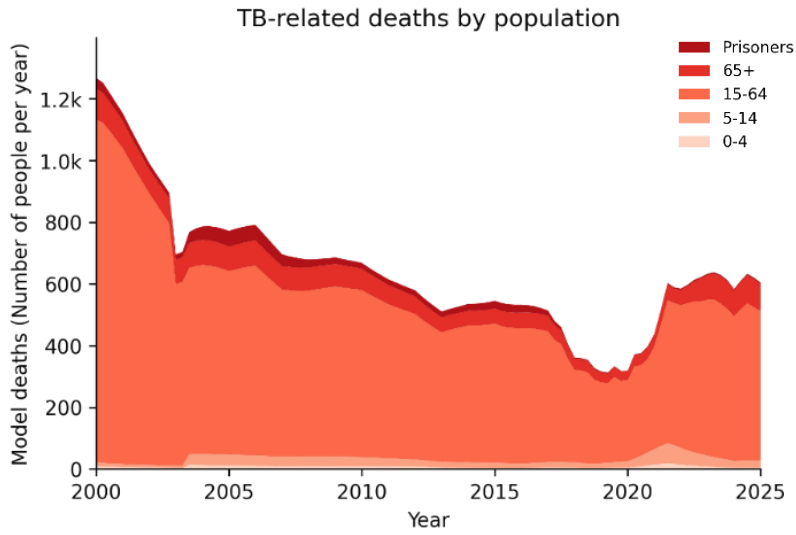


Source: Optima TB Kyrgyz Republic model output, 2023. Notification data from National TB programme.
Note: Shaded area indicates uncertainty range for TB incidence

TB mortality

Optima TB modelling estimates that TB-related deaths have declined in Kyrgyz Republic from 1,218 in 2000 to 381 in 2020, in line with decreasing incidence and advances in diagnosis and treatment (Figure 4). However, due to COVID-19-related increases in TB incidence and disruptions to TB treatment, annual deaths have since increased, reaching an estimated 610 in 2022, although a lower number of TB patients are dying during treatment in national program data. With current conditions maintained, Optima TB estimates that there may cumulatively be 3,736 TB-related deaths from 2023-2030.

Figure 4. TB-related deaths by population, 2015–2025

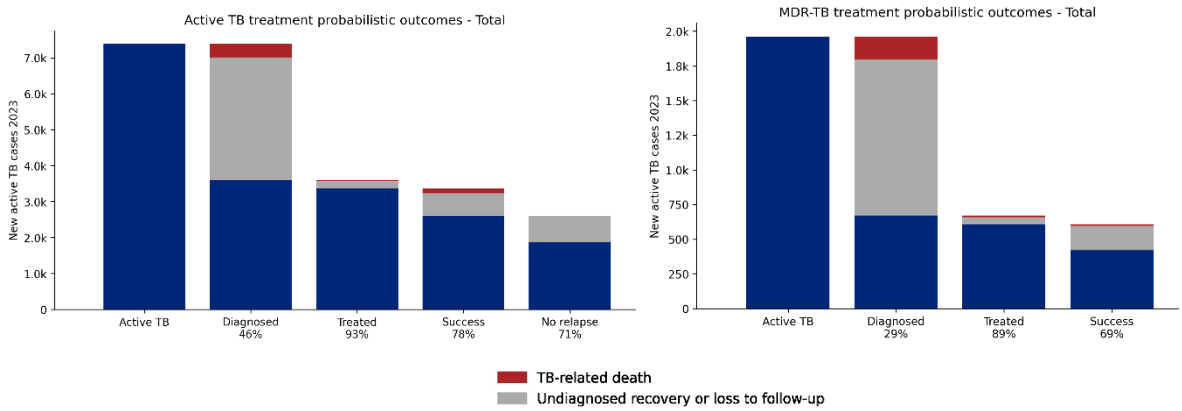


Source: Optima TB Kyrgyz Republic model output, 2023.

TB cascade

A probabilistic cascade is reported representing the estimated long-term outcomes of the cohort of people progressing to active TB in 2023. Based on the most recent estimated diagnosis and treatment rates prior to quarter 3, 2022, only 46% of all people progressing to active TB in Kyrgyz Republic would be projected to be diagnosed prior to natural outcome (recovery or death). Of those diagnosed, 93% are projected to be treated (Figure 5). These projected outcomes likely reflect ongoing impacts of COVID-19-related disruptions to care-seeking and diagnosis for TB and are a substantial decline from the 87% of active TB cases projected to be diagnosed in 2018 (12).

Figure 5. The projected final cohort outcomes for people progressing to active TB (left) and MDR-TB (right) in 2023 in the status quo scenario

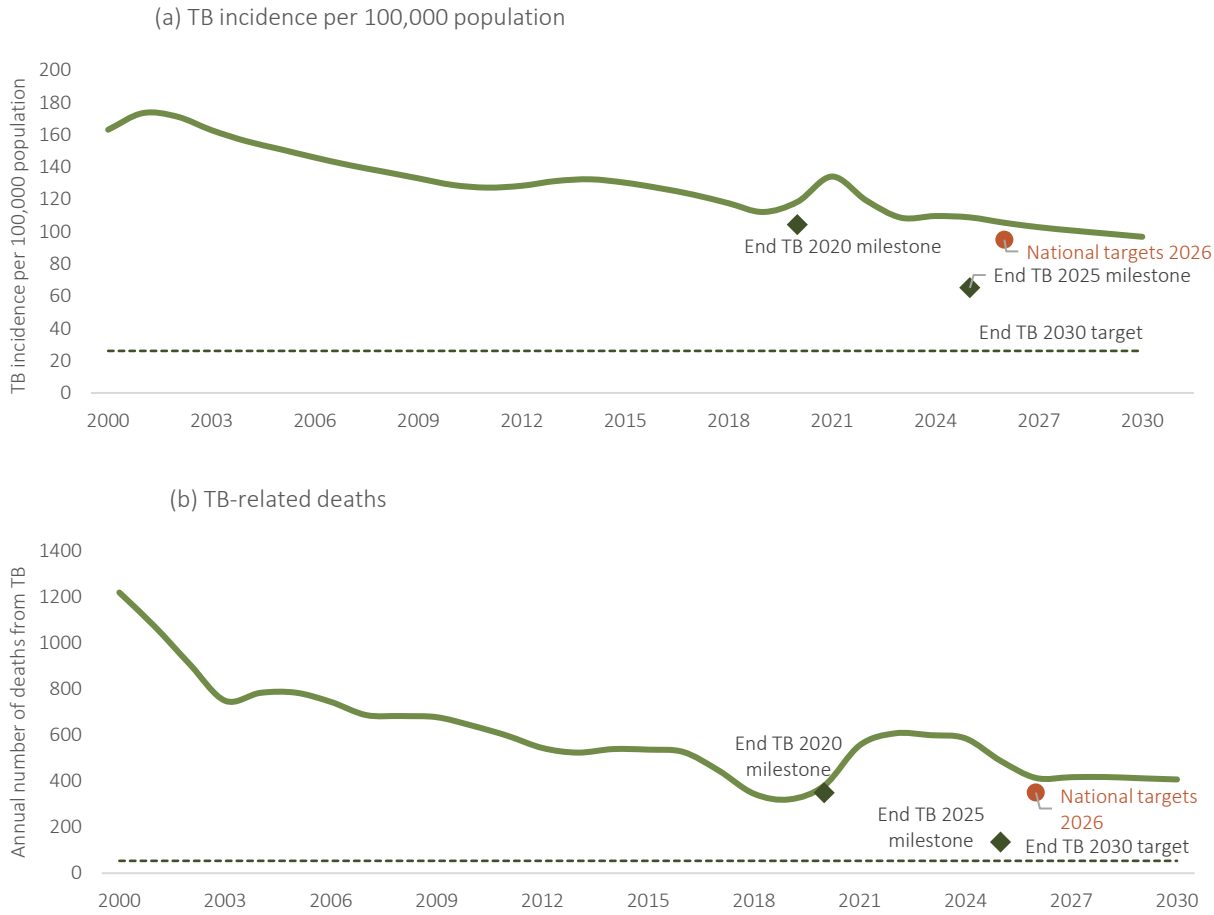


Overall, the probability of treatment success was 78% for all active pulmonary TB and slightly lower (69%) for MDR-TB. For both MDR-TB and XDR-TB, treatment failure rates have reduced substantially since 2010, from 28% to 5% for MDR-TB and from 57% to 10% for XDR-TB. Reported loss to follow has declined for MDR-TB, although up to 15% of MDR-TB patients were reported as "not evaluated" for cohorts initiating treatment since 2018.

Progress towards TB targets

The national targets aim for a TB incidence of 95 per 100,000 and 3.5 TB deaths per 100,000 by 2026. Similar ambitious targets have been set by the global End TB strategy (13). To evaluate progress towards the 2030 targets of reaching an 80% reduction in incidence rate and 90% reduction in TB deaths relative to 2015, the strategy defines country milestones for 2020 and 2025. Based on Optima TB modeled incidence, Kyrgyz Republic was on track to reach the 2020 End TB milestone for 20% reduction in incidence from 2015, but this may have been hindered by the reversal of trends in 2020-21 due to COVID-19. With continuation of current conditions, Kyrgyz Republic is not predicted the reach the End TB 2025 milestone nor 2030 target for reduction in TB incidence rate (Figure 6a), but may meet the national targets for incidence by 2026. While Kyrgyz Republic achieved the End TB 2020 milestone for 35% reduction in TB-related deaths relative to 2015 and may be able to meet the 2026 national target, the 2025 End TB milestone and 2030 End TB target are not in reach with current conditions continued (Figure 6b).

Figure 6. Optima TB estimated trends in (a) TB incidence rate and (b) TB mortality in relation to End TB targets



Source: Optima TB Kyrgyz Republic model, 2023. End TB milestones (diamond markers) and 2030 targets (dashed line) defined as percentage reduction from 2015 (14). Baseline based on Optima modelled values.

CURRENT TB SPENDING

Based on most recent spending estimates, in 2022 an estimated US$14.2 million was spent on direct TB prevention, screening and treatment programs. Of this, the majority was spent on treatment (88%). Treatment predominantly utilized standard, longer-course regimens, but 20% of

MDR-TB patients were initiated on shorter, all-oral treatment regimens, accounting for 10% of spending for MDR-TB treatment.

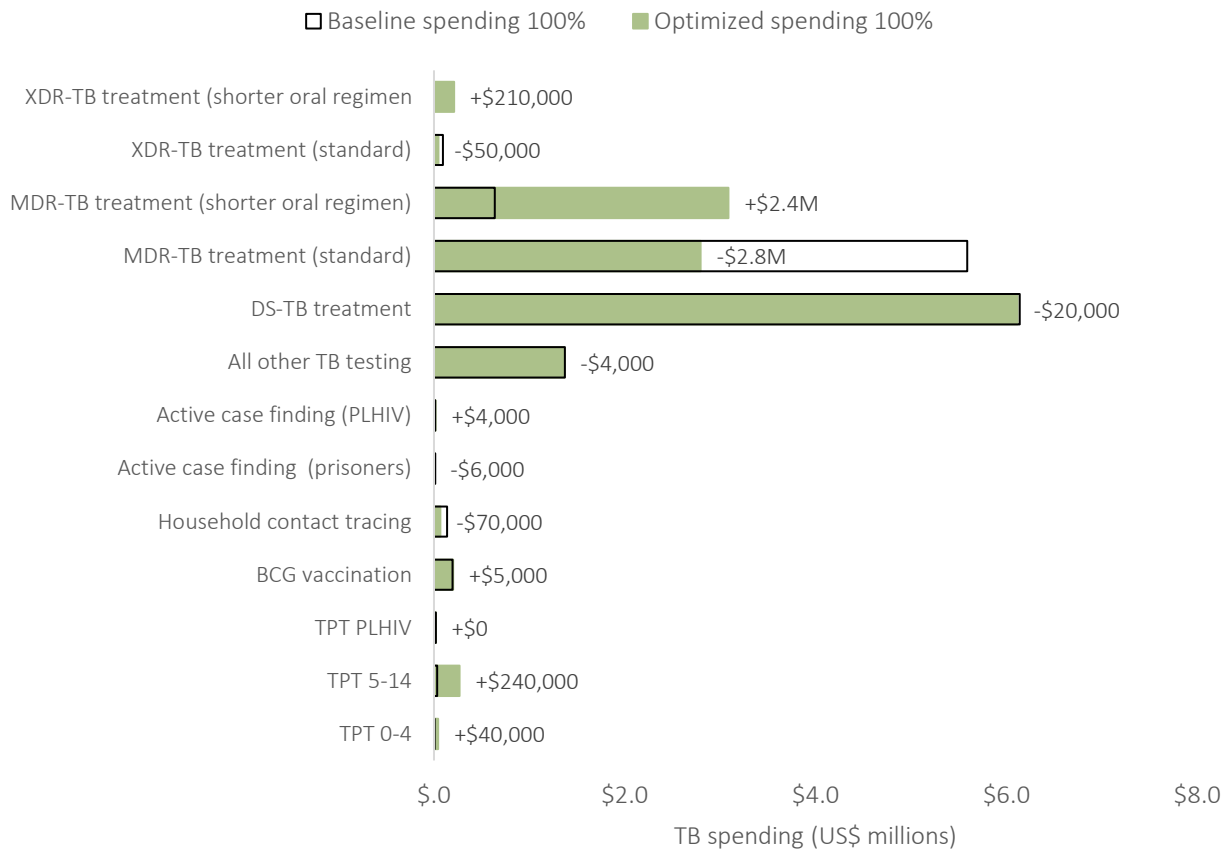
Among all spending for TB screening and testing, 11% was spent on active case finding among household contacts of people with active TB, prisoner populations, and people living with HIV.

WHAT IS THE OPTIMIZED ALLOCATION OF THE TB BUDGET TO MINIMISE DRUG-RESISTANT TB?

Optimized allocation of TB spending

With 100% of baseline spending maintained, the optimized allocation of the TB budget prioritizes short-course MDR and XDR treatment (+US$ 2.6M) rather than the standard course MDR and XDR treatment to minimize prevalence of drug-resistant TB by 2030 (Figure 7). Preventive TB treatment for children 0 to 14 (+US$ 275,000) as well as BCG vaccination (+US$ 5,000) were recommended to be scaled up. Active case finding for people living with HIV was also recommended to improve diagnosis rates, in lieu of household case finding and case finding in prisons. The number of people covered by each intervention can be found in Appendix E. As a result of the shorter course treatment, an additional 1,000 MDR-TB and XDR-TB cases could be treated from 2024 to 2030 for the same amount of spending and 4,700 more MDR-TB cases could be averted over the same period.

Figure 7. Baseline and optimized allocation of current TB spending for TB prevention, testing and treatment interventions

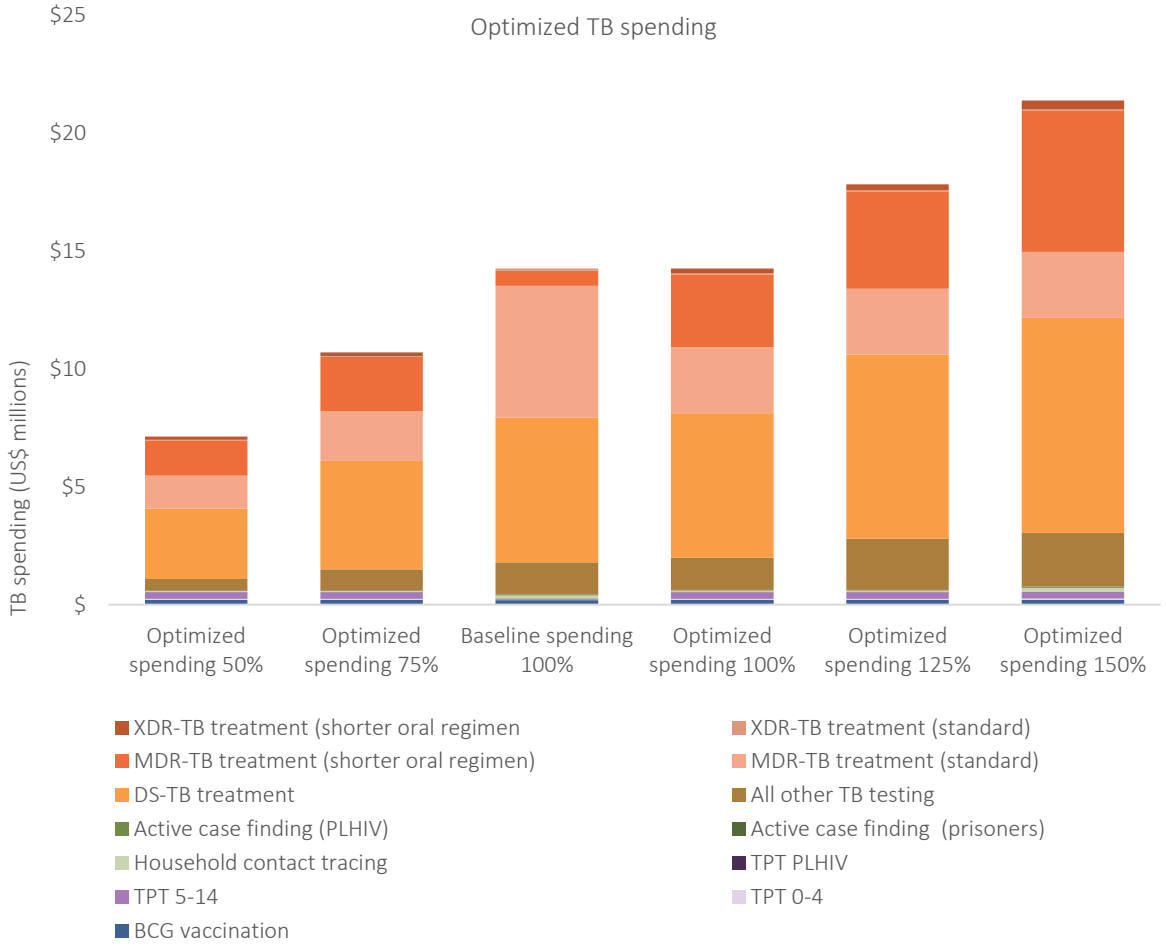


Notes: BCG, Bacillus Calmette-Guérin; DS, drug susceptible; MDR, multi-drug resistant; PLHIV, people living with HIV; TB, tuberculosis; TPT, TB preventive treatment; XDR, extensively drug-resistant.
Source: Optima TB Kyrgyz Republic model, 2023

As budgets increase, allocating more to shorter course treatment as well as expanding other TB testing is prioritized to reduce the burden of DR-TB and TB-related deaths. This expansion of other TB testing would enable a return to levels of baseline testing and diagnosis that were present in Kyrgyz Republic prior to COVID-19-related disruptions from 2020 to 2022. More budget also means more funding for drug sensitive treatment, increasing the potential number of treated DS-cases from 23,800 to 31,000 (+7,200) at 150% budget level. Investment levels above 150% are not included as there is limited impact as the modelled interventions reach close to the maximum coverage level at 150% spending.

At lower budget levels below 100%, it is imperative to ensure treatment for DS, MDR and XDR-TB are maintained, while BCG vaccination and preventive TB treatment for children 0 to 14 are recommended to be scaled up compared with the baseline spending allocations. Detailed spending by budget level can be found in Appendix E.

Figure 8. Recommended allocation of funding by program to minimize drug-resistant TB for varying budget levels (50% to 150%)



Notes: BCG, Bacillus Calmette-Guérin; DS, drug susceptible; MDR, multi-drug resistant; PLHIV, people living with HIV; TB, tuberculosis; TPT, TB preventive treatment; XDR, extensively drug-resistant.
Source: Optima TB Kyrgyz Republic model, 2023

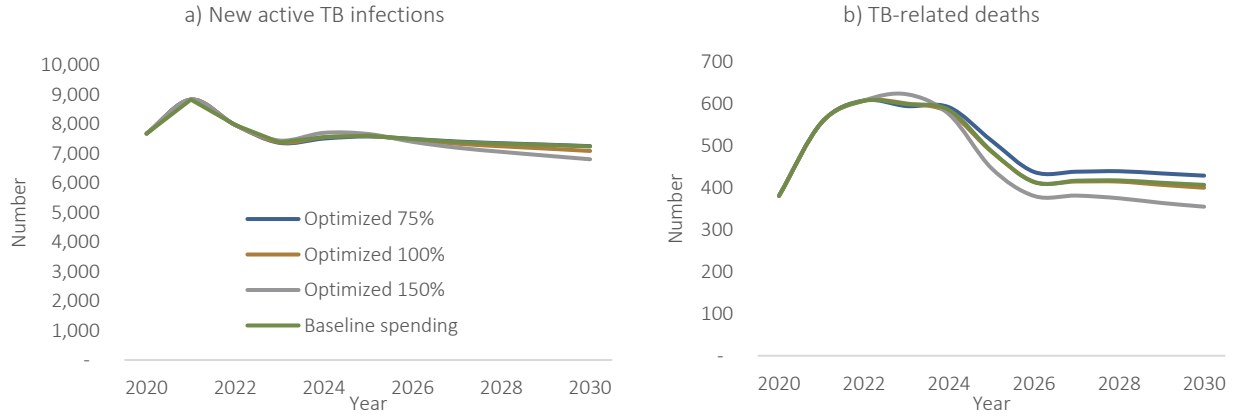
Projected impact of optimized TB spending

Optima TB estimates that with current conditions maintained, incidence of TB will 97 per 100,000 population by 2030, equivalent to 7,329 new/relapse cases.

With 100% of TB spending optimized, it is estimated that approximately 470 (1%) new TB infections and 25 (1%) TB-related deaths could be averted from 2024 to 2030 compared with if baseline spending were continued (Figure 9). The impact of optimized spending is limited because following a COVID-19 related reduction in TB spending since 2019, the 2022 baseline represents primarily treatment for people diagnosed through passive case finding and other TB testing, which is the highest priority to maintain. This presents limited opportunity for reinvestment in prevention or active case finding, although prioritizing short-course all-oral MDR-TB treatment regimens over standard MDR-TB treatment will allow additional treatment and TB preventive treatment for household child contacts of active TB cases.

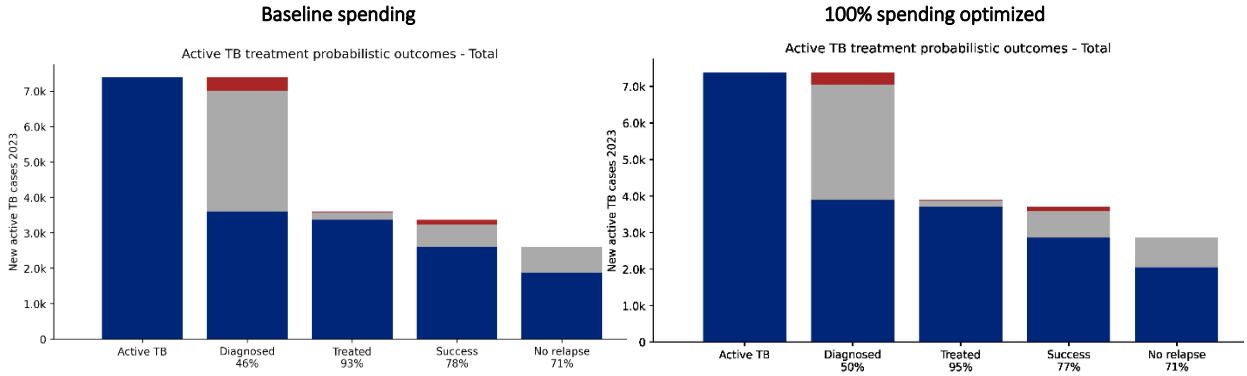
With resources increased 150% of baseline spending, 260 (-8%) deaths could be averted from 2024 to 2030. Importantly, a reallocation of resources could increase the number of people initiating treatment for DR-TB by 1,000 (17% increase). The 2023 cohort cascade could improve +4 percentage points more people diagnosed, of those diagnosed +2 percentage points more people could be treated, increasing treatment to 95% (Figure 10). This analysis did not consider treatment success to change as a result of shorter treatment regimens, therefore no impact is seen there.

Figure 9. Projected impact of optimization at varying budget levels on (a) TB incidence and (b) TB-related deaths, 2020–2030



Source: Optima TB Kyrgyz Republic model, 2023

Figure 10. Active TB probabilistic cascade in baseline spending (left) and 100% optimized spending (right) in 2024

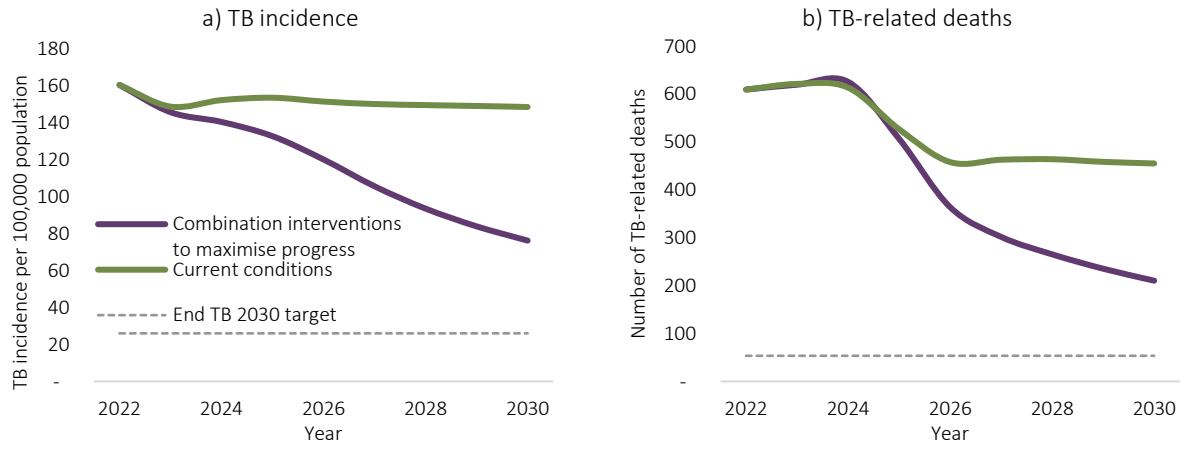


Source: Optima TB Kyrgyz Republic model, 2023

WHAT COMBINATION OF INTERVENTIONS WILL MAKE IT FEASIBLE TO ACHIEVE END TB TARGETS BY 2030?

Reaching the national TB targets may be within reach if resources are allocated optimally, however reaching the End TB targets is projected to be out of reach with the current set of interventions. A combination of targeted screening that may improve diagnosis rates, short durations of treatments and full implementation of preventive treatment and vaccination, and reductions in the social determinants of TB may be required to advance progress towards reaching End TB targets (Figure 11).

Figure 11. Projected impact of implementing rapid diagnosis and treatment toward End TB targets for reducing (a) TB incidence and (b) TB-related deaths, 2022–2030



Notes: *Current conditions* refers to continuation of baseline spending and existing interventions. *End TB 2030 target* ((dashed line) defined as percentage reduction from 2015 (14). 2015 baseline based on Optima modelled values. TB, tuberculosis.
Source: Optima TB Kyrgyz Republic model, 2023

The modelled combination of interventions included:

- Increased awareness, expanded service availability, and improved testing algorithms may allow for a reduction in the average time until diagnosis for people with active TB to less than 12 months, for all populations and all strains and smear status of active TB. Under status quo conditions, it is common for patients to delay care-seeking at clinics and diagnosis can often take more than 12 months from first symptoms, and individuals with subclinical TB may never seek care.
- Rapid treatment initiation following diagnosis for all diagnosed individuals.
- Contact tracing of diagnosed individuals and preventive treatment for all household contacts (estimated to reach up to 13% of adults and 35.5% of children with early latent TB due to recent exposure to active TB and a smaller proportion of people with late latent TB) (15, 16).
- A 20% reduction in social determinants leading to TB activation, e.g. through nutrition and other public health interventions.

Further reductions in TB incidence become more challenging even with a substantial scale-up in the rate of active case finding and preventive treatment for all contacts that reduces TB transmission to very low levels. A large proportion of progression from latent infection to active TB disease is estimated to come from people exposed more than five years previously when the

burden of TB prevalence was higher in Kyrgyz Republic, combined with relapse cases expected to be reported following a scale-up of treatment.

4 Study limitations

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

The size and profile of the TB epidemic in Kyrgyz Republic was aligned with the 2022 WHO Global TB Programme modelled estimates (1). If these estimates are revised in future years subject to emerging data, Optima TB estimates would need to be considered in context of the new estimates. The current analysis includes pulmonary tuberculosis only and excludes extrapulmonary tuberculosis to maintain consistency with previous analyses.

TB expenditure and program definitions: There was very limited data on the coverage and costs of costs of TB interventions in Kyrgyz Republic, and the latest data originated from 2016. Available TB spending data were reported in very broad expenditure areas only, while this analysis uses discrete TB interventions. Subsequently, unit costs for interventions are subject to some levels of uncertainty. There were insufficient cost data to consider the resource required to reach the End TB targets.

Resource needs for treatment of drug resistant strains were projected based on the proportion of incident drug resistant cases in 2022, but this may continue to evolve based on either suitability of new drugs to treat previously extensively drug resistant cases as per the WHO reclassification of XDR in 2021 (17), or further emergence of new drug resistance in Kyrgyz Republic.

Implementation efficiency: Detailed modelling of implementation efficiency was beyond the scope of the study, and this analysis only included considerations of implementation efficiency in a limited way. For instance, reduced drug prices (leading to lower unit costs, better efficiency and cost-effectiveness) were not modelled.

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

This analysis did not model other potential benefits of shorter treatment regimens on treatment completion, adherence and effectiveness (18). Subsequently, findings likely underestimated the positive impact of scaling up shorter treatment regimens for MDR-TB and XDR-TB.

Priority populations: Insufficient data were available to consider the burden of TB and population-specific interventions for other priority populations at increased risk of TB or with poorer health outcomes, including migrants and people living with HIV. The number of people living with HIV has doubled in Kyrgyz Republic from 2013 to 2019, so they may become a higher priority population for TB in the future. This may mean that preventive treatment for people living with HIV, though not prioritized in this analysis, could become more important in future.

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.

5 Conclusions

This allocative efficiency analysis for TB prevention and treatment in the Kyrgyz Republic highlights the necessity to invest in short-duration treatment regimens for drug-resistant TB, more targeted testing strategies among populations at higher risk of TB, and scale up of TB preventive treatment among children.

Rates of diagnosis and treatment decreased in 2020 due to COVID-19 and have not since recovered. A total 50% increase in most recent estimated spending, allocated to additional targeted TB prevention, would equate to less than a 10% increase in 2019 spending, and could enable rates of care seeking and testing to return to and exceed 2019 levels. National TB targets could be within reach if resources are allocated optimally. However, End TB targets may be out of reach by 2030 with the current set of interventions.

KEY RECOMMENDATIONS

1. Shorter treatment regimens based on Bedaquiline are more cost-effective, allowing for a larger number of people to be treated for the same amount of spending, as well as better adherence and limiting side-effects for people with TB.
2. Continued and expanded prioritization of case finding among vulnerable populations such as people living with HIV could improve diagnosis rates from 46% in 2023 to 50% in 2024.
3. Expand prevention strategies for children - including preventive treatment coverage for children 0 to 14 (+3,200 annually) and vaccinate 4,000 more children aged 0-4 annually.
4. Kyrgyz Republic may need to revisit and expand the available set of TB interventions in order to achieve further reductions in TB incidence and deaths and approach End TB 2030 targets.

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7 Appendices

APPENDIX A. OPTIMA TB MODEL OVERVIEW

A.1. Tuberculosis model structure

The Optima TB tool is based on a dynamic, population-based TB model encapsulated within an intervention and costing framework (19). The model uses a linked system of ordinary differential equations to track the movement of people among health states (Figure A1). The overall population is partitioned in two ways: by population group and by TB health state. TB infections occur through the interactions among different populations. Each compartment in Figure A1 corresponds to a single differential equation in the model, and each rate (Figure A1 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.

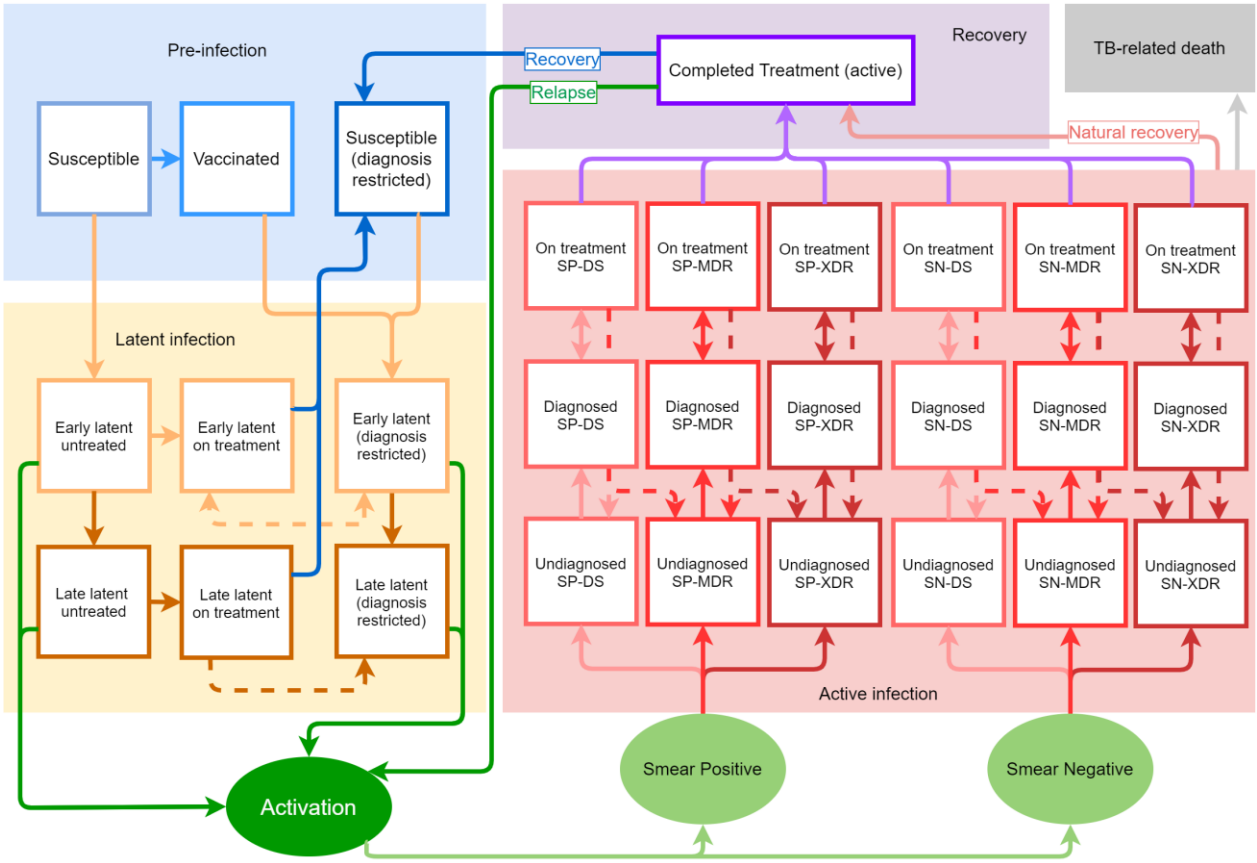
The WHO definition for incident TB cases includes both new and relapse cases. In the model, incident TB cases correspond to the following transitions between compartments (Table A1):

- 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 a new episode of TB disease after previous completion of treatment or natural recovery.

Treatment success includes 'cured' and 'treatment completion', as per the WHO definition:

- Death during TB treatment is not included in treatment failure, but is considered separately
- Treatment failure and 'loss to follow-up' during treatment are included as separate outcomes in the model.

Figure A1. Optima TB model diagram



Source: Goscé (2021)
Notes: Each compartment represents a single population group with the specified health state. Each arrow represents the movement of numbers of individuals between health states. All compartments except for "susceptible" and "vaccinated" represent individuals with either latent or active TB. Death can occur for any compartment, but TB related mortality varies between compartments. SN-DS, smear-negative drug susceptible; SP-DS, Smear-positive drug susceptible; SP-MDR, smear-positive-multi-drug resistant; SN-MDR, smear-negative multi-drug resistant; SN-XDR, smear-negative extensively drug-resistant; TB, tuberculosis.

A.2. TB Resource Optimization

Optima TB is able to calculate allocations of resources that optimally address one or more TB-related objectives (for example, impact-level targets in a country's TB national strategic plan). Because this model also calculates the coverage levels required to achieve these targets, Optima TB can be used to inform TB strategic planning and the determination of optimal program coverage levels. The key assumptions influencing resource optimization are the relationships among (1) the cost of TB interventions for specific target populations, (2) the resulting coverage levels of targeted populations with these TB programs, and (3) how these coverage levels of TB programs for targeted populations influence screening and treatment outcomes. Such relationships are required to understand how incremental changes in spending (marginal costs) affect TB epidemics. To perform the optimization, Optima uses a global parameter search algorithm, which is an adaptive stochastic descent algorithm (19).

Table A1. Overview of key Optima TB Model features and definitions

TB parameters	Model features and definitions
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 a new episode of TB disease after previous completion of treatment or natural recovery.
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 definition. Other outcomes of treatment in the model include 'loss to follow-up' during treatment, 'treatment failure', 'treatment failure with escalation of drug resistance', 'death during treatment'. Where data is reported as 'not evaluated' it may be assumed to be allocated proportionally to other compartments or based on other evidence.
Population structure, key populations and People living with HIV	Age-structured populations can be user defined Ability to specify additional key populations with defined transition rates to/from general population groups People living with HIV represented as a separate key population disaggregated by HIV treatment status

A.3. Uncertainty Analyses

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

APPENDIX B. MODEL INPUTS

B.1. Demographic inputs by sub-population group

Parameter	2022	Source or assumptions
Population sizes		
0-4	797,905	UN Population Division 2023; country-provided estimate of prison population
5-14	1,486,085	
15-64	4,039,463	
65+	301,146	
Prisoners	6,000	
Percentage of people who age into the next age category per year		
0-4	21.4%	UN Population Division 2023
5-14	9.4%	
15-64	2.2%	
Annual number of births	154,510	UN Population Division 2023
Annual non-TB death rate		
0-4	0.29%	All-cause mortality based on UN Population Division 2023
5-14	0.02%	
15-64	0.43%	
65+	6.54%	
Prisoners	0.36%	
Number of departing immigrants		
0-4	602	UN Population Division 2023. Based on net migration of -10,000 allocated based on population distribution and assumed relative likelihood of emigrating between age groups
5-14	672	
15-64	7,321	
65+	681	
Prisoners	602	

Notes: ART, antiretroviral therapy; PLHIV, people living with HIV; TB, tuberculosis; UN, United Nations

B.2. Tuberculosis notifications

Table A2. Number of notified TB infections per population group, 2022

Population group	Sputum positive			Sputum negative			Total notified
	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB	
0-4	19	16	1	32	4	0	72
5-14	67	39	1	115	9	0	231
15-64	911	568	16	1668	137	2	3302
65+	189	70	2	330	17	0	608
Prisoners	17	8	0	7	2	0	34
Total	1203	701	20	2152	169	2	4247

Notes: ART, antiretroviral therapy; DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; PLHIV, people living with HIV; XDR, extensively drug-resistant. No new data regarding smear status were available, and notifications were divided by smear status based on fixed proportions of SP versus SN from 2018.
Source: National TB Programme data, 2023

B.3. TB treatment

Active TB treatment

Table A3. Treatment outcomes, latest year

	Number of treatment initiations			Average treatment duration (days)			Treatment success			Loss to follow up			Treatment failure (no escalation)			Treatment failure (escalation to MDR/XDR)			Died		
	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB	DS-TB	MDR-TB	XDR-TB
0-4	200	80	2	209	504	600	92%	69%	62%	2%	3%	20%	4%	16%	10%	0%	0%	N/A	0%	2%	8%
5-14	713	187	5	209	504	600	92%	69%	62%	2%	3%	20%	4%	16%	10%	0%	0%	N/A	0%	2%	8%
15-64	10,110	2764	70	209	504	600	78%	69%	62%	9%	3%	20%	5%	16%	10%	0%	0%	N/A	4%	2%	8%
65+	2,034	340	9	209	504	600	78%	69%	62%	9%	3%	20%	5%	16%	10%	0%	0%	N/A	6%	2%	8%
Prisoners	94	38	1	209	504	600	88%	69%	62%	10%	0%	0%	0%	22%	18%	0%	0%	N/A	0%	2%	8%

Notes: DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; N/A, not applicable; XDR, extensively drug-resistant. Treatment initiations based on 2022. Treatment outcomes based on 2021 for DS-TB and 2019 for MDR and XDR-TB.
Source: National TB Programme, 2023.

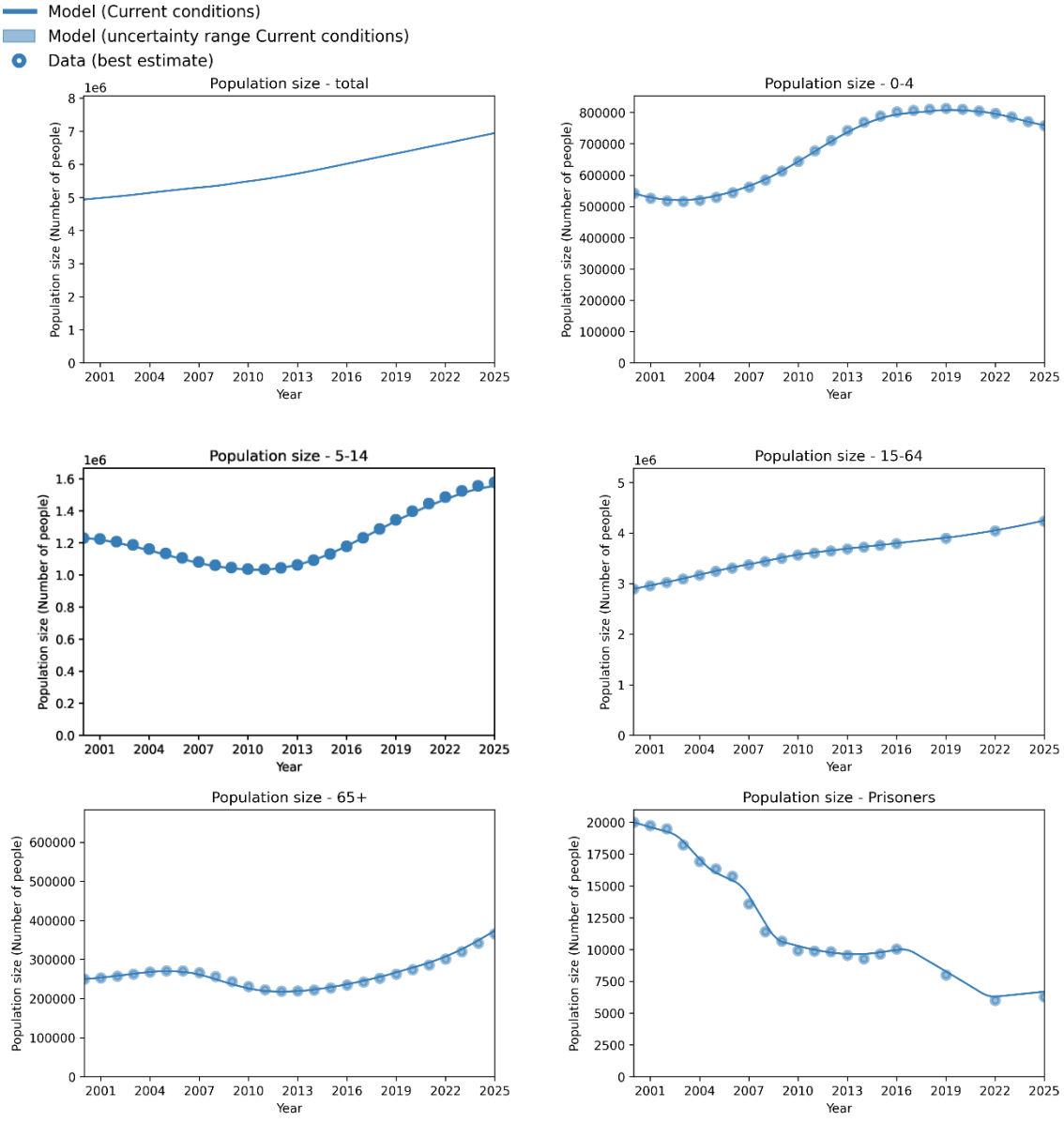
B.4. Epidemiological parameters

Description	Value	Population	Source or assumption
Vaccinations administered (/year)	143,581 (2022)	0-4	Estimated based on proportion vaccinated in 2016, National TP Programme data
Early Latency Departure Rate	0.2 0.2-0.26 0.3-0.39 0.25	All populations unless specified 15-64 65+ Prisoners	Houben (2016) - appendix of TIME model. 0.1%/year reactivation rate (0.01-0.25). Assumed higher early latency departure rate in 2021 due to COVID-19
Late Latency Departure Rate*	0.003 0.0032	All populations unless specified Prisoners	Andrews (2012)- risk of progression to active. Assumed higher rate (0.0039) among adults in 2021 due to COVID-19
Probability of Early-Active vs. Early-Late LTBI Progression*	0.2 0.15 0.18-0.23 0.2 0.25	0-4 5-14 15-64 65+ Prisoners	Andrews (2012)- risk of progression to active Assumed higher rate among 15-64 in 2021 due to COVID-19.
Infection Vulnerability Factor (Vaccinated vs. Susceptible)	0.5 1.0	0-14 15+	Mangtani (2014) (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.
Infection vulnerability factor (relative population susceptibility)	1.5-1.8 2.4-2.88 2.1-4.2 3-9 30	0-4 5-14 15-64 65+ Prisoners	A value of '1' is the default, but this is likely to be significantly higher in vulnerable populations such as people living with HIV.
Smear-positive DS-TB Infectiousness*	1.0	All populations	A value of '1' is the default
Smear-negative TB Infectiousness (Compared to SP-TB)	0.22	All populations	Behr (1999)
Duration of active TB until natural outcome (years)	3.5 3.0-3.5 2.5-3.0	All populations unless specified 15-64 65+	WHO, Tiemersma (2011)
Smear-positive untreated-TB death rate	12-20% 24-40% 18-30%	All populations unless specified 0-4 65+	WHO, Tiemersma (2011), adjusted to reflect proportion of natural outcome rather than annual rate.
Smear-negative untreated-TB death rate	2.0-3.3% 4.0-6.7%	All populations unless specified 65+	WHO, Tiemersma (2011), adjusted to reflect proportion of natural outcome rather than annual rate.

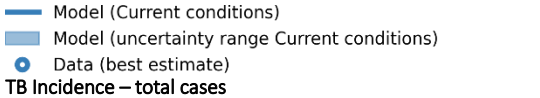
Notes: LTBI, latent tuberculosis infection; PLHIV, people living with HIV; SN, smear-negative; SP, smear-positive; TB, tuberculosis.

APPENDIX C. CALIBRATION

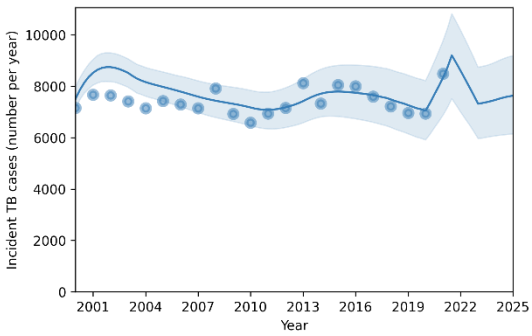
C.1. Populations size calibration figures



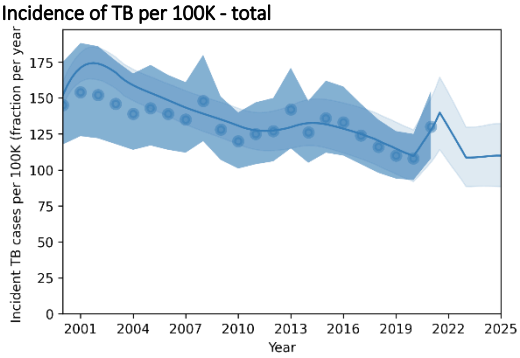
C.2. Selected TB epidemic calibration figures



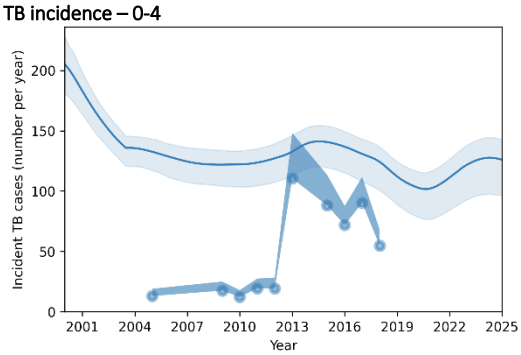
TB Incidence – total cases



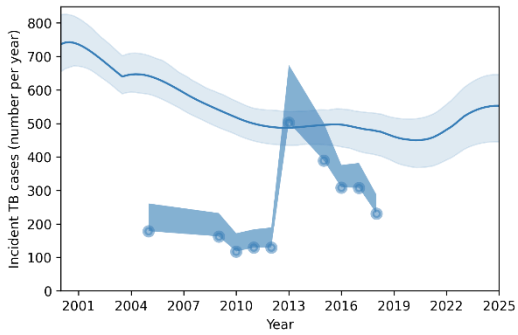
Incidence of TB per 100K - total



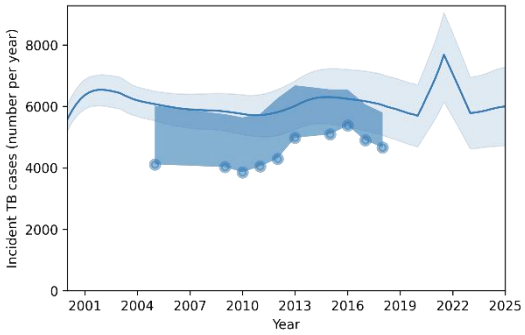
TB incidence – 0-4



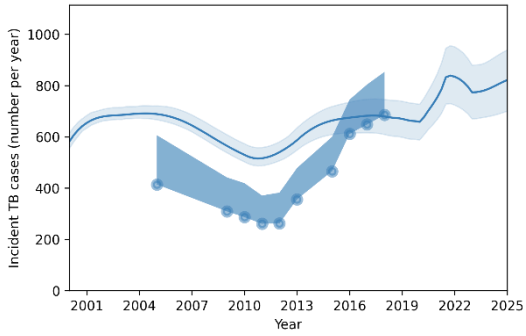
TB incidence – 5-14



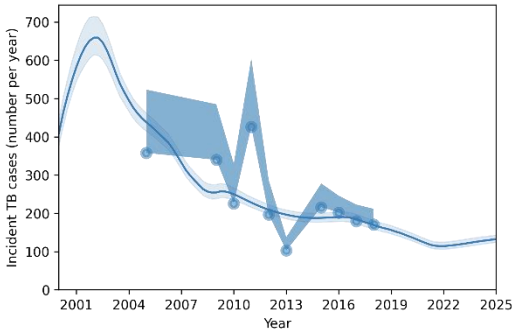
TB incidence – 15-64



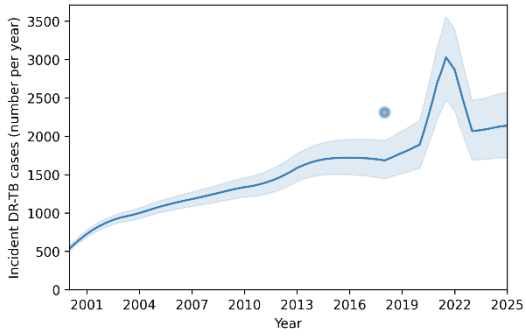
TB incidence – 65+

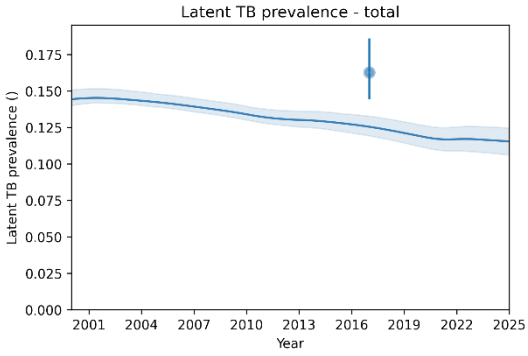


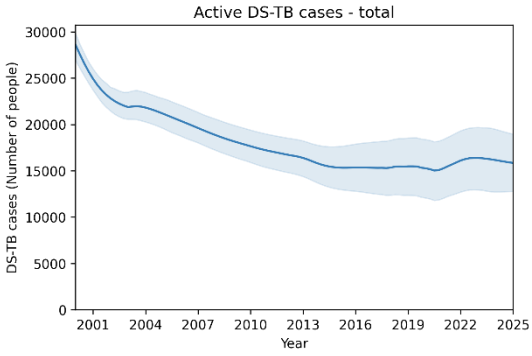
TB incidence – Prisoners

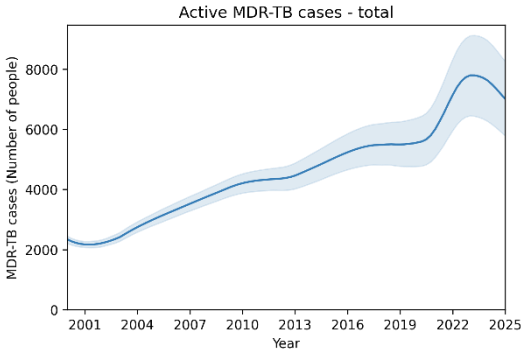


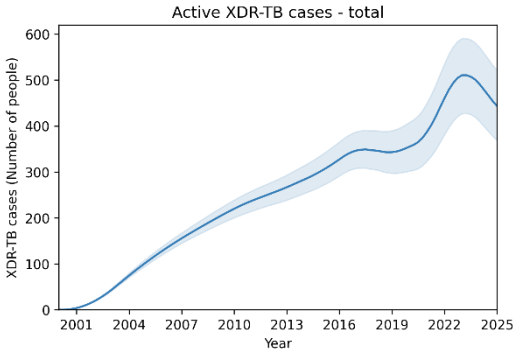
DR-TB incidence – total cases

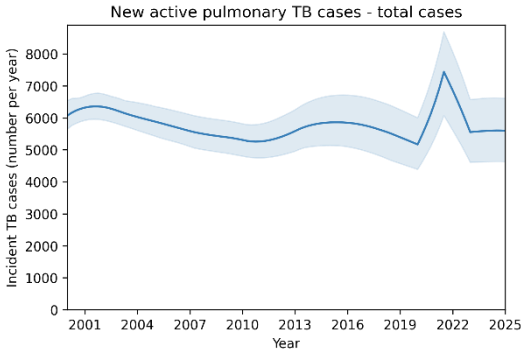


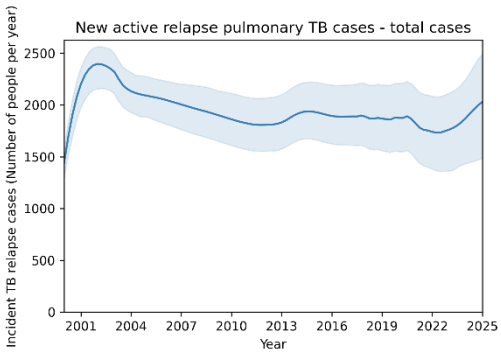

Latent TB prevalence - total
Latent TB prevalence ()
0.175
0.150
0.125
0.100
0.075
0.050
0.025
0.000
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year

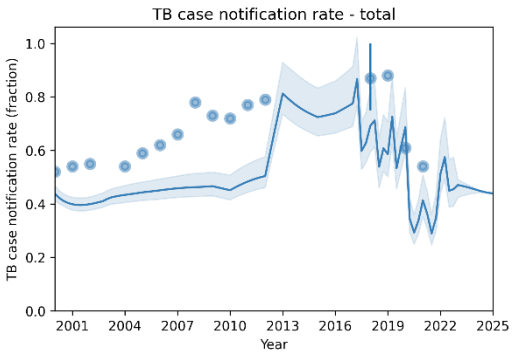

Active DS-TB cases - total
DS-TB cases (Number of people)
30000
25000
20000
15000
10000
5000
0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year

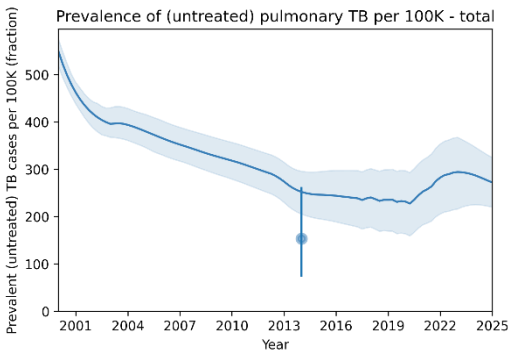

Active MDR-TB cases - total
MDR-TB cases (Number of people)
8000
6000
4000
2000
0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year

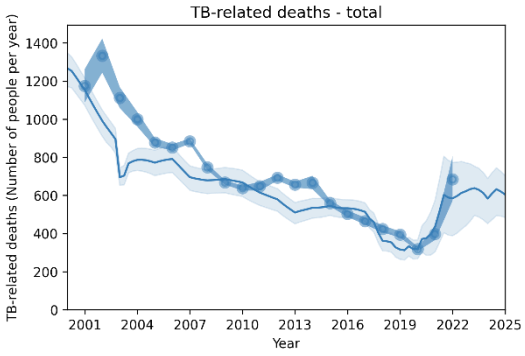

Active XDR-TB cases - total
XDR-TB cases (Number of people)
600
500
400
300
200
100
0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year

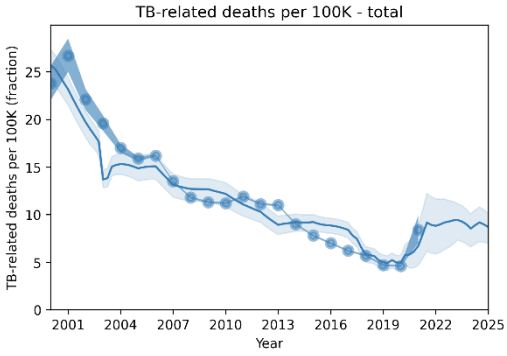

New active pulmonary TB cases - total cases
Incident TB cases (number per year)
8000
7000
6000
5000
4000
3000
2000
1000
0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year

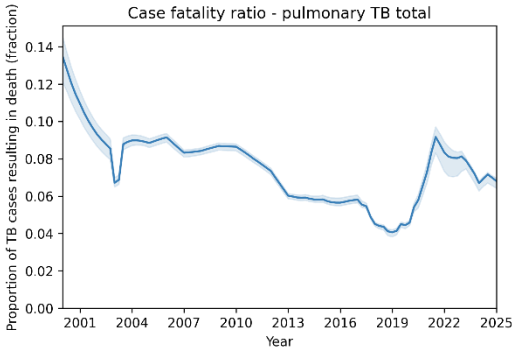

New active relapse pulmonary TB cases - total cases
Incident TB relapse cases (Number of people per year)
2500
2000
1500
1000
500
0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year


TB case notification rate - total
TB case notification rate (fraction)
1.0
0.8
0.6
0.4
0.2
0.0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year

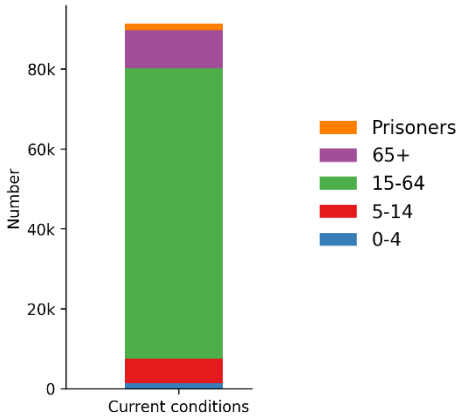

Prevalence of (untreated) pulmonary TB per 100K - total
Prevalent (untreated) TB cases per 100K (fraction)
500
400
300
200
100
0
2001 2004 2007 2010 2013 2016 2019 2022 2025
Year



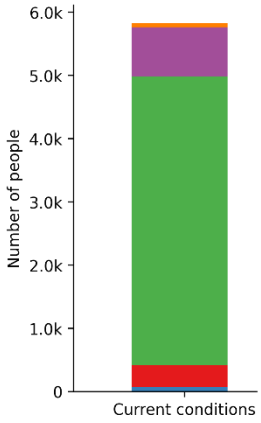




Cumulative TB incidence 2018 to 2030



Cumulative TB-related deaths 2018 to 2030



APPENDIX D. PROGRAM DEFINITIONS

D.1. Program details

Table D1. Program details and estimated unit costs for TB interventions in Kyrgyz Republic

		Unit	Unit cost (USD)	Assumptions
TB PREVENTION PROGRAMS				
BCG vaccination		Cost per infant vaccinated	$1.39	National estimate 2021 (assumed same as 2018)
TB preventive treatment (TPT) for people living with HIV		Cost per person per year	$31.49	National estimate 2021 (assumed same as 2018)
TPT (DS only) for household contacts aged:	0-4 years	Cost per person who is a contact of active TB, per preventive treatment initiation	$31.49	National estimate 2021 (assumed same as 2018)
	5-14 years		$117.41	
SCREENING AND DIAGNOSIS PROGRAMS				
Contact tracing (household)		Per person diagnosed	$504.55	Assumes same positive yield as 2018 (1.46%), National TB Programme data
Active case finding (prisoners)		Per person diagnosed	$75.10	Assumes same positive yield as 2018 (2.94%), National TB Programme data, (25)
Active case finding (PLHIV)		Per person diagnosed	$50.78	Assumes same positive yield as 2018 (6.67%), National TB Programme data, (25)
All other TB testing		Cost per person in total population to have testing available when presenting with symptoms	$0.30	Based on reported $276.46 per notification in 2018, implying total spending of $1.86M, and a unit cost of $0.30 per person (6.2M persons). Spending estimated to be $1.37M in 2021 based on reduced demand due to COVID-19 related disruptions.

TB TREATMENT PROGRAM	Unit	Total unit cost	Drug regimen cost	Inpatient costs	Outpatient costs	Monitoring/ lab costs
DS-TB treatment (standard)	Per person initiating treatment	$1597.99	$95.70	$1,285.52	$188.48	$28.29
MDR-TB treatment (standard)	Per person initiating treatment	$8114.42	$4,672.00	$2,631.02	$621.92	$189.47
MDR-TB treatment (shorter oral regimens)	Per person initiating treatment	$3765.78	$1,251.00	$1,754.01	$650.24	$110.53
XDR-TB treatment (standard)	Per person initiating treatment	$8212.27	$ 4,672.00	$2,631.02	$698.72	$210.53
XDR-TB treatment (shorter oral regimens)	Per person initiating treatment	$3811.20	Assumed based on cost of XDR-TB treatment (standard) and relative cost of shorter oral MDR-TB treatments compared to MDR-TB treatment (standard).			

Notes: DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; XDR, extensively drug-resistant.

D.2. Relative diagnosis probability by program

Relative probability of diagnosing TB by program case finding modality was informed by the number of pulmonary diagnoses reported by population group, estimated number of undiagnosed active pulmonary TB infections, number of people screened and diagnosed through each case finding modality in most recent available data from 2018, and qualitative assumptions about the effectiveness of screening modalities for reaching and diagnosing each population (Table D2).

Table D2. Relative probability that each case finding modality will diagnose each population

	0-4	5-14	15-64	65+	Prisoners	Assumptions
All other TB testing	1.85	0.85	0.9	2.75	0	Includes passive case finding which is more likely to diagnose people 65+ and 0-4 due susceptibility to infection, potential disease severity due to comorbidities, and higher care seeking.
Contact tracing (household)	4	1	1	2	0	Contact tracing prioritizes screening children 0-4, with assumed higher rates of screening for 65+ in line with screening through all other TB testing.
Active case finding (prisoners)	0	0	0	0	1	Program only diagnoses prisoners.
Active case finding (PLHIV)	0	0	1	0	0	Most people living with HIV in Kyrgyz Republic are aged 15-64.

Notes: TB, tuberculosis; MDR, multi-drug resistant; PLHIV, people living with HIV.

Relative probability of diagnosis by TB smear and strain combination was based off the relative probability by case finding modality and actual number of diagnosis by modality, adjusted to align with actual number of TB notification by population and smear/strain (Table D3).

Table D3. Relative probability of diagnosis by TB smear and strain status

	SP-DS	SP-MDR	SP-XDR	SN-DS	SN-MDR	SN-XDR
All other TB testing	1.11	0.84	0.34	1.15	0.45	0.09
Contact tracing (household)	1.11	0.84	0.34	1.15	0.45	0.09
Active case finding (prisoners)	1.94	1.18	0.47	0.48	0.63	0.12
Active case finding (PLHIV)	1.11	0.84	0.34	1.15	0.45	0.09

Notes: DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; PLHIV, people living with HIV; SP, smear-positive; SN, smear-negative; XDR, extensively drug-resistant.

APPENDIX E. DETAILED MODEL FINDINGS

Table E1. Annual TB program spending in baseline and optimized spending scenarios (USD)

	Baseline 2022	Optimized 75% spending	Optimized 100% spending	Optimized 125% spending	Optimized 150% spending
TB preventive treatment for 0-4	$6,771	$44,945	$44,891	$45,021	$44,880
TB preventive treatment for 5-14	$33,346	$269,482	$269,484	$269,686	$269,541
TB preventive treatment for PLHIV	$20,215	$15,162	$20,215	$20,215	$20,244
BCG vaccination	$194,663	$200,752	$200,055	$198,476	$210,167
Household contact tracing	$136,865	$51,326	$68,433	$68,909	$181,173
Active case finding among prisoner populations	$12,404	$4,652	$6,202	$6,202	$33,110
Active case finding among PLHIV	$13,955	$18,316	$18,060	$18,179	$17,948
All other TB testing	$1,371,541	$887,241	$1,367,233	$2,166,011	$2,269,452
DS-TB treatment	$6,140,472	$4,605,484	$6,117,406	$7,801,505	$9,108,393
MDR-TB treatment (standard)	$5,590,834	$2,096,622	$2,795,417	$2,795,417	$2,799,357
MDR-TB treatment (shorter oral regimen)	$636,418	$2,303,101	$3,085,822	$4,130,595	$5,995,735
XDR-TB treatment (standard)	$92,900	$34,839	$46,450	$46,450	$46,516
XDR-TB treatment (shorter oral regimen)	$0	$155,868	$210,715	$246,313	$379,059
Total	**$14,250,383**	**$10,687,788**	**$14,250,383**	**$17,812,979**	**$21,375,575**

Source: Optima TB Kyrgyz Republic model output, 2023

Notes: BCG, Bacillus Calmette-Guerin; DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; PLHIV, people living with HIV; XDR, extensively drug-resistant.

Table E3. Annual TB program coverage in baseline and optimized spending scenarios

	Baseline spending 2022	Optimized 75% spending	Optimized 100% spending	Optimized 125% spending	Optimized 150% spending
TB preventive treatment for 0-4	215	1,425	1,425	1,425	1,425
TB preventive treatment for 5-14	284	2,295	2,295	2,296	2,296
TB preventive treatment for PLHIV	642	481	642	642	643
BCG vaccination	140,244	144,630	144,128	142,991	151,308
Household contact tracing	271	102	136	137	358
Active case finding among prisoner populations	165	62	83	83	440
Active case finding among PLHIV	275	353	353	353	353
All other TB testing	4,571,603	2,957,339	4,557,243	6,765,323	6,765,292
DS-TB treatment	3,843	2,882	3,828	4,882	5,700
MDR-TB treatment (standard)	689	258	345	345	345
MDR-TB treatment (shorter oral regimens)	169	612	819	1,097	1,592
XDR-TB treatment (standard)	11	4	6	6	6
XDR-TB treatment (shorter oral regimens)	0	41	53	63	70

Source: Optima TB Kyrgyz Republic model output, 2023

Notes: BCG, Bacillus Calmette-Guerin; DS, drug susceptible; TB, tuberculosis; MDR, multi-drug resistant; PLHIV, people living with HIV; XDR, extensively drug-resistant.

Table E2. Projected incidence of TB per 100,000 people and TB-related deaths by spending scenario from 2022 to 2030

	2022	2023	2024	2025	2026	2027	2028	2029	2030
NEW AND RELAPSE TB CASES									
Baseline spending	7,964	7,371	7,555	7,607	7,480	7,385	7,331	7,287	7,239
Optimized 75% spending	7,964	7,359	7,506	7,575	7,490	7,404	7,345	7,299	7,247
Optimized 100% spending	7,964	7,376	7,550	7,590	7,456	7,329	7,241	7,165	7,083
Optimized 125% spending	7,964	7,395	7,597	7,600	7,426	7,267	7,134	7,015	6,890
Optimized 150% spending	7,964	7,437	7,698	7,658	7,393	7,194	7,054	6,926	6,802
TB INCIDENCE PER 100,000 PEOPLE									
Baseline spending	2,291	2,313	2,369	2,402	2,403	2,396	2,388	2,378	2,365
Optimized 75% spending	2,291	2,313	2,363	2,398	2,408	2,403	2,392	2,379	2,364
Optimized 100% spending	2,291	2,316	2,368	2,399	2,405	2,398	2,386	2,372	2,356
Optimized 125% spending	2,291	2,319	2,372	2,399	2,402	2,395	2,380	2,364	2,346
Optimized 150% spending	2,291	2,331	2,408	2,423	2,393	2,371	2,358	2,345	2,332
ACTIVE DR-TB CASES									
Baseline spending	8,043	8,263	7,826	7,244	7,077	7,007	6,894	6,772	6,664
Optimized 75% spending	8,043	8,205	7,648	6,897	6,494	6,318	6,181	6,055	5,951
Optimized 100% spending	8,043	8,170	7,568	6,811	6,394	6,200	6,033	5,876	5,744
Optimized 125% spending	8,043	8,128	7,510	6,812	6,382	6,070	5,838	5,636	5,459
Optimized 150% spending	8,043	7,930	6,953	6,126	5,885	5,743	5,563	5,393	5,248
TB-RELATED DEATHS									
Baseline spending	607	599	585	487	413	417	417	412	407
Optimized 75% spending	608	594	591	512	438	438	439	434	429
Optimized 100% spending	607	600	579	485	414	415	414	407	400
Optimized 125% spending	607	607	569	460	396	392	387	378	368
Optimized 150% spending	607	622	575	446	380	381	375	364	355
TB-RELATED DEATHS PER 100,000 PEOPLE									
Baseline spending	607	599	585	487	413	417	417	412	407
Optimized 75% spending	608	594	591	512	438	438	439	434	429
Optimized 100% spending	607	600	579	485	414	415	414	407	400
Optimized 125% spending	607	607	569	460	396	392	387	378	368
Optimized 150% spending	607	622	575	446	380	381	375	364	355

Source: Optima TB Kyrgyz Republic model output, 2023
Notes: DR, drug-resistant; TB, tuberculosis. Status quo refers to continued 100% baseline spending and allocation from 2022 to 2030.

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