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Optimizing Investments in Belarus' Tuberculosis Response

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OPTIMIZING INVESTMENTS IN BELARUS' TUBERCULOSIS RESPONSE

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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.

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ACRONYMS AND ABBREVIATIONS

AE	allocative efficiency
AIDS	acquired immune deficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral drug
DALY	disability-adjusted life year
DOT	directly observed treatment
DS	drug susceptible
ECA	Europe and Central Asia
FSW	female sex worker
GBD	global burden of disease
GDP	gross domestic product
GGHE	general government health expenditure
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IMF	International Monetary Fund
LRI	lower respiratory infection
LTBI	latent tuberculosis infection
MDG	Millennium Development Goal
MDR	multi-drug resistant
NASA	National AIDS Spending Assessment
NHA	national health accounts
NTD	neglected tropical disease
PLHIV	people living with HIV
PWID	people who inject drugs
RSPC MT	Republican Scientific and Practical Centre for Medical Technologies
RSPC PT	Republican Scientific and Practical Centre for Pulmonology and Tuberculosis
SDG	Sustainable Development Goal
STI	sexually transmitted infections
TB	Tuberculosis
THE	total health expenditure
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme
UNGASS	United Nations General Assembly
USAID	United States Agency for International Development
US$	United States dollar
WHO	World Health Organization
XDR	extensively drug resistant
YLL	years of life lost

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KEY MESSAGES

- Despite progress made in reducing TB incidence and deaths, Belarus' TB response continues to face challenges, in particular in relation to drug resistant TB. **The current TB response and allocation of resources—if continued—would sustain a moderate decline of the TB epidemic, but would be insufficient to achieve national and global TB targets set for 2020 and 2035.**
- The allocative efficiency study presented in this report identified potential for reallocation of resources. The same budget available for TB-related activities in 2015 (US$ 61.8 million) could,—if allocated optimally—achieve the following changes by 2035:
  - **Reduce prevalence in the general adult population by up to 45%;**
  - **Reduce the total number of TB deaths by up to 60%;**
- In order to achieve these changes specific reallocations are required in relation to how TB programs are delivered. **Transitioning from hospital care to ambulatory care could free up approximately 40% of TB treatment cost for reallocation to higher-impact programs.** Additional resources could be freed up in the area of involuntary isolation department treatment, the service modality with the highest unit cost, in palliative care and in mass screening.
- **Resources freed up by changing treatment modalities would need to be invested in selected higher-impact interventions and delivery solutions.** These include provision of incentives for providers of ambulatory TB care, procurement of new, more efficacious drug regimens for MDR-TB and XDR-TB, scale up of rapid molecular diagnostics, enhanced active case finding among high-risk populations and enhanced contact tracing.
- **Findings of this study can inform the reform of TB care and TB care financing in Belarus as well as expanded pilots of these reforms at Oblast (province) level.**

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EXECUTIVE SUMMARY

This report summarizes the findings of an allocative efficiency study of Belarus' Tuberculosis (TB) response, which was conducted using the Optima-TB model in 2016-17.

TB EPIDEMIC SITUATION AND RESPONSE

TB incidence, active TB prevalence and TB-related deaths declined in Belarus in the period between 2000 and 2015, while the relative share of multi-drug resistant (MDR) and extensively drug resistant (XDR) TB increased during that same period. Belarus' TB response has achieved treatment success rates of 88% for new and relapse cases (2014 cohort), 54% for multi-drug resistant TB (2013 cohort) and 38% for extensively drug resistant TB (2013, cohort). (WHO 2017b). Ambitious targets have been set nationally including a 35% reduction in TB related deaths, a 12% reduction in TB incidence and an increase in MDR-TB treatment success to 75% by 2020. Globally the End-TB strategy aims to reduce TB deaths by 95% and TB incidence by 90% (or below 10/100,000) by 2035.

Epidemic projections made in the Optima-TB model suggest that with the current level of TB spending (US$61.8 million in 2015) and the current allocation of resources to different TB response interventions, TB incidence, prevalence and deaths would continue to decline moderately in Belarus up to 2035, but 2020 national targets and global milestones as well as 2035 End-TB targets would be missed.

ALTERNATIVE TB RESPONSE SCENARIOS

Mathematical modelling analyses suggest that alternative program scale up scenarios and different service delivery modalities could improve outcomes of the TB response:

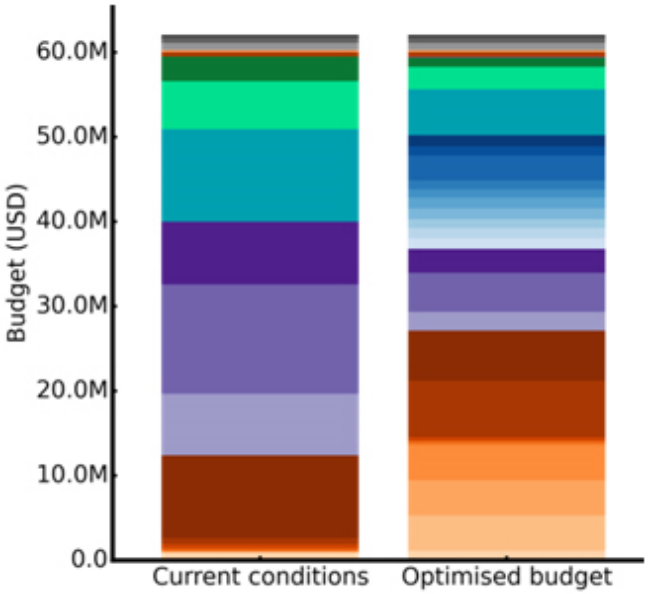
- Scaling up diagnosis and treatment to 90% coverage by 2020 is projected to avert 40% of active TB infections and 27% of expected TB related deaths compared with current coverage by 2020. Scaling up to 95% treatment coverage by 2035 is projected to avert 52% of active TB infections and 53% of expected TB related deaths compared with current coverage.
- A shift from the current model of hospital-based care to a model of extended ambulatory care would reduce TB treatment cost by up to 40% with the same treatment outcomes. Data from a global review suggests that ambulatory care enhanced by incentives has improved outcomes by approximately 16% in other settings. (Nguyen 2016)
- With current treatment success rates for extensively drug resistant (XDR) TB, even increased diagnosis and treatment coverage for XDR-TB, would only lead to moderate reductions in XDR-TB. If treatment success rates can be improved through introduction of new drugs such as bedaquiline, clofazimine and linezolid, this could reduce the prevalence of active XDR-TB by more than half by 2035 compared to scale up with current drugs.
- Current rates of TB diagnosis could be achieved more cost-efficiently by changing the mix of screening modalities and reducing the coverage of mass screening, while increasing active

case finding among key populations such as people living with HIV, people who inject drugs, homeless populations, people with problematic alcohol use and diabetes as well as contact tracing.

OPTIMIZED ALLOCATIONS

Optimization analysis was carried out using a formal mathematical algorithm to establish, which mix of TB response interventions is expected to produce the largest reductions in TB incidence, prevalence and deaths. Figure ES.1 shows current allocations of resources and the optimized allocation of resources.

Figure ES.1 Current allocation of TB resources and optimized allocations to minimize TB incidence, prevalence and deaths



Source: Populated Optima-TB model for the Belarus.

The optimized budget allocation differs from current allocations across several different areas. The allocation to several program areas would decrease by more than 50% each. This includes involuntary isolation department treatment, hospital-based treatment modalities, mass-screening and palliative care. In the optimized allocation, funds are reallocated to incentivized ambulatory care, new MDR- and XDR-TB drug regimens, rapid-molecular testing and enhanced /incentivized contact tracing and active case finding among key populations.

By 2035, optimized allocation of resources would reduce adult TB prevalence by 45% in comparison to current allocations. In addition, the optimized allocation would also reduce TB related deaths by 60% in comparison to current allocations, and by 70% compared to 2015 levels.

CONCLUSIONS AND RECOMMENDATIONS

Based on the analyses conducted, 13 conclusions and recommendations were formulated (see Chapter 7 for details):

1. **Transitioning from hospital-focused to ambulatory treatment modalities** could reduce the cost of TB treatment by up to 40% and free up resources for reallocation to high-impact interventions.
2. **Strengthening ambulatory care through incentives** for health worker outreach support and for patients' adherence through a mix of delivery solutions is likely to improve treatment outcomes.
3. Enhanced ambulatory care requires a **reform of tuberculosis care financing** to replace bed-based payment modalities by results-based modalities based on patient-centred care.
4. Since **involuntary isolation department treatment is the most expensive modality** for delivering treatment, reducing and over time phasing out this delivery modality, would free up resources for other high-impact interventions.
5. **Mass screening and screening of obligatory groups are the treatment modalities with the lowest testing yield** and reducing their coverage in favor of more targeted screening approaches could increase diagnostic yield.
6. The **contribution of contact tracing and active case finding among key populations** to the total number of TB cases identified could be increased by introducing service delivery modalities using provider incentives.
7. The **scale up of rapid molecular diagnostics** will be an important step towards reducing time from screening to treatment initiation and thereby reduce the infectious period.
8. Reallocating savings from palliative care and involuntary isolation department treatment to **new drug regimens** including bedaquiline, linezolid and clofazimine is projected to improve treatment outcomes, in particular for XDR-TB.
9. Introducing **alcohol screening for all adult TB patients and provision of a brief alcohol intervention** for TB patients with problematic alcohol use, are low-cost interventions with the potential to improve treatment adherence and outcomes.
10. The number of TB notifications in prisons has declined substantially, but **enhanced TB care and screening for prisoners post-release** remains a priority.
11. Considering the country's growing HIV epidemic, there is need for **strengthened linkages between HIV and TB services**.
12. Reaching the 2035 target of a reduction in TB incidence to less than 10/100,000 would require addressing **latent TB**, a major source of new cases, post 2020.
13. **Closing strategic information gaps through operational research**, will be essential in informing Belarus' TB care reform.

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1. INTRODUCTION: WHY ALLOCATIVE EFFICIENCY ANALYSIS NOW?

1.1 NECESSITY FOR ALLOCATIVE EFFICIENCY

The adoption of the sustainable development goals (SDGs) agenda (UNGASS 2015) and the World Health Organization's new End TB Strategy (WHO 2015a) have introduced a new era for national TB responses. While the Millenium Development Goals (MDGs) had aimed to halt and reverse the epidemics of HIV, TB and Malaria, the SDG agenda sets out a more ambitious pathway towards ending TB. (Lönnroth 2016) This has been translated into ambitious targets of reducing TB incidence by 80% (or to less than 20/100,000) and TB deaths by 90% by 2030. The WHO End TB strategy has set additional targets with a longer time frame of 2035 aiming for a 90% reduction in TB incidence (or <10/100,000) and a 95% reduction in TB deaths.

The 2015 Global TB report by WHO (WHO 2015b) demonstrated that TB responses needed to change if these targets were to be achieved. The decline in global TB incidence was negligible (then estimated at just 1.5% annually), despite doubled TB funding in 2015 compared to 2006. It was also reported that there were now more TB deaths than AIDS deaths, and that there was a large gap between knowledge of what works and implementation.

The new frameworks imply that national TB responses are faced with the need to scale up programs for screening, diagnosis and treatment to achieve substantially higher coverage and treatment success rates than in the past. Since the vast majority of TB epidemics affect low- and middle income countries, national TB responses are commonly faced with resource constraints. While enhanced domestic and international resource mobilization for health continues to be desirable, international assistance for disease response programs has stagnated in recent years and domestic financing remains constrained by competing health, social and other public financing priorities. Focused design and efficiency in TB program delivery are therefore essential to ensure that programs can do more with what is available.

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. Within the broader support towards enhancing efficiency and effectiveness of health programs, the concept of allocative efficiency refers to the maximization of health outcomes, with the least costly mix of health interventions.[1] .

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 is currently being expanded

[1] Technically, allocative efficiency can be achieved within a fixed budget envelope (maximize impact with given amount of money); or within defined impact targets (minimize cost to achieve a given impact).

towards TB, hepatitis, nutrition, malaria and child health. TB allocative efficiency studies generally try to answer the question, "*How can TB funding be optimally allocated to the combination of TB response interventions that will yield the highest impact?*"

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 optimized TB resource allocation.

An allocative efficiency study of Belarus' HIV response was carried out and informed national strategic planning and the country's Global Fund application in 2015. (World Bank; Government of Belarus 2016) On the basis of this previous collaboration it was agreed to carry out a similar analysis of the national TB response in order to support Belarus in its decision-making on strategic TB investments in the coming years.

1.2 TUBERCULOSIS IN THE CONTEXT OF OVERALL DISEASE BURDEN

Belarus' overall burden of disease is characterized by a high proportion of deaths and years of life lost attributable to non-communicable diseases, in particular ischemic heart disease, stroke and cancer. TB accounts for 0.3% of all deaths, 0.4% of all disability adjusted life years and 0.5% of all years of life lost. Although the contribution to overall disease burden is relatively small, TB remains one of the three major causes of death related to communicable diseases, in addition to HIV and lower respiratory infections. The country's overall success in reducing the burden of preventable communicable diseases therefore heavily depends on the results achieved in the responses to TB and HIV.

1.3 FINANCING OF TB IN THE CONTEXT OF HEALTH CARE FINANCING

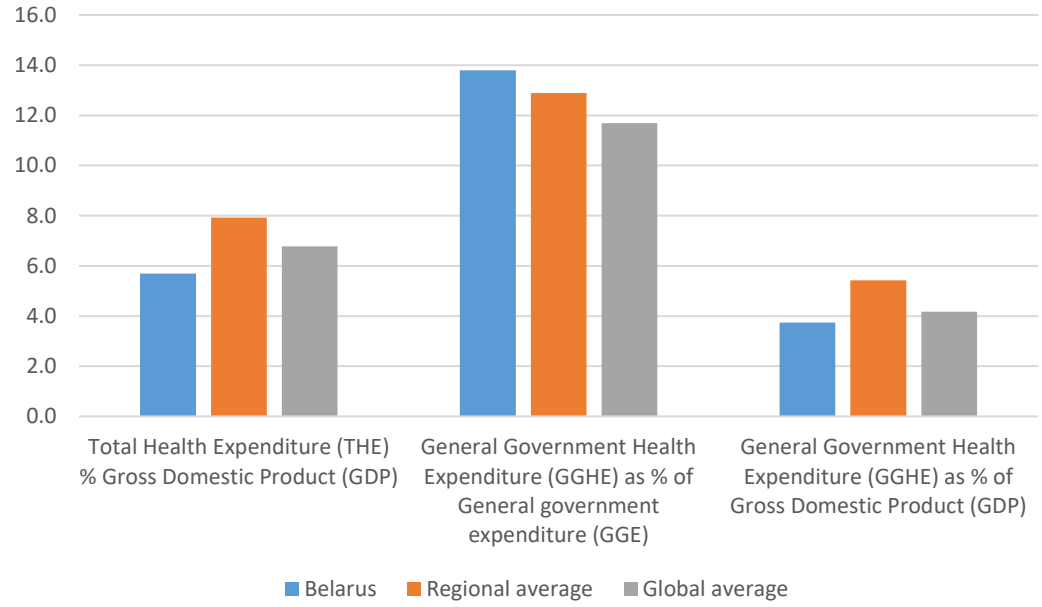
Table 1.1 provides a summary of health spending in Belarus according to the WHO national health accounts database. Although health spending per capita in Belarus increased substantially from US$75 to US$450 between 2000 and 2014, total health expenditure relative to GDP remained fairly stable since 2000 and stood at 5.7% of GDP in 2014, which is below regional (7.9%) and global (6.8%) averages (WHO 2017a). In 2014, the majority of health expenditure (65.8%) was government funded and private health expenditure was mostly out-of-pocket spending. Government health spending relative to GDP declined since 2000 and was 3.7% of GDP in 2014, which is also below regional and global averages. Nevertheless, as illustrated in Figure 1.1, the share of Belarus' government health spending relative to total government spending was 13.8%, which is above regional and global averages of 12.8% and 11.7% (WHO 2017a). In other words, the relatively low level of government health spending relative to GDP is not due to a low allocation to health within government resources, but needs to be seen in the context of the lower tax revenue collection of 14.7% compared to many countries in the region and to the global average of 15.8% in 2015 (World Bank 2017).

Table 1.1 Overview of health expenditure in Belarus, 2000–14

Belarus	2000	2005	2010	2011	2012	2013	2014	Regional average*	Global average**
Total health expenditure vs. GDP									
Total Health Expenditure (THE) % Gross Domestic Product (GDP)	6.1	6.9	5.6	4.9	5.0	6.1	5.7	7.9	6.8
General Government Health Expenditure (GGHE) as % of Gross Domestic Product (GDP)	4.6	5.0	4.3	3.5	3.9	4.0	3.7	5.4	4.2
Health expenditure by source									
General Government Health Expenditure (GGHE) as % of Total Health Expenditure	75.5	72.9	77.7	70.5	77.2	66.2	65.8	67.4	60.1
Private Health Expenditure (PvtHE) as % of Total Health Expenditure (THE)	24.5	27.1	22.3	29.5	22.8	33.8	34.2	32.4	39.9
General Government Health Expenditure (GGHE) as % of General government expenditure (GGE)	10.1	10.5	13.4	13.0	13.2	13.9	13.8	12.9	11.7
Per capita spending									
Total Health Expenditure (THE) per Capita in US$	75.0	215.9	322.5	293.1	336.0	465.2	450.2	2288.1	1140.2
Total Health Expenditure (THE) per Capita in Int$ (Purchasing Power Parity)	356.5	666.9	854.3	816.2	859.5	1068.2	1031.0	2265.1	1305.8
General Government Health Expenditure (GGHE) per Capita in US$	56.6	157.5	250.6	206.7	259.3	308.1	296.2	1754.6	823.4
General Government Health Expenditure per Capita in Int. $ (Purchasing Power Parity)	269.1	486.4	663.7	575.7	663.4	707.6	678.3	1694.9	910.4

Source: Authors
*Note: * Regional average refers to countries in Europe and Central Asia (2014)*
*** Global average refers to 192 countries including in the WHO national health accounts database (2014)*
Source: Table prepared by authors based on WHO global health expenditure database (WHO 2017a).

Figure 1.1 Health expenditure in Belarus compared to regional and global averages (2014)

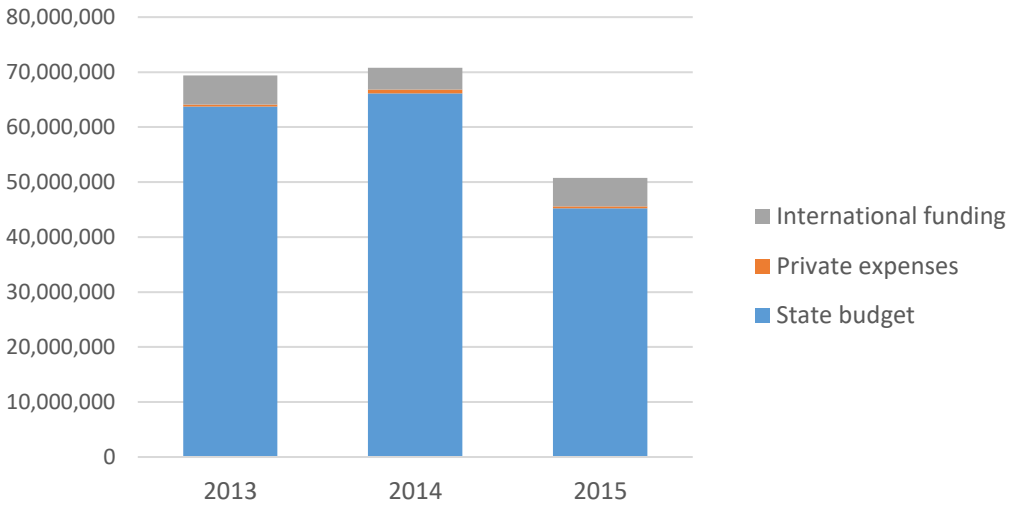


Source: Figure prepared by authors based WHO global health expenditure database (WHO 2017a).

1.4 FINANCING OF THE TB RESPONSE IN BELARUS

Total spending in the national TB program in Belarus declined from US$69.3 million and US$70.8 million in 2013 and 2014 to US$50.8 million in 2015 (Figure 1.2). This decline was recorded despite an increase in TB spending in national currency from 616.2 billion BYR to 808.7 billion BYR and can be attributed to the declining rate of exchange between the Belarusian Ruble and the US Dollar. The majority of TB funding in Belarus is provided from the state budget. In 2015, the state budget accounted for 89.1% of TB spending, private expenditure for 0.6% and international funding for 10.3%. In addition, as outlined in more detail later in this report, an estimated US$11 million were allocated to other TB related health services such as screening programs in 2015, which are not part of the TB program expenditure but accounted for in other parts of the health system.

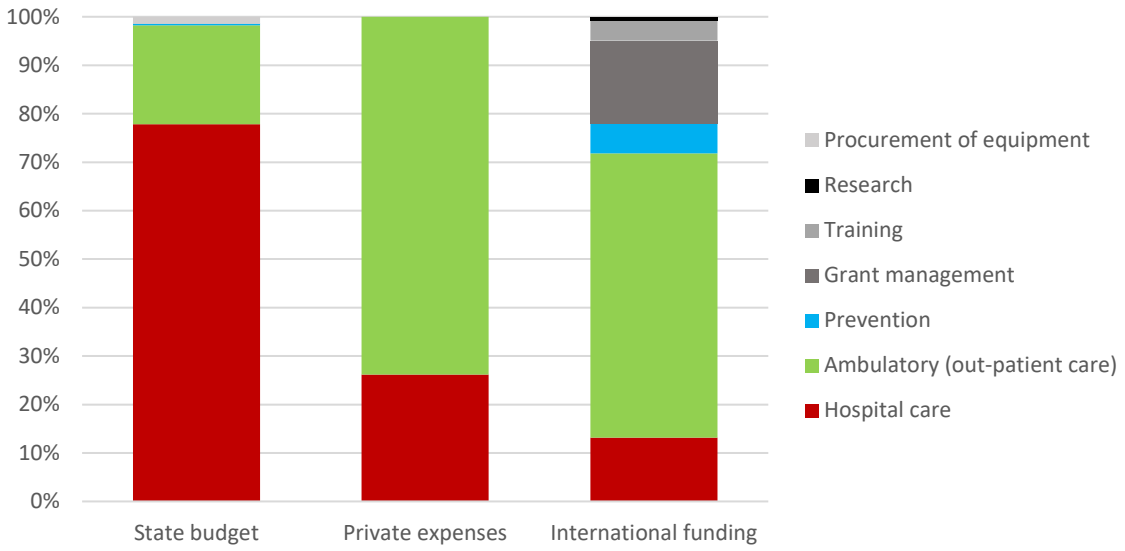
Figure 1.2 Belarus: TB spending by year and source of financing, US$ (%)



Source: WHO national health accounts, TB sub-accounts

Figure 1.3 illustrates the thematic focus of TB program spending by funding source. State budget funding for TB is primarily allocated to hospital care and secondarily to ambulatory care. Private expenses primarily cover out-patient care. International funding is also primarily allocated to ambulatory care with a focus on new diagnostic and treatment options, while also including spending on grant management, hospital-care and prevention.

Figure 1.3. Belarus: TB spending by source of financing and thematic focus, 2015 (%)



Source: WHO national health accounts, TB sub-accounts

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2. WHAT ARE THE KEY QUESTIONS AND WHICH METHODS WERE USED TO ANSWER THEM?

This section outlines the main steps taken and tools applied to carry out the analyses presented in this report. Additional details are available in appendices A and B.

To support the national strategy priorities and assist Belarus in meeting its set targets, this report answers the following questions:

1. What are the current trends in Belarus TB epidemic?
2. What is the impact of current tuberculosis spending?
3. What is the expected future impact of different program implementation scenarios?
4. What is the projected future trajectory of Belarus' TB epidemic with and without investment in specific programs, or with/without attaining program-specific targets?

The scenarios will cover the following aspects:

- Treatment scale up
- Hospital-focused vs. ambulatory treatment
- Enhanced XDR treatment
- Different TB case finding modalities

4. How close are we to National Strategic Plan targets under current funding?

Over the National Strategic Plan period, how close will Belarus get to their National Strategic Plan's disease-related targets:

a. With the current volume of funding, allocated according to current expenditure?

b. With the current volume of funding, allocated optimally?

Additional more detailed questions on epidemiology and cost-effectiveness also are answered in this report.

2.1 OPTIMA MODEL

To carry out the analyses, the team used Optima-TB, a mathematical model of TB transmission and disease progression integrated with an economic and program analysis framework. Optima-TB incorporates evidence on biological transmission probabilities, detailed infection progression and population mixing patterns, in a compartmental 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 into drug susceptible (DS), multi-drug resistant (MDR) and extensively drug resistant (XDR). A more detailed illustration of the compartmental model structure is included in Appendix A.

In consultation with national experts and in the absence of a TB prevalence survey, Optima-TB was calibrated to Belarus' TB epidemic primarily based on data on TB case notifications and registered TB deaths.

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

Using the relationships among cost, coverage, and outcome in combination with Optima's epidemic module, it is possible to calculate how incremental changes in the level of funding allocated to each program will impact on overall epidemic outcomes. Furthermore, by using a mathematical optimization algorithm, Optima-TB is able to determine an optimized allocation of funding across different TB programs. Additional details about Optima-TB are included in appendices A and B.

2.2 ANALYTICAL FRAMEWORK

In partnership between the Government of Belarus, World Bank, Optima Consortium of Decision Sciences, the Burnet Institute and University College London, it was agreed to carry out the region's first Optima-TB study in Belarus. An in-country study group was formed involving RSPC PT, RSPC MT, WHO and the World Bank. Country-specific objectives of the analysis and parameters were outlined in a Scope of Work document. Epidemiological, program, and cost data were collected by in-country experts in collaboration with international experts using an adapted MS-Excel-based Optima data entry spreadsheet. In order to establish baseline spending on TB, 2015 expenditure data from TB sub-accounts within the WHO national health accounts were used. This data was triangulated with other unit cost data to establish estimated TB spending by intervention. Input data, model calibration and cost-coverage-outcome relations were reviewed and validated by the in-country study group. The team then consulted with government experts and other in-country partners on the preliminary results and summarized them in this report.

Table 2.1 Modelling parameterization

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+
	PLHIV	Males and Females aged 15-64 living with HIV
	Prisoners	Male and Female prison populations aged 15-99. Assumed to be equivalent to the total national prison population

Table 2.1 Modelling parameterization (continued)

Program expenditure areas defined in the model and included in optimization analysis	**Hospital Focused Modality**	**Current treatment delivery for DS/MDR/XDR-TB implemented in Belarus. Equivalent to the number of hospitalization days for a given 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
	Incentivised Ambulatory Delivery Modality	Incentivised outpatient treatment. Similar to the ambulatory modality, but incorporates financial incentives (food packages, outcome based financing) initiative from the Mogilev District
	Short-Course Regimen for MDR-TB	Short-course regimen considered for both Ambulatory and Incentivised Ambulatory modalities. Targets only those 9% of MDR-TB patients who are eligible for short-course treatment, according to the GLC Report (Gurbanova 2017) and country experts
	New and Repurposed M/XDR-TB Drugs	Given the precautions necessary to prevent the development of resistance to new/repurposed drugs, these regimens are only considered for the incentivised ambulatory modality to MDR/XDR-TB patients
	Involuntary Isolation for M/XDR-TB	The country has decreased involuntary isolation and is planning to further reduce this practice. The modality has been included to assess the impact of 50% and 80% reductions in isolation
	Prison TB-Treatment	Prison based treatment of DS-TB, MSR-TB and XDR-TB
	Palliative Care Services	Palliative care targeting M/XDR-TB patients with a history of non-adherence, extended drug-resistance and adverse reactions
	Isoniazid Preventative Therapy	Treatment of Latent-TB Infections with 6-months Isoniazid therapy to prevent the progression to active TB in general population TB-contacts and the PLHIV population
	BCG Vaccination	Vaccination with Bacillus Calmette-Guérin targeting the 0-4 population
	Passive case finding	Diagnosis package for people who present to the health facility with symptoms; includes a Chest X-ray, X-pert, two Sputum Smear Microscopies and two Culture tests or culture couple with LPA
	Mass Screening	Current practice of mass screening the general population with chest X-rays
	Active Case Finding	Active case-finding by targeted screening of high-risk groups (Alcohol, PWID, PLHIV, HCWs, Prisoners, etc.) with chest X-rays
	Incentivised Active Case-Finding	Active case-finding in high-risk groups, incentivised through financial incentives and rewards in order to improve the yield
	Contact Tracing	Investigation of TB-contacts and follow-up treatment with IPT preventative therapy for suspected LTBI
	Incentivised Contact Tracing	Investigation of TB-contacts, incentivised through financial incentives and rewards in order to improve the yield

Table 2.1 Modelling parameterization (continued)

Expenditure areas not optimized	The components of TB spending that will not be included in the optimization analysis include:	Some program areas have not been optimized but instead were fixed at agreed amounts. This was done for different reasons including either due to a program's effect on TB incidence, morbidity or mortality not being clear, or because the expenditure was central systems expenditure that is essential for several program areas, or because no country data to estimate effects was available. In addition, some cost categories like specific diagnostic tests or the brief alcohol interventions only account for a small proportion of the TB response budget and would have been too complex to model.
	Solid Culture Testing	Cost of solid culture testing to identify and confirm resistance types of MDR-TB and XDR-TB
	Line Probe Assay (LPA)	Cost of LPA testing to identify and confirm resistance types of MDR-TB and XDR-TB
	Tuberculin Skin Test (TST)	Cost of conducting TST test to diagnose LTBI
	Management	Administrative costs
	Procurement	As per TB sub-accounts of NHA
	Other costs	As per TB sub-accounts of NHA
	Alcohol Interventions	Cost of alcohol programmes to help improved adherence to TB treatment regimens estimated based on internationally available cost-estimates
Time frames over which the optimization was considered	2000	Starting year for data entry
	2016–20	Government's timeline for achievements of national strategic plan targets
	2020/2025	Interim accelerated and standard timeline for international targets set by End-TB Strategy
	2030	Time frame for achievement of SDG targets
Baseline scenario funding	As per TB sub-accounts of NHA	Total spending on TB in 2015 as per TB sub-accounts of the NHA plus TB related costs not recorded as part of the TB program

Source: Authors.

Based on program spending per person reached, cost-coverage outcome relations were developed. Calibrations and cost-coverage outcome relations were produced in collaboration with national experts and are further explained in appendix B, while unit costs are included in appendix C.

2.3 NATIONAL TARGETS AND HOW THEY WERE TRANSLATED INTO OPTIMA

The strategic goals under the National Strategic Plan (NSP 2015-2020) and National Tuberculosis Program (NTP) include: i) to decrease the 2020 TB notified cases rate by 12 percent points compared to the 2013 baseline, or to reduce annually the TB notified cases rate by 2 percent points; ii) to reduce the number of notified MDR-TB cases by 12 percent points by 2020 compared to the 2013 baseline; and iii) to reach a 75 percent treatment success rate among MDR-TB patients by 2020. The resource needs of the TB program (2016-2018) were estimated at US$ 201.7 million with a remaining financial gap of US$ 11.9 million.

In the analysis of long-term trends, global targets were used in the study including 2025 milestones, 2030 SDG goals and 2035 End-TB Strategy targets. (Table 2.2)

Table 2.2 National and global targets

Indicator	Baseline value (2015 or most recent year)	Targets			
		2020 (NSP)	2025 (Milestone)	2030 (SDG)	2035 (End TB)
Reduction in number of TB deaths	730 (excl. PLHIV) 80 (among PLHIV)	35%	75%	90%	95%
Reduction in TB incidence rate (per 100,000)	51.9/100,000 (2013)	12% (NSP*) 20% (WHO)	50%	80% (<20/100,000)	90% (<10/100,000)
Reduction in number of notified MDR-TB cases		12% (NSP)	30%	50%	75%
Treatment success rate among MDR patients	54%	75%	80%	85%	90%

Source: Authors.
Note: * refers to notified cases rate

2.4 LIMITATIONS OF THE ANALYSES

Similar to any mathematical modelling analysis, this study is based on a number of assumptions, which necessarily imply specific limitations:

- As for all complex modelling studies of diseases, there are some gaps in data. The majority of countries globally including Belarus do not have actual TB prevalence surveys. This implies that routine data on TB notifications formed the basis for estimating disease burden, which implies that estimates on the size of the undiagnosed populations had to be made.
- Unlike HIV, there are no standardized national TB spending assessments undertaken in countries and current templates for national health accounts including TB sub-accounts do not provide sufficiently detailed breakdowns of costs by intervention area. As mentioned, above, unit cost assumptions based on national and international spending data had to be made.
- The modeling approach used to calculate relative cost-effectiveness among programs includes assumptions concerning the impact of increases or decreases in funding for programs. These assumptions are partially based on costs per person reached and observed ecological relationships among outcomes of program coverage and the amount of money spent on programs in the past or in other contexts.
- The analysis did not determine the implementation efficiency of several programs. Gains in implementation efficiency were mainly considered when analyzing delivery models for TB treatment. Additional implementation efficiencies such as reductions in drug prices would lead to different unit costs, which would affect resource allocation.
- Modelling the optimization of allocative efficiencies depends critically on the availability of evidence-based parameter estimates of the effectiveness of individual interventions. Although these estimates were derived from a global systematic literature review, they may vary in specific countries and populations depending on various factors, particularly the quality of implementation and levels of adherence to interventions. All programs and spending categories, for which such parameters cannot be obtained could not be included in the mathematical optimization. Because they still have important functions in the TB response, they were treated as fixed costs and, in some specific scenarios, adjusted with specific justifications.

- Effects outside the TB endpoints are complex to consider (such as non-health benefits of different TB treatment modalities). Given the complexity of interactions among interventions and their non-TB benefits the model does not seek to take into account 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.

3. WHAT ARE THE CURRENT TRENDS IN THE TB EPIDEMIC?

Chapter 3 summarizes the current status of the TB epidemic in Belarus. The model assumed that current conditions would continue until 2020, i.e. that the coverage of individual interventions would remain constant.

3.1 SUMMARY OF KEY NATIONAL DATA ON THE STATUS OF THE TB EPIDEMIC

Despite a decline in TB incidence and mortality between 2000 and 2014, Belarus remains one of the countries highly affected by TB within the European region. As shown in Table 3.1, WHO estimated that 5,200 incident TB infections (including both new and relapse as well as HIV+TB) occurred in 2015 and that an estimated 520 TB related deaths occurred in 2015. (WHO 2017b)

Table 3.1 Key TB epidemiological data for Belarus (2015)

Estimates of TB burden, 2015	**Number (thousands)**	**Rate (per 100 000 population)**
Mortality (excludes HIV+TB)	0.45 (0.42–0.49)	4.8 (4.5–5.1)
Mortality (HIV+TB only)	0.072 (0.021–0.15)	0.76 (0.22–1.6)
Incidence (includes HIV+TB)	5.2 (3.9–6.8)	55 (41–71)
Incidence (HIV+TB only)	0.3 (0.2–0.44)	3.2 (2.1–4.6)
Incidence (MDR/RR-TB)	3.5 (2.8–4.2)	37 (29–44)
Estimated TB incidence by age and sex (thousands), 2015		
	0-14 years	**> 14 years**	**Total**
Females	0.11 (0.021–0.2)	1.3 (0.48–2.2)	1.4 (0.5–2.4)
Males	0.22 (0.14–0.3)	3.6 (2.7–4.5)	3.8 (2.8–4.8)
Total	0.33 (0.23–0.43)	4.9 (4.1–5.7)	5.2 (3.9–6.8)
TB case notifications, 2015		
Total cases notified	4,177	
Total new and relapse	3,765	
% tested with rapid diagnostics at time of diagnosis	72%	
% with known HIV status	99%	
% pulmonary	92%	
% bacteriologically confirmed among pulmonary	78%	

Source: Prepared based on WHO TB epidemic profile for 2015 (WHO 2017b)

Belarus recorded 4,177 total notified TB cases in 2015, of which 3,765 were new and relapse cases. This suggests that 72% of the estimated 5,200 incident new and relapse cases were notified and 28% remained undiagnosed. Among notified TB cases, 72% were tested using rapid molecular diagnostics at the time of diagnosis and virtually all (99%) were tested for HIV. Overall, 92% of notified cases were pulmonary TB cases, among which 78% were bacteriologically confirmed.

An epidemic highly affecting men

Approximately 75% of incident TB cases are estimated to occur among males and the number of notified cases among males is substantially higher in all age groups, except older people aged 65 and above (WHO 2017b). The sex-disaggregated data suggests that there are specific risk factors among men causing increased incidence of active TB. These are likely to include higher use of alcohol, higher HIV prevalence, higher drug use, higher likelihood of imprisonment and potentially a range of other factors. In older people, the higher prevalence of diabetes mellitus in females compared to males as well as the larger number of women in this age group due to higher mortality among men due to other causes are likely to affect the sex pattern of TB notifications. (IHME 2015)

Exceptionally high levels of drug resistance

Belarus experiences one of the highest levels of TB drug resistance world-wide. In 2015, there were 1,800 MDR/RR-TB cases among notified TB cases and MDR/RR-TB cases represented 37% of new cases and 69% of previously treated cases. In the same year, 69% of new cases and 65% of previously treated cases were tested for rifampicin resistance. (WHO 2017b) Analysis of 2016 data suggests that within 1808 MDR-TB cases 65% were XDR-TB or pre-XDR-TB (resistance against second line injectable agents or fluoroquinolones).

Table 3.2 Drug resistance status

Drug-resistant TB care, 2015	New cases	Previously treated cases	Total number***
Estimated MDR/RR-TB cases among notified pulmonary TB cases			1 800 (1 700–1 800)
Estimated % of TB cases with MDR/RR-TB	37% (35–39)	69% (66–72)	
% notified tested for rifampicin resistance	69%	65%	2 825
MDR/RR-TB cases tested for resistance to second-line drugs			1 281

Source: Prepared based on WHO TB epidemic profile for 2015 (WHO 2017b)

Large variation in treatment outcomes

There is substantial variation in treatment outcomes in Belarus. As mentioned above, and in line with a vast majority of countries the largest break point in the country's treatment cascade is likely at the initial step of diagnosis, as 72% of the estimated TB cases are diagnosed in 2015 (Table 3.3). Based on WHO's global TB database (WHO 2017c) a summary of the TB cascade was prepared for 2014 when an estimated 70% of incident TB cases were notified (Figure 3.1 a). Additional analysis based on the WHO database is presented for specific TB treatment cohorts. These TB treatment cohort cascades use the people initiated on treatment as the denominator.

When considering new and relapse TB cases, the losses in the TB cascade from initiation of treatment to completion are 12% and attributable to a combination of loss-to-follow up, death, treatment failure and lack of evaluation (Figure 3.1 b) leading to a treatment success rate of 88%.

Among TB patients with known HIV status 6% were HIV positive and 84% on antiretroviral therapy in 2015. An analysis of the TB treatment cohort cascade for 2014 suggests that treatment outcomes for HIV positive patients were substantially less favorable than for HIV negative TB patients with a success rate of 74% and death being the largest breakpoint in the treatment cohort cascade. (Figure 3.1c)

Among people with MDR-TB, there are major losses in the TB-treatment cohort cascade. Reported data suggest that loss-to-follow up, death and treatment failure are major breakpoints in the cascade, which contributed to a treatment success rate of 54% in 2013. (Figure 3.1d)

The treatment cohort cascade for XDR-TB for 2013 was based on a relatively small sample (60) and suggests a treatment success rate of 38%. Major breakpoints in the cascade were death and treatment failure. (Figure 3.1e)

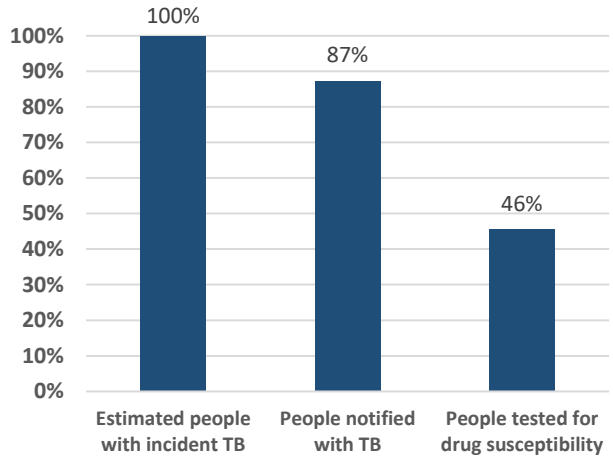
Table 3.3 Key treatment indicators

Universal health coverage and social protection			
TB treatment coverage (notified/estimated incidence), 2015		72% (56–97)	
TB case fatality ratio (estimated mortality/estimated incidence), 2015		0.1 (0.08–0.14)	
TB/HIV care in new and relapse TB patients, 2015		**Number**	**(%)**
Patients with known HIV-status who are HIV-positive		206	6%
- on antiretroviral therapy		174	84%
Laboratory-confirmed cases	MDR/RR-TB: 1 340, XDR-TB: 460		
Patients started on treatment ****	MDR/RR-TB: 1 949, XDR-TB: 508		
Treatment success rate and cohort size		**Success**	**Cohort**
New and relapse cases registered in 2014		88%	2 706
Previously treated cases, excluding relapse, registered in 2014		73%	249
HIV-positive TB cases, all types, registered in 2014		74%	135
MDR/RR-TB cases started on second-line treatment in 2013		54%	2 136
XDR-TB cases started on second-line treatment in 2013		38%	60
TB preventive treatment, 2015			
% of HIV-positive people (newly enrolled in care) on preventive treatment		10%	
% of children (aged < 5) household contacts of bacteriologically-confirmed TB cases on preventive treatment		100% (100–100)	

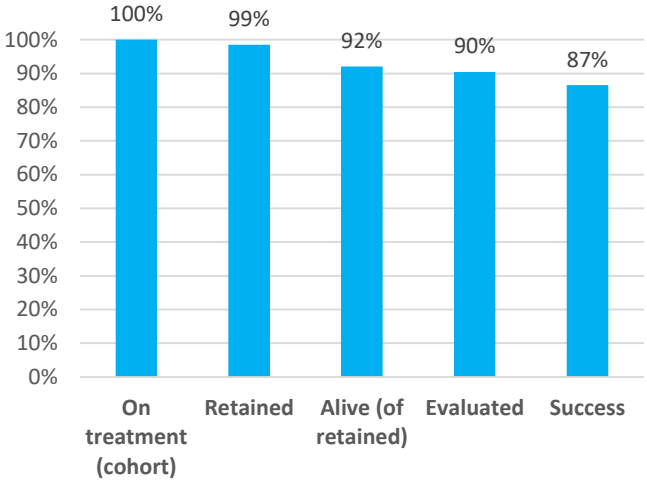
Source: Prepared based on WHO TB epidemic profile for 2015 (WHO 2017b)

Figure 3.1 TB treatment cascade and treatment cohort cascades

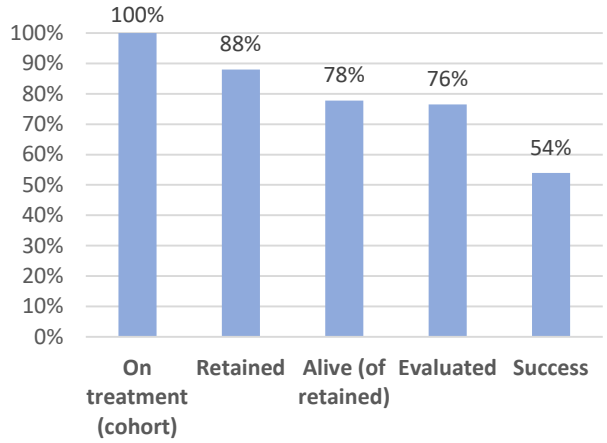
a. TB care cascade of all incident cases (new and relapse cases), first part from infection to diagnosis 2014



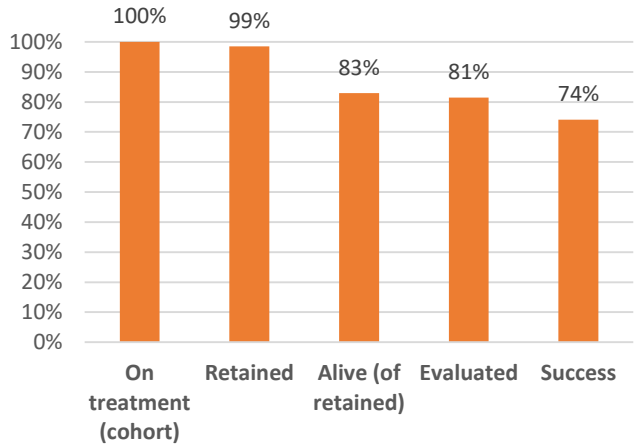
b. Treatment cohort cascade, all new relapse cases



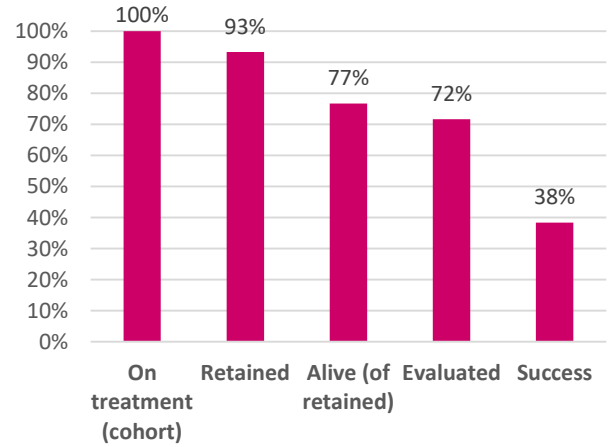
c. TB treatment cohort cascade, PLHIV, 2014



d. Treatment cohort cascade, MDR-TB, 2013



e. Treatment cohort cascade, XDR-TB, 2013



Source: Prepared by authors based on WHO global TB database, (WHO 2017c)

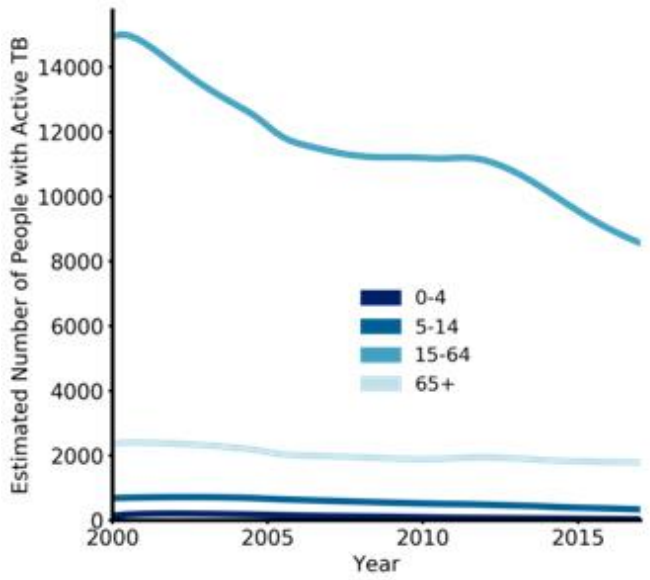
3.2 EPIDEMIC TRENDS ESTIMATED IN OPTIMA

The Optima-TB model was used to estimate trends of TB prevalence, incidence and mortality in Belarus. Estimates were made based on detailed epidemiological and program data received, which are summarized in the Appendix B of this report.

The prevalence of active TB declined since 2000

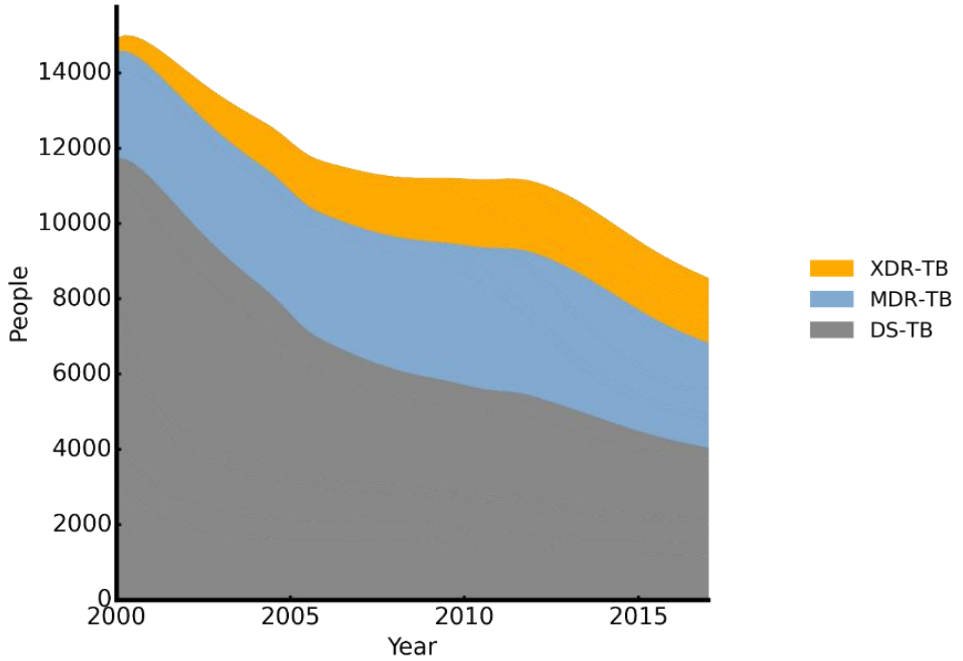
Optima-TB results suggest that the prevalence of TB has declined since the year 2000 (Figure 3.2) in the general population. Although the number of TB cases declined across different age groups, the decline was less pronounced among populations aged 65+. While drug-resistant types of TB accounted for less than one quarter of active TB cases in 2000, more than half of people with active TB in 2016 were estimated to be infected with a drug resistant type of TB. (Figure 3.3). The declining trend in the epidemic is in line with WHO estimated TB prevalence and the declining trend in TB notifications according to national TB program records. According to Optima-TB the number of people with active TB among all populations declined from 17,000 people with active TB in 2004 to 12,000 in 2015. The estimated number of active TB cases in Optima-TB is within the confidence bounds of WHO TB prevalence estimates for Belarus between 2004 and 2015, but close to the upper margins. Given the absence of a TB prevalence survey for Belarus, it is not possible to validate model estimates for TB prevalence with empirical data. Higher estimates of TB prevalence in Optima-TB are likely due to different disease input assumptions on parameters such as disease duration, which in the context of Belarus is likely high due to the high prevalence of drug-resistant types of TB and a relatively large number of people on palliative care who do not access any form of treatment.

Figure 3.2 Trends in the estimated number of people with active TB in the general population in Belarus by age group (2000-16)



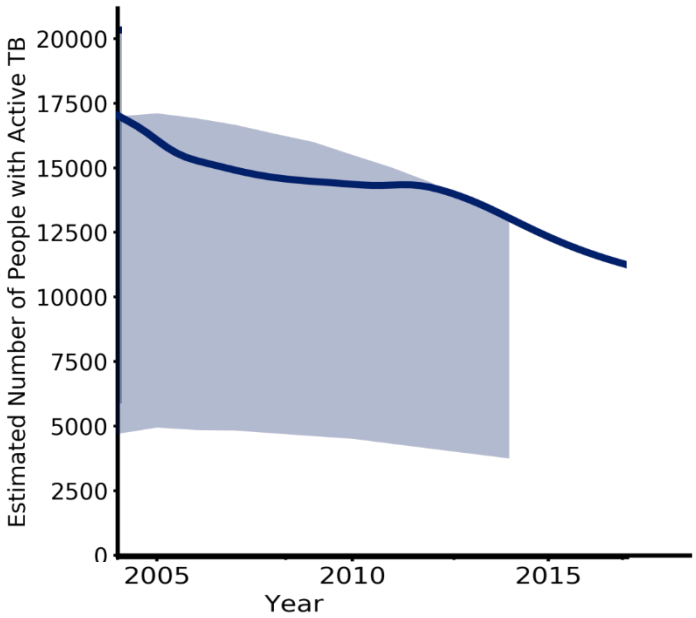
Source: Populated Optima-TB model for Belarus.

Figure 3.3 Trends in the estimated number of people aged 15-64 with active TB in Belarus by drug resistance type (2000-16)



Source: Populated Optima-TB model for Belarus.

Figure 3.4 Trends in the estimated number of people with active TB in Belarus, all ages and sub-populations (2004-16)

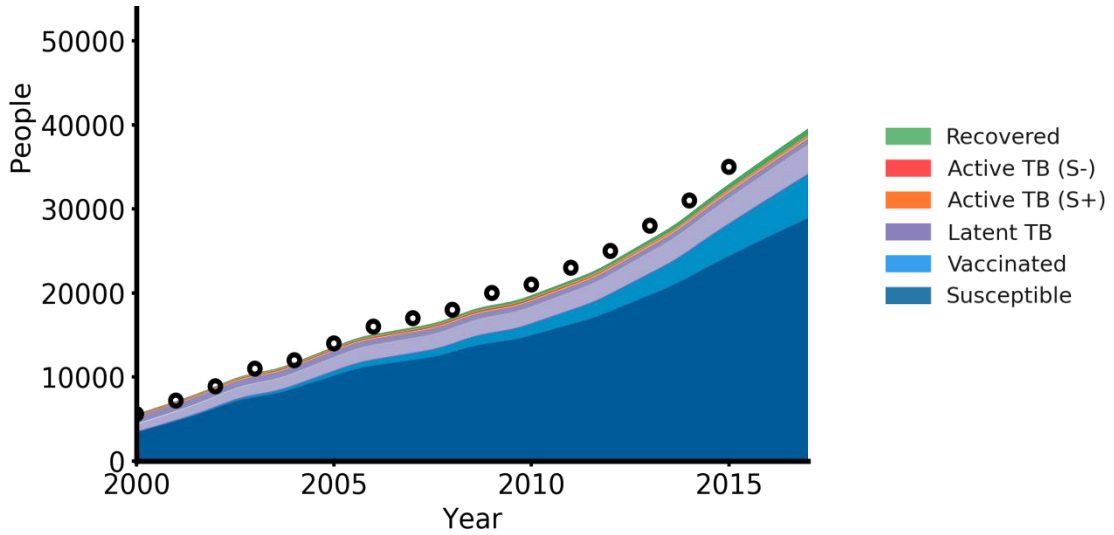


Source: Populated Optima-TB model for Belarus.
Note: Shaded areas represent confidence bounds of WHO TB prevalence estimates.

An increasing contribution of HIV to the TB epidemic

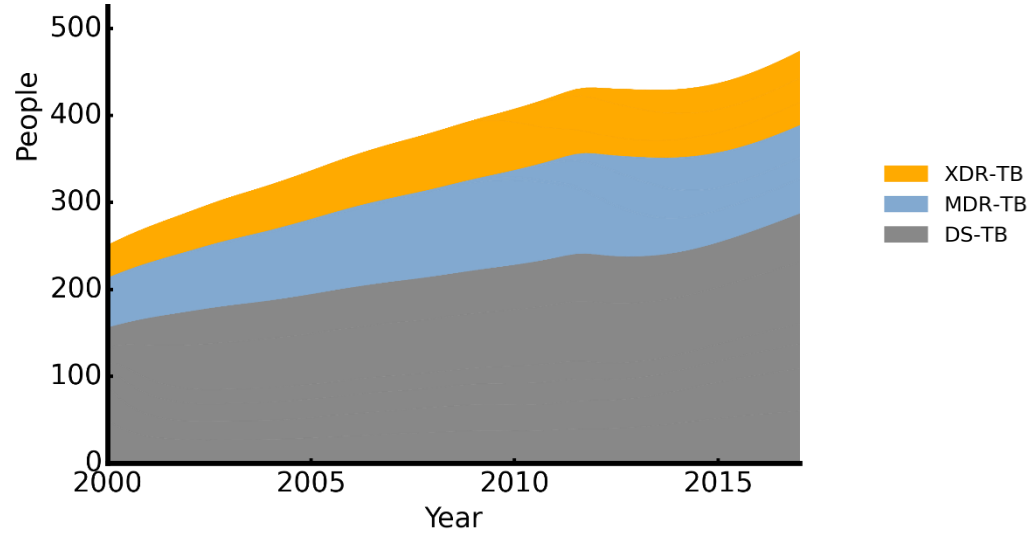
While the prevalence of TB decreased by more than one third in Belarus between 2000 and 2015, Belarus' HIV epidemic increased more than six-fold over the same time period from an estimated 5,600 people living with HIV in 2000 to 35,000 in 2015. (UNAIDS 2016) Figure 3.5 illustrates the growing number of PLHIV in Belarus by TB disease status. Despite the decline in TB prevalence, the estimated number of active TB cases among PLHIV nearly doubled between 2000 and 2016 (Figure 3.6). Optima projections suggest that the proportion of people with active TB who are HIV positive increased from less than 2% of people with active TB in 2000 to approximately 6% in 2016 with a growing share of MDR and XDR-TB among PLHIV.

Figure 3.5 People living with HIV by TB disease status



Source: Populated Optima-TB model for Belarus.

Figure 3.6 People living with HIV who have active TB by drug resistance strain

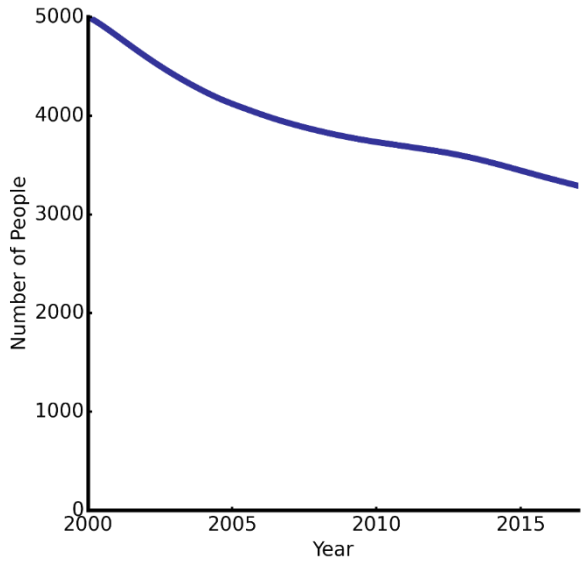


Source: Populated Optima-TB model for Belarus.

TB incidence declines in all general population groups except older populations

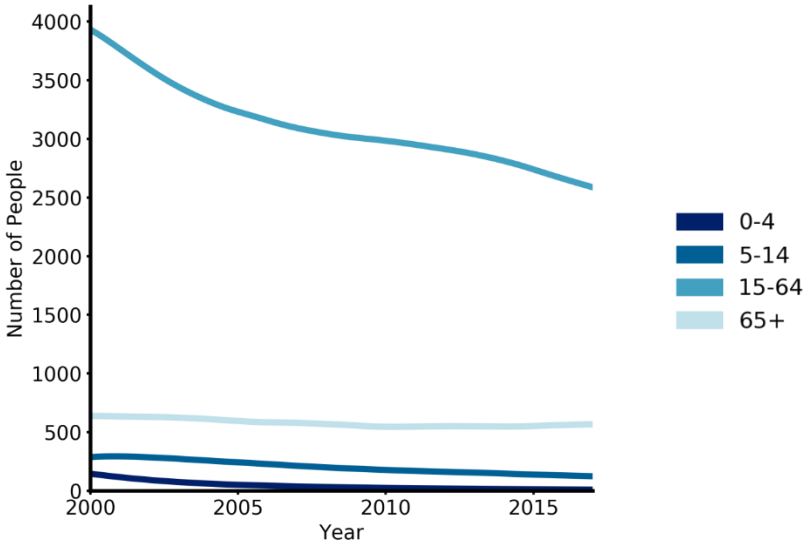
The estimated incidence of TB in Optima suggests that new infections declined in the general population overall since the year 2000 by approximately one third (Figure 3.7). While the decline was sustained among 0-4, 5-14 and 15-64 year age groups, the number of incident TB cases was estimated to have stabilized in about 2010 among populations aged 65 and older (Figure 3.8). The model suggests that this is due to the continued activation of latent-TB infections among this age group.

Figure 3.7 Estimated total number of active TB infections in Belarus (2000–16)



Source: Populated Optima-TB model for Belarus.

Figure 3.8 Estimated number of active TB infections in the general population in Belarus by age (2000–16)



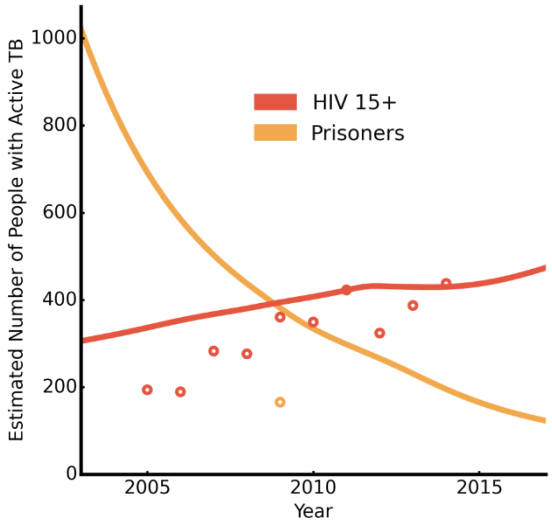
Source: Populated Optima-TB model for Belarus.

Key populations - TB declined among prisoners but increased among PLHIV

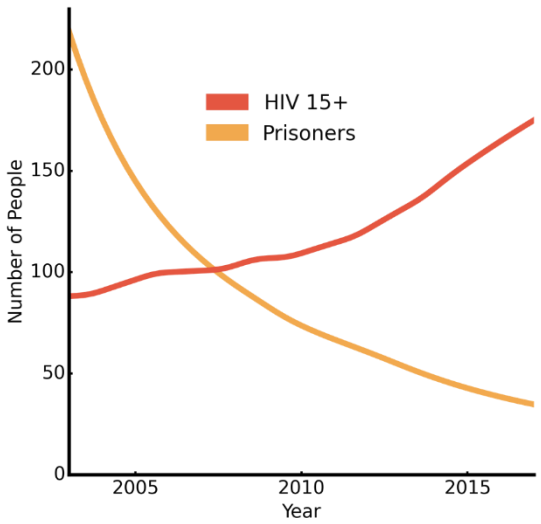
Optima estimates suggest that the TB epidemic declined among prisoners, but increased among PLHIV between 2003 and 2016. Optima projections suggest that TB prevalence and incidence among prisoners declined faster than among the general populations. This projection is supported by data on TB notifications, which declined nearly five-fold between 2003 and 2015 according to national program records.

Figure 3.9 New and active TB infections in key populations in Belarus (2003–16)

a. Estimated number of people with active TB infections



b. Estimated incident TB infections



Source: Populated Optima-TB model for Belarus.

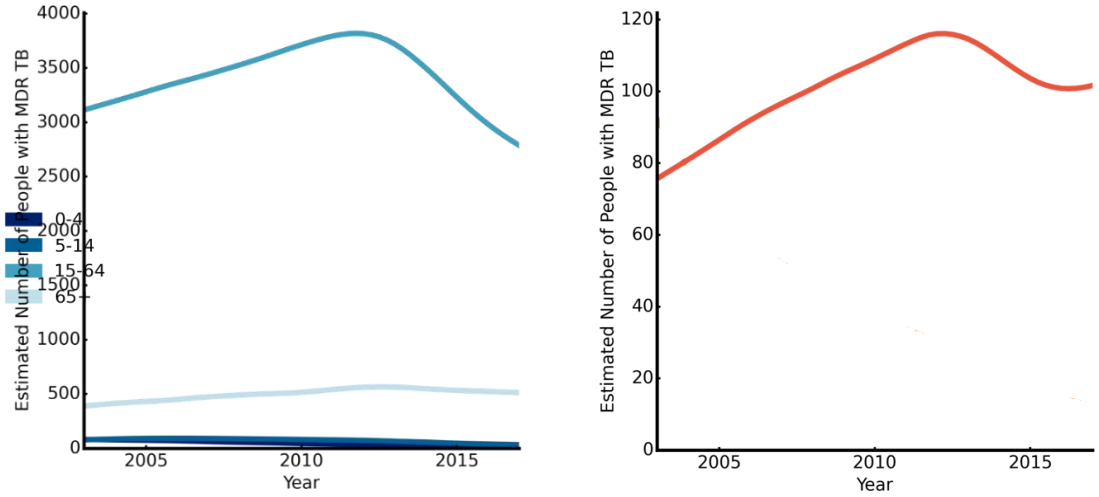
Continued high MDR-TB prevalence

Despite the overall reductions in TB prevalence in Belarus between 2000 and 2010, Optima projections suggest that the number of people with MDR-TB continued to increase up to 2010. (Figure 3.10) Disaggregated data on MDR-TB notifications is not available for the time period prior to 2010 and therefore model estimates could not be compared to actual data points for this period. Our model estimates suggest that while the share of MDR-TB among all TB infections remains stable at a high level after 2010, absolute numbers of active MDR-TB (excluding XDR-TB) began to decline in 2012. This reduction is due to the combined effects of overall reduction in TB prevalence, the increasing coverage of diagnosis and treatment of MDR-TB, and the increasing number of people who moved from being classified as MDR-TB to being XDR-TB cases.

When disaggregated by age, Optima-TB estimates suggest that the reduction in MDR-TB (excluding XDR) was primarily due to a reduction in active MDR-TB in the 15-64 age group, while the estimated number of people with active MDR-TB among older people aged 65+ remained stable. Among PLHIV, the number of people with active MDR-TB stabilized at a high level.

Figure 3.10 People with active MDR-TB in Belarus (2003-2016)

a. MDR-TB in the general population by age **b. MDR-TB among PLHIV**



Source: Populated Optima-TB model for Belarus.

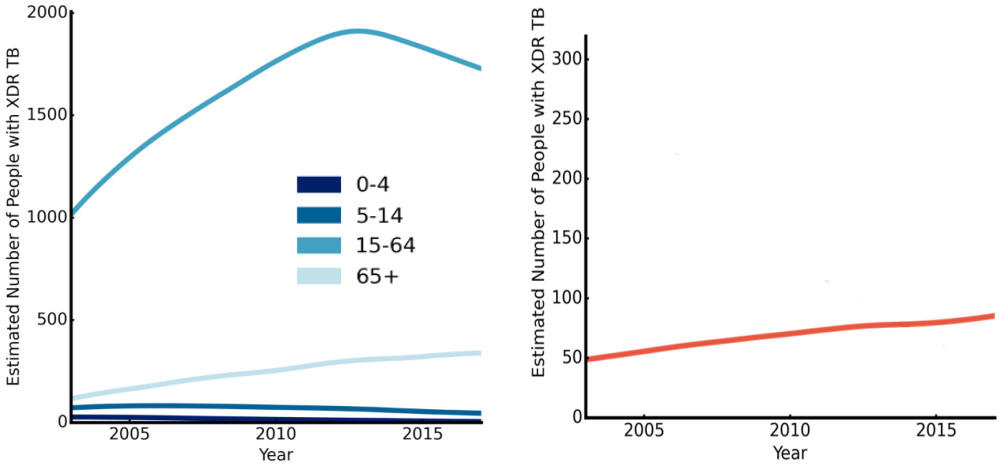
XDR-TB: Exceptionally high prevalence

As outlined above (Figure 3.3) the proportion of people with active TB who are diagnosed as XDR-TB is exceptionally high in Belarus. Correspondingly, Optima-TB estimates suggest that in the period between 2000 and 2013 the number of people with active XDR-TB must have increased rapidly (Figure 3.11). Disaggregated data on XDR-TB notifications is not available for the time period prior to 2014 and therefore model estimates could not be compared to actual data points for this period.

The available data is insufficient to produce precise estimates and projections of trends. Based on the limited available data, Optima-TB projections suggest that the number of people with active XDR-TB stabilized in children and people aged 15-64, but continues to increase among people aged 65+ and among people living with HIV.

Figure 3.11 People with active XDR-TB in Belarus (2003-2016)

a. XDR-TB in the general population by age **b. XDR-TB among PLHIV**



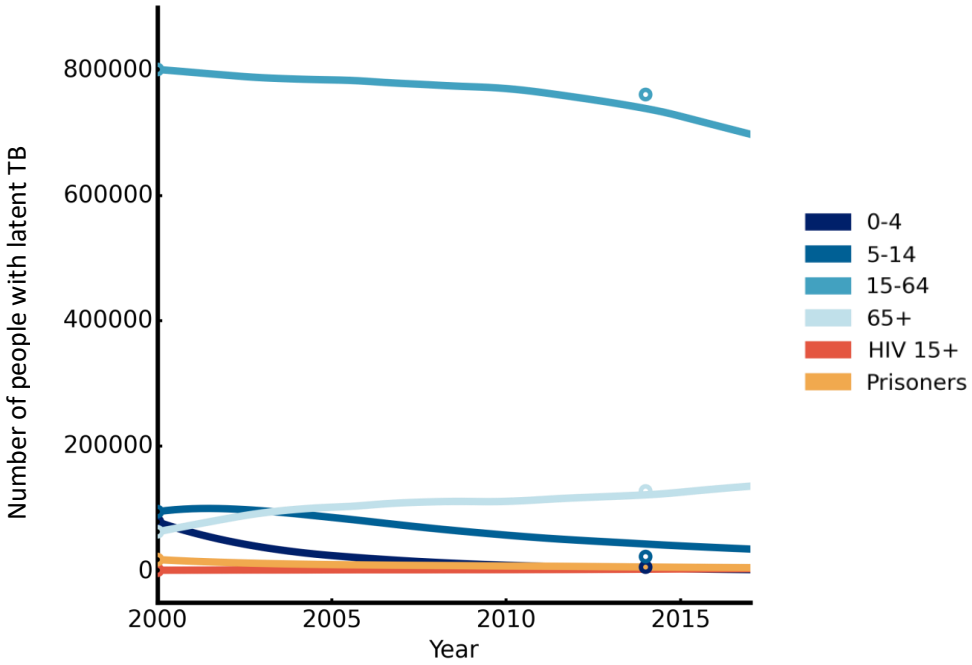
Source: Populated Optima-TB model for Belarus.

Latent TB: The reservoir sustaining the TB epidemic

The actual prevalence of latent TB in Belarus is currently unknown. While earlier estimates suggested that up to one third of the world's population was infected with latent TB, the most recent global estimate suggests that global latent TB prevalence is less than 25%. (Houben 2016)

Estimates of the prevalence of latent TB in Belarus have been produced using the Optima-TB model, based on observed active TB cases. Optima-TB estimates the number of latent TB cases to be approximately 900,000 in 2015. Optima-TB estimates suggest that the number of latent TB infections is stable or declining in most populations in Belarus (Figure 3.12). Latent infections were estimated to be increasing slightly in older populations (aged 65+). Further work is needed to understand whether there is an increase in latent infection among populations aged 65+ and what possible causes may be. Hypotheses for explaining an increase in latent TB among people aged 65+ might include aging of cohorts of people with higher exposure to people with active TB prior to 2000 including in the 1990s when active TB incidence in Belarus was higher than after 2000. Independent estimates suggest that the number of people with latent TB in Belarus is between 770,000 and 1,400,000 - with an estimated total of 920,000 cases (Houben 2016)

Figure 3.12 People with latent TB infection in Belarus (2003–16)



Source: Populated Optima-TB model for Belarus, data points represented in small disks are from Houben 2016.

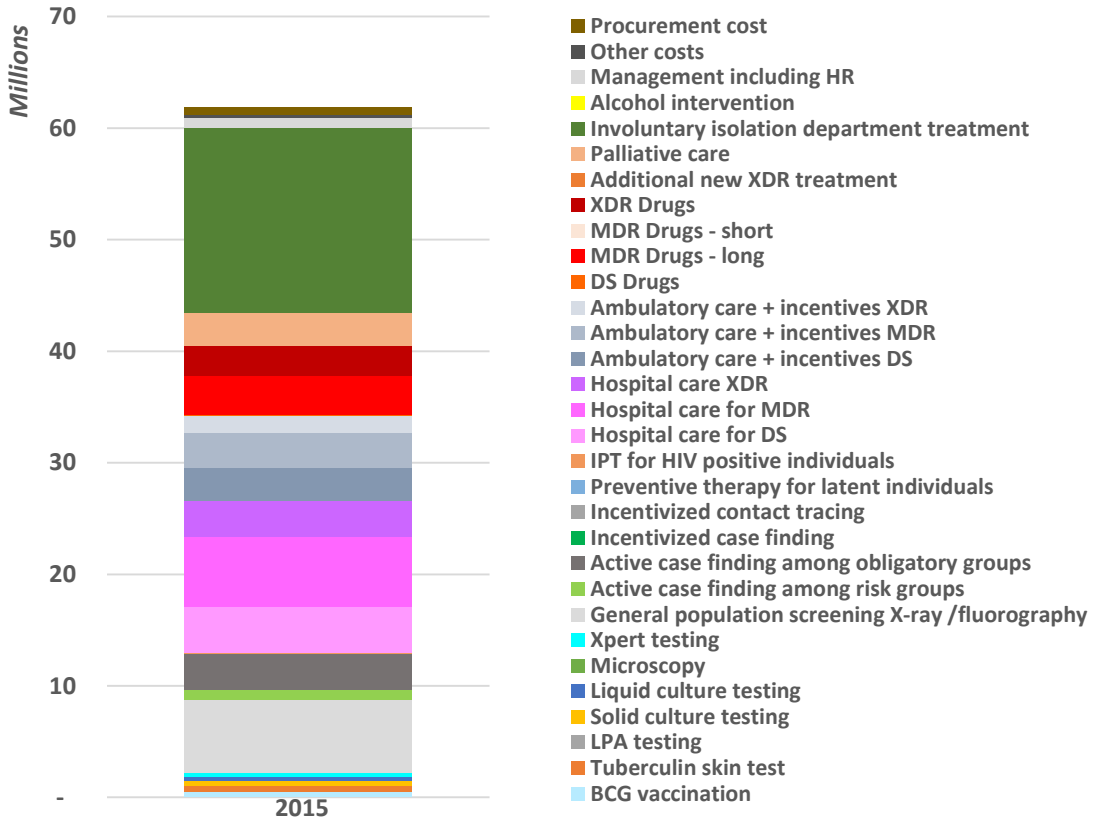
4. WHAT ARE THE IMPACTS OF CURRENT TUBERCULOSIS SPENDING?

This chapter describes the programmatic focus of TB spending in Belarus and the corresponding epidemiological outcomes if current spending patterns would be sustained.

4.1 FOCUS OF CURRENT TB PROGRAMS IN BELARUS

In 2015, an estimated US$61.8 million were spent on TB programs and TB related activities in other parts of the health system as outlined in Chapter 2 of this report. Figure 4.1 provides a detailed breakdown of TB spending in 2015 in Belarus by intervention area.

Figure 4.1 TB expenditure in Belarus by program area, 2015 (US$ million)



Source: Populated Optima data entry spreadsheet for the Belarus, based on WHO national TB sub-accounts and other cost data from program records.

More than half of TB spending in Belarus was allocated to hospital-based treatment. Involuntary isolation department treatment was estimated to absorb 26.8% of all TB related spending. Hospital-based care for DS, MDR and XDR-TB accounted for another 22.1%. Palliative care for TB patients for whom suitable drugs were not available was estimated to account for 4.7% of TB spending based on an estimated number of 537 palliative care patients (WHO GLC report) receiving hospital-based care. When considering that 364 patients were covered under involuntary isolation department treatment, spending of US$16.6 million in this program area translated into an annual cost of US$45,600 per patient in 2015, by far the highest cost of all treatment modalities.

Ambulatory care for all types of TB was estimated to absorb 12.3%. Screening for the general population and professional groups at risk of elevated TB transmission accounted for 15.8% of TB spending, while all other diagnostic interventions accounted for 4.3% of total TB spending. Management, administrative and procurement costs were 2.9% of total TB spending.

4.2 WITHOUT TB PROGRAMS, TB INCIDENCE AND DEATHS WOULD RISE SUBSTANTIALLY

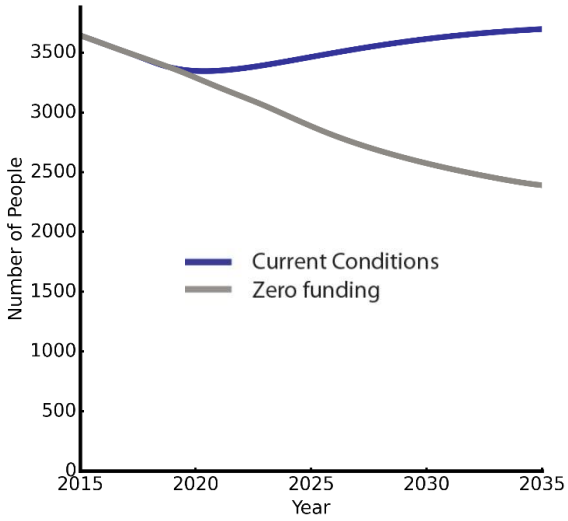
A scenario analysis was performed to assess the impact of current TB programs. This analysis assumed that the level of 2015 resources would be sustained up to 2035 and funding allocated in the same way as it was allocated in 2015 (see Figure 4.1). The effect of this 'current conditions' scenario was compared to a scenario of zero-spending on TB. The effects of 'current conditions' and 'no TB funding' on TB incidence, prevalence (number of people with active TB) and TB deaths were established (Figure 4.2).

The scenario analysis suggests that current funding for TB programs is making a significant impact on the TB epidemic and would have continued effects on the TB epidemic up to 2035 compared to zero-TB spending. Compared to zero-spending, current investment would avert approximately 25% of new infections, an estimated annual 6,000 active TB cases in 2035 and more than 1,500 TB related deaths in the year 2035. (Figure 4.2).

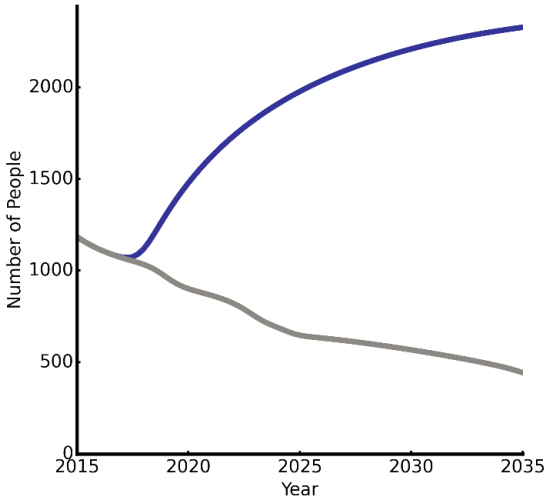
While current TB spending is clearly beneficial *compared to no public spending* on TB, current spending and allocations would only achieve moderate reductions in TB *compared to 2015 epidemic levels*. This implies that according to projections performed in Optima –TB, national and global targets outlined in chapter 2 of this report would not be achieved with current allocations of resources. The following chapters explore alternative resource allocation scenarios.

Figure 4.2 Epidemiological outcomes of current TB spending patterns versus no TB-spending between 2015 and 2035

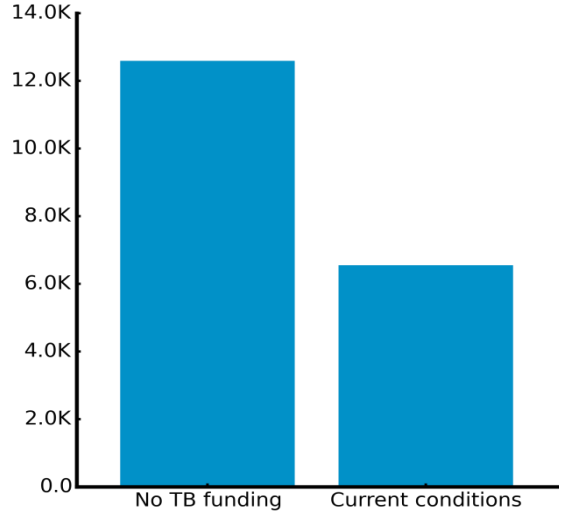
a. Number of people with incident TB infection per year



b. Number of TB related deaths per year



c. Number of people with active TB infection in 2035



Source: Populated Optima model for Belarus.
Note: Current conditions refers to continued coverage of services at 2015 levels.

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5. WHAT WILL BE THE IMPACT OF DIFFERENT PROGRAM IMPLEMENTATION SCENARIOS?

This chapter summarizes different scenario analyses, which were conducted to understand the effect that specific programmatic changes would have on Belarus' TB epidemic.

5.1 SCENARIO GROUP 1: SCALING UP COVERAGE OF KEY DIAGNOSTIC AND TREATMENT INTERVENTIONS

A scenario analysis was performed to understand the level of changes to the TB epidemic that would occur if key national targets and global milestones were achieved by 2020 and if global targets were achieved by 2035. Table 5.1 summarizes the parameters, which were modified in the model to assess the effect of the scenarios. Three scenarios were defined to compare the effect of current coverage to achievement of 2020 milestones for coverage and achievement of 2035 coverage targets. 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. Although in the 2020 target scenario, coverage targets are achieved by 2020, the impact of achieving and sustaining 2020 coverage levels is tracked up to 2035.

Table 5.1 Parameters for scenario group 1 – scaling up coverage of key diagnostic and treatment interventions

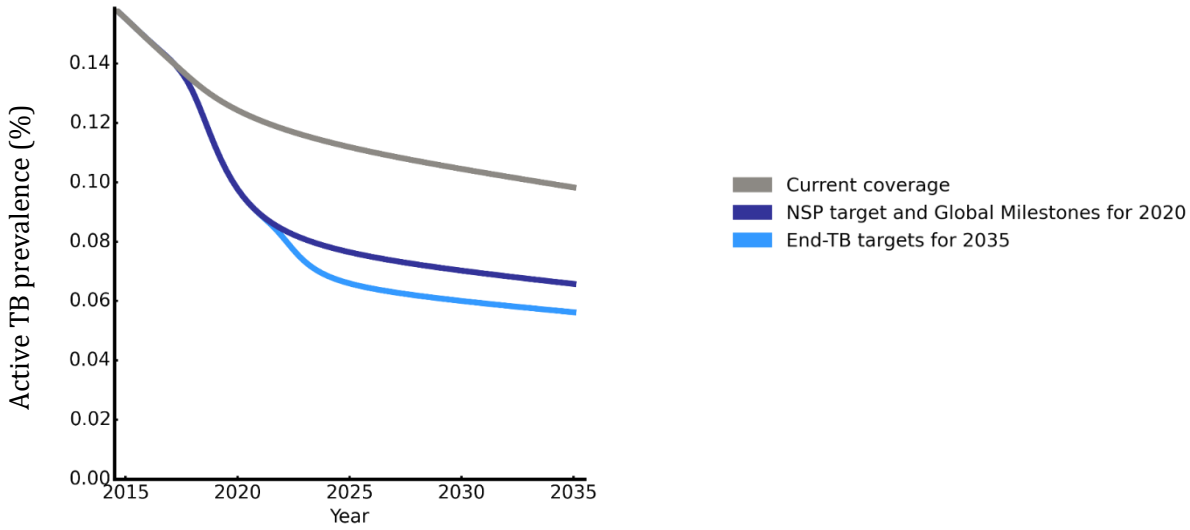
	Current coverage	NSP Targets and Global Milestones for 2020	Global End-TB Targets for 2035
Proportion of all DS-TB diagnosed	76%	90%	95%
Proportion of all MDR-TB diagnosed and initiated on treatment	76%	90%	95%
Proportion of all XDR-TB diagnosed and initiated on treatment	76%	90%	95%
Proportion of DS-TB patients successfully completing treatment	87%	95%	98%
Proportion of MDR-TB patients successfully completing treatment	52%	75%	90%
Proportion of XDR-TB patients successfully completing treatment	38%	60%	80%
Time frame for change to occur:		**2017-2020*	***2021-2035*
Time frame for tracking impact:		**2017-2035*	***2017-2035*

Source: Prepared by authors in consultation with national experts.

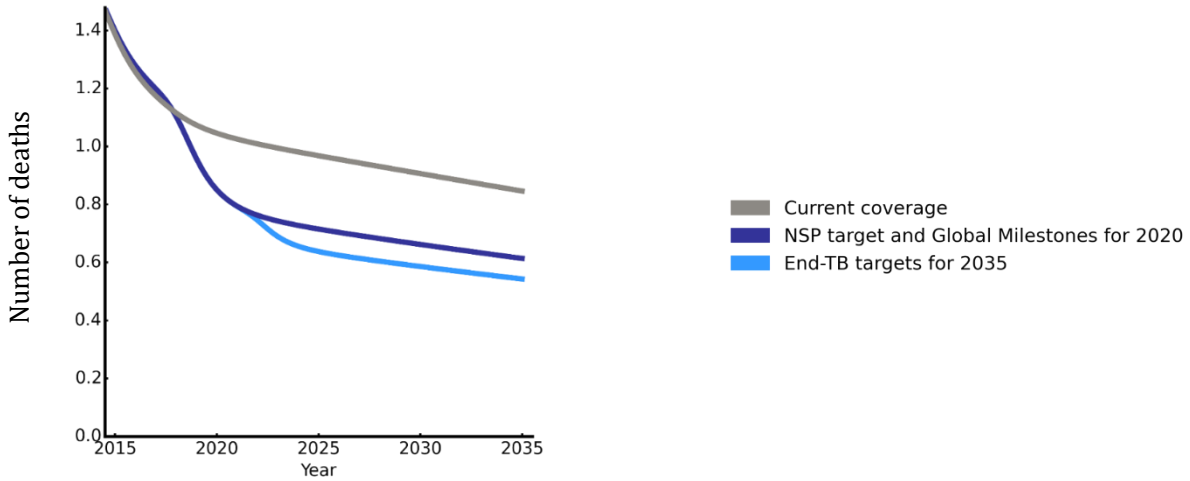
Figure 5.1 illustrates the effect of achievement of 2020 and 2030 targets on prevalence of active TB in the general population aged 15-64 and among PLHIV. As already established in chapter 4, current coverage levels would lead to a continued decline in prevalence of active TB, but the decline would gradually slow down and both 2020 and 2030 targets would be missed. The results on PLHIV also illustrate that while the number of active TB cases among PLHIV will continue to increase due to the increasing population of PLHIV as shown in chapter 4, the prevalence of active TB among PLHIV is actually expected to decline even with current coverage. Optima-TB analyses suggest that achievement of 2020 targets will reduce prevalence of active TB by approximately one third compared to sustaining only current coverage up to 2030. Compared to 2015 levels of TB prevalence, achievement of 2020 targets would imply more than a 50% reduction in active TB, both in the general population aged 15-64 and among PLHIV. Achievement of 2035 targets would imply greater impact with more than 40% reduction compared to business as usual and more than 60% reduction of active TB prevalence by 2035 compared to 2015 levels.

Figure 5.1 Estimated prevalence of active TB in Belarus (2015–35)

a. General population aged 15–64



b. People living with HIV

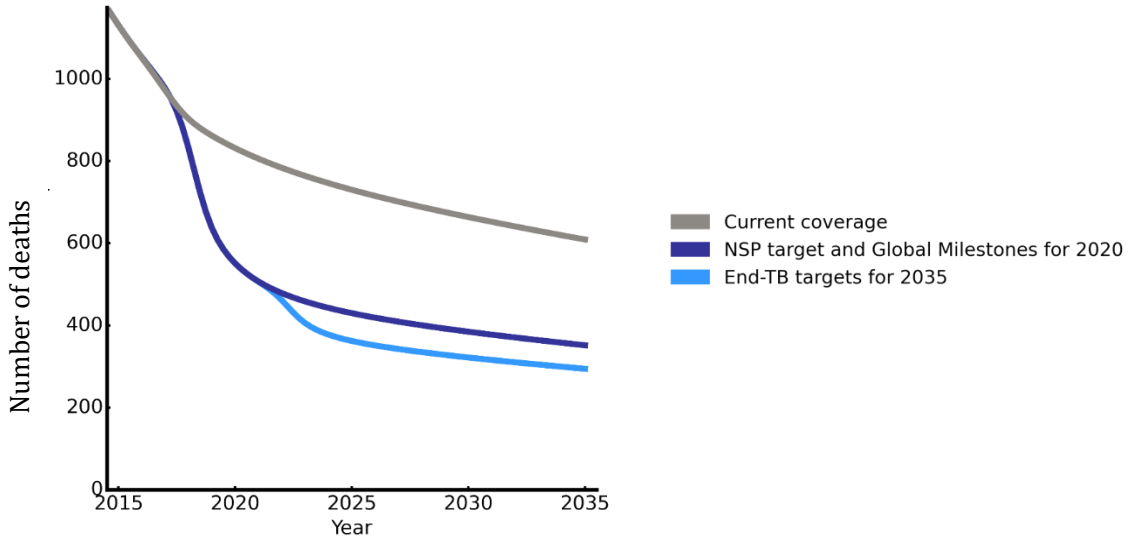


Source: Populated Optima model for Belarus.

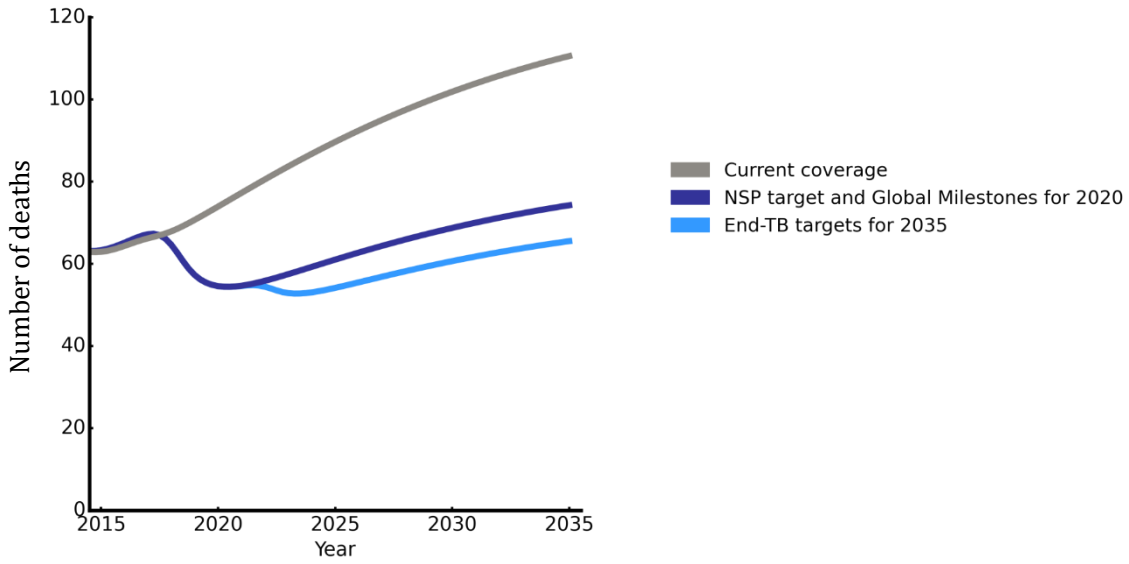
Figure 5.2 shows the effect of the same scenarios on TB-related deaths. With current coverage of interventions, the number of TB deaths per year would continue to decline among the general population aged 15-64. The projected increase in the number of TB-related deaths among PLHIV occurs in a context of a rapidly increasing number of PLHIV and despite moderately declining TB prevalence as shown in Figure 5.1. The effect of scaling up diagnosis and treatment on mortality is slightly larger than on active TB prevalence. Achieving 2020 targets would lead to more than 40% reduction of TB deaths by 2020 and more than 50% reduction by 2035 in the general population aged 15-64. This corresponds to a reduction by approximately two-thirds when compared to 2015 levels. Among PLHIV, scaling up TB diagnosis and treatment would halt the increase in TB related deaths. However, in the absence of scaled up HIV prevention and treatment interventions – which were not included in the Optima-TB analysis – the number of TB related deaths among PLHIV is projected to increase again moderately after 2020. This suggests that TB-related mortality among PLHIV can only be reversed if HIV prevention and treatment interventions are scaled up in parallel to TB treatment.

Figure 5.2 Estimated TB-related deaths in Belarus

a. General population, aged 15–65



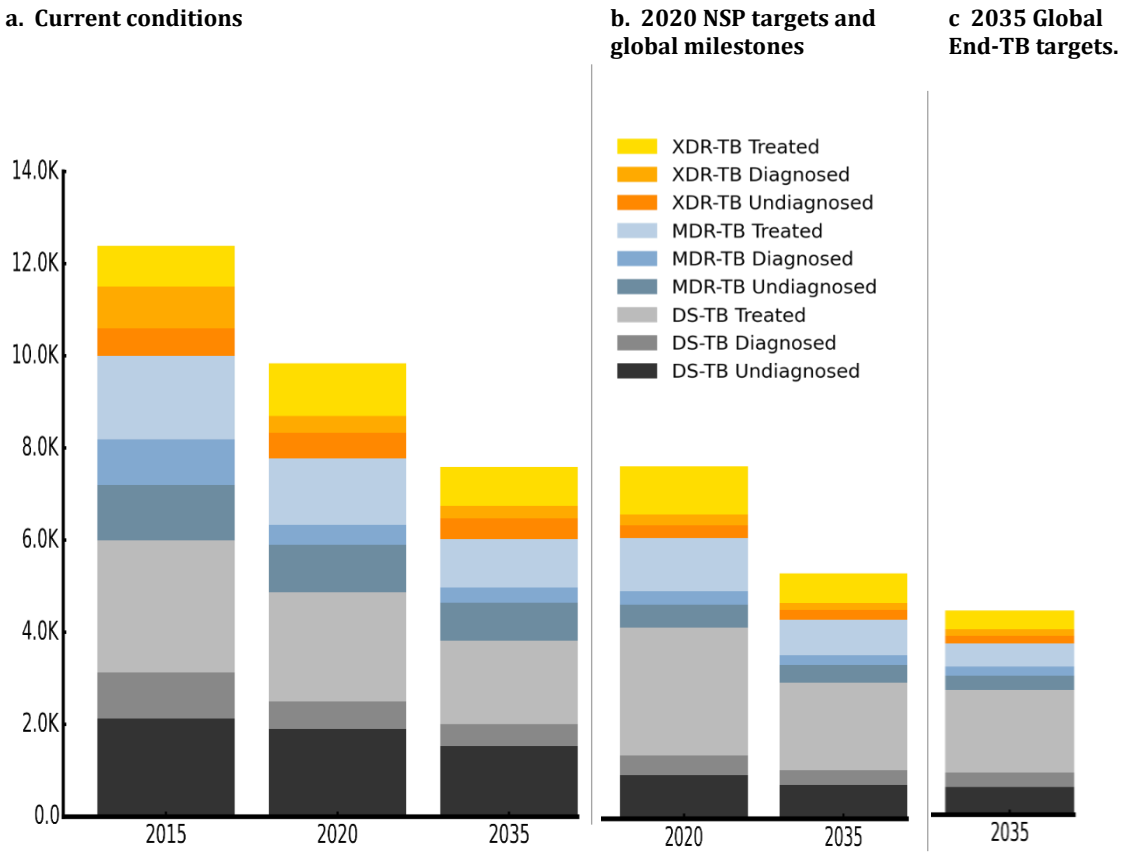
b. People living with HIV



Source: Populated Optima model for Belarus.

Figure 5.3 illustrates the effect of the same scenarios on the number of active TB cases disaggregated by drug resistance type (DS, MDR, XDR) and by treatment status (undiagnosed, diagnosed, treated) among all populations. The analysis confirms that reductions in active TB prevalence will be achieved across different drug resistance types. The undiagnosed population is also projected to decline substantially with the scale up of interventions.

Figure 5.3 Number of active TB cases by drug resistance type and treatment status with different scale up scenarios



Source: Populated Optima-TB model for Belarus.

Overall, scaling up to meet 2020 national targets and key global milestones is projected to avert 40% of active TB infections and 27% of expected TB related deaths by 2020 compared with current coverage. Scaling up to meet 2035 global End-TB targets is projected to avert 52% of active TB infections and 53% of expected TB related deaths compared with current coverage.

5.2 SCENARIO GROUP 2: SHIFTING FROM IN-PATIENT TO OUT-PATIENT MODALITIES OF TB TREATMENT

A specific scenario analysis was conducted in order to assess the potential effect of a shift from in-patient to out-patient treatment modalities for TB treatment. This analysis compares current hospital-focused treatment to modalities with standard ambulatory care and a modality with incentivized ambulatory care. All modalities include both hospital-costs and ambulatory costs.

What differs between hospital-focused and ambulatory modalities is the duration of hospitalization. Table 5.2 summarizes the durations of TB-treatment, which were assumed for the different treatment modalities based on WHO recommendations and consultation with in-country experts. The assumed reduction in in-patient days for ambulatory modalities corresponds to the estimated time required to achieve smear conversion suggesting that the patient is no longer highly infectious. Available data suggest that current average duration of hospitalization in Belarus is substantially longer than required on average to achieve smear conversion.

Table 5.2 Parameters for scenario group 2 – in-patient and out-patient modalities of TB treatment

		Current (Hospital-based)	Standard ambulatory	Incentivized ambulatory
Total days	DS treatment	180	180	180
	MDR - long	600	600	600
	MDR - short	–	315	315
	XDR	720	720	720
Number of Out-patient Days	DS treatment	120	166	166
	MDR - long	390	555	555
	MDR - short	–	285	285
	XDR	450	660	660
Number of In-patient Days	DS treatment	60	14	14
	MDR - long	210	45	45
	MDR - short	–	30	30
	XDR	270	60	60
Relative increase in treatment success rate	All (DS, MDR-long, MDR-short, XDR)	Standard (baseline)	No Change	16%

Source: Populated Optima-TB data spreadsheet based on consultations with national experts.

Table 5.3 provides a breakdown of the estimated cost for different treatment modalities based on a combination of estimated drug costs, costs of hospitalization per day, duration of hospitalization and costs for any incentives. The costs in the table represent the cost for a full course of treatment for one patient in different treatment modalities. Detailed assumptions used are summarized in Appendix C. A shift to ambulatory treatment modalities would reduce costs per patient on treatment by 25-28% for the DS, MDR and XDR-TB treatment courses. Even if incentives for health workers providing ambulatory services were included, an estimated 15-20% reduction in cost per patient could be achieved. The largest saving could be made by reducing involuntary isolation department treatment.

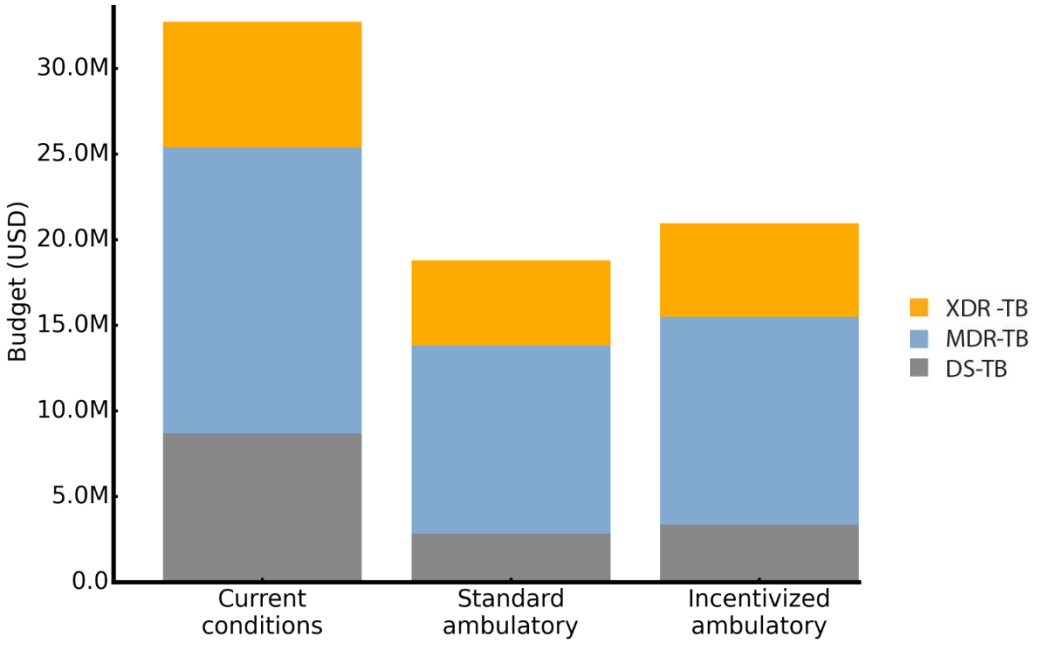
Table 5.3 Estimated cost of a full course of treatment for different drug regimens by treatment modality

	DS	MDR - long	MDR - short	XDR
Hospital-focused	2,610	14,158	–	20,483
Standard ambulatory	1,878	10,196	4,520	15,441
Incentivized ambulatory	2,215	11,325	5,100	16,783
Involuntary isolation	–	21,482	–	28,840

Source: Populated Optima data entry spreadsheet for the Belarus

Figure 5.4 shows the effect of three treatment modalities on overall cost of TB treatment considering current levels of treatment coverage. Using current modalities, treatment cost was estimated at approximately US$32 million per year versus US$18 million per year for standard ambulatory treatment and approximately US$20 million for incentivized ambulatory treatment.

Figure 5.4 Total cost of TB treatment using three different TB treatment modalities



Source: Populated Optima-TB model for Belarus.

Optima-TB analyses suggest that a transition from the current hospital focused modality to ambulatory care could save 40% of treatment costs and that these resources could be reallocated to more effective TB interventions.

There was insufficient in-country data to estimate the epidemiological impact of a transition from a hospital-focused system to ambulatory modalities. An international systematic review of the evidence supports the assumption that ambulatory care could achieve current coverage levels in target populations. (Bassili 2013) A meta-analysis of 540 articles reported no statistical difference for treatment outcome rates (success, death, default and failure), between ambulatory and hospital-based delivery of TB care. The review found that standard ambulatory care can be as effective as hospital-based care (Bassili 2013) There is also evidence to suggest that ambulatory care that is enhanced by specific incentives might be more effective than standard ambulatory care alone. A Cochrane review suggested that ambulatory care coupled with cash-incentives for patients may be more effective than un-incentivized ambulatory care, particularly among high-risk groups. (Lutge 2015) A WHO review of evidence also suggests improvements in treatment adherence through food and financial support as well as TB care enhanced through a mix of incentives. (Nguyen 2016) Within Belarus, the Mogilev pilot included food packages for patients and financial incentives for providers and a transition away from bed-based to outcomes-based financing. (Gurbanova 2017)

5.3 SCENARIO GROUP 3: ENHANCED DRUG REGIMENS AND COVERAGE OF XDR-TB TREATMENT

As outlined earlier in this report, rising levels of drug resistance are the key challenge for Belarus' TB response. In 2016, two thirds of all MDR-TB patients were classified as being infected with pre-XDR or XDR-TB. In the same year, 537 patients were receiving only palliative care and no drugs. Understanding the benefits of scaling up programmatic interventions for XDR-TB is therefore essential. Since pre-XDR-TB cases were not analyzed separately within Optima-TB, patients diagnosed with pre-XDR TB were included among the MDR-TB diagnoses. Therefore the analyses presented here only refer to patients diagnosed as XDR-TB cases.

As shown in chapter 3 of this report, the treatment success rate for XDR-TB in Belarus was 38% for the 2013 treatment cohort, which is substantially lower than for DS-TB and MDR-TB. New alternative XDR drug regimens containing linezolid, clofazimine and bedaquiline are available and have higher success rates than current drug regimens. In this context, it is important to examine whether interventions to minimize XDR-TB should focus primarily on identifying XDR cases or whether new drug regimens would substantially increase population-level impact.

Table 5.4 describes the key parameters used for this scenario analysis. Current conditions are compared to a scenario of scaling up XDR diagnosis and treatment using currently available drug regimens versus increased coverage of new XDR drug regimens. For the new drug regimens, a treatment success rate of 60% was assumed based on international literature.

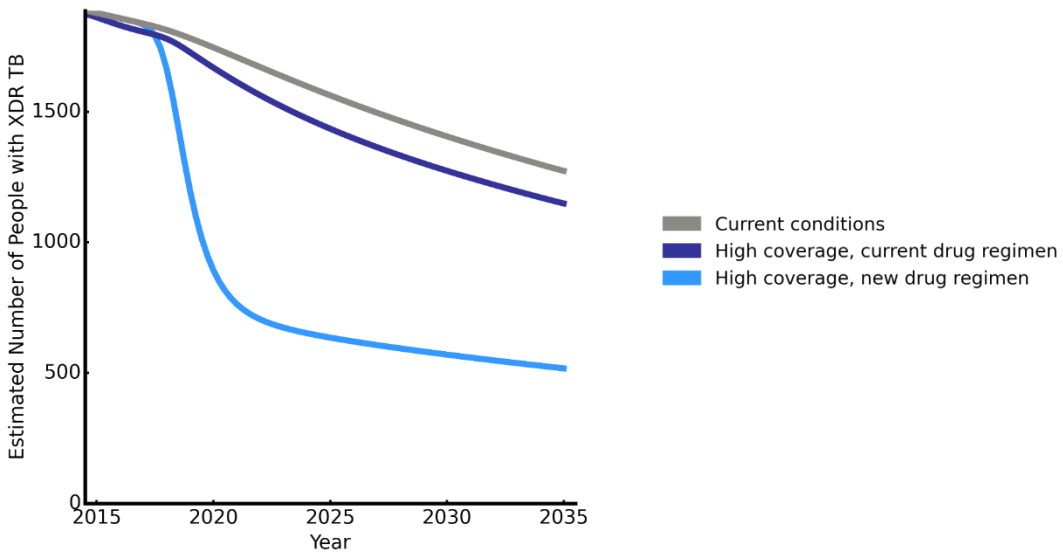
Figure 5.5 shows the effect of the different scenarios of XDR treatment on the total number of active XDR-TB cases.

Table 5.4 Parameters for scenario group 3 – enhanced diagnosis drug regimens and coverage of XDR-TB treatment

	Current conditions (2015)	Increased coverage of current XDR drug-regimen	Increased coverage of new XDR drug-regimen
Percent of XDR-cases correctly diagnosed	56%	90%	90%
Percent of XDR-TB cases initiated on treatment	85%	97%	97%
Percent of XDR-TB cases treated with current regimen	100%	100%	
Percent of XDR-TB cases treated with new drug regimen			100%
Treatment failure rate and Loss to Follow-up, with current regimen	62%	62%	
Treatment failure rate and Loss to Follow-up, with new regimen			40%
Treatment success rate, current regimen	38%	38%	
Treatment success rate, new drug regimen			60%

Source: Prepared by authors in consultation with national experts.
Note: * Time frame for tracking impact: 2017–35.

Figure 5.5 Estimated number of people with XDR-TB in Belarus with different types of XDR-TB treatment

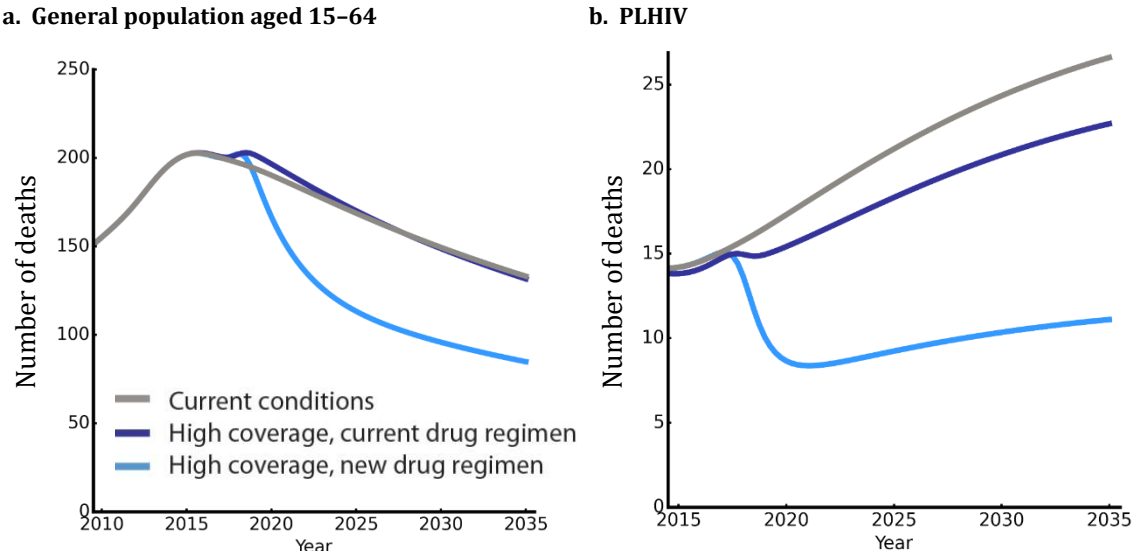


Source: Populated Optima model for Belarus.

The comparison of scenarios suggests that provision and increased coverage of new XDR drugs reduces the prevalence of XDR cases by approximately 65%. Increased coverage through the correct diagnosis of XDR cases is an important step for scaling up, but our analysis suggests that the higher treatment success rate of new drug regimens is the most important factor to reducing the number of XDR cases. Analyses also suggest that XDR treatment requires sustained support beyond the current NSP funding period to make an impact by 2035.

Figure 5.6 summarizes the effect of the different XDR-TB treatment scenarios on mortality. Optima-TB analysis suggests that while there is a small mortality-related benefit of scaling up XDR-TB diagnosis with current drug regimens, impact can be substantially enhanced by using more efficacious drug regimens, both for adults in the general population and among PLHIV.

Figure 5.6 Number XDR-TB related deaths per year with different types of XDR-TB treatment

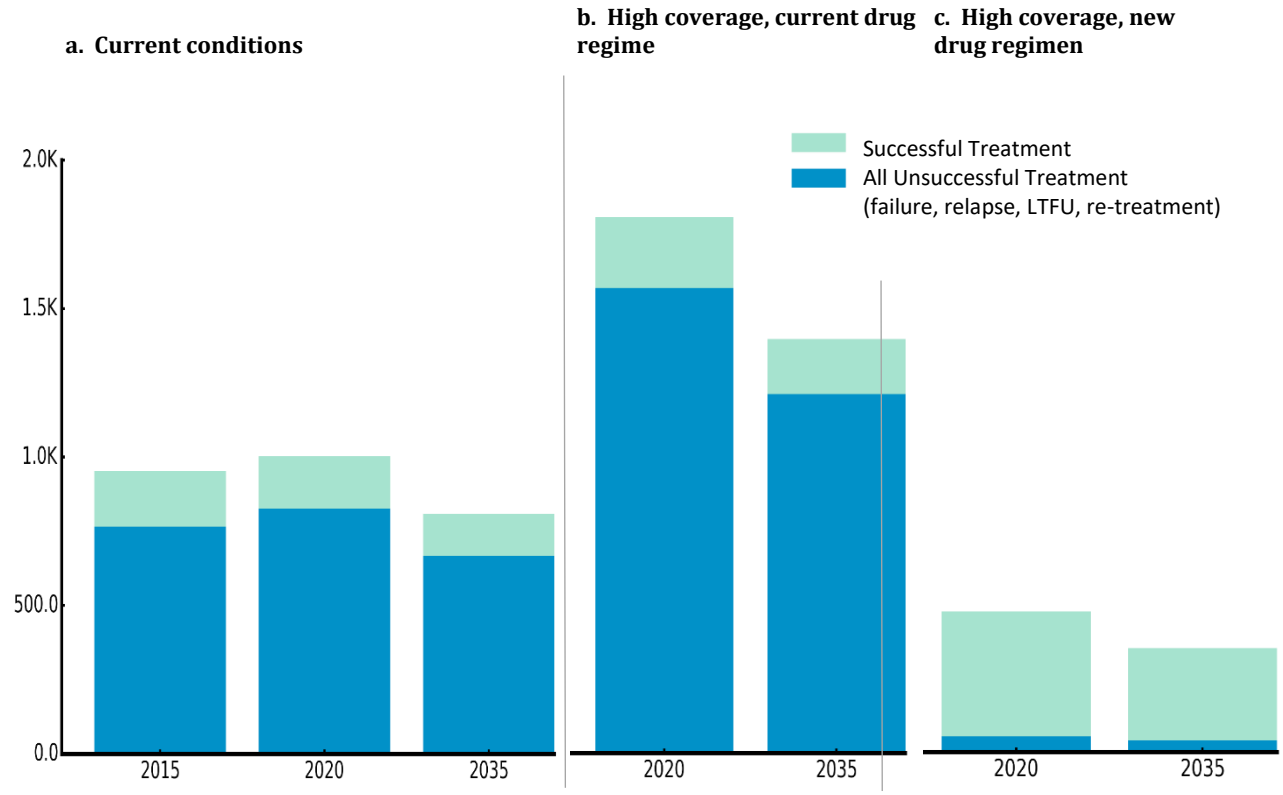


Source: Populated Optima model for Belarus.

Figure 5.7 summarizes successful and unsuccessful treatment outcomes for the three XDR-TB treatment scenarios for all populations. As shown above, current conditions will imply a continued relatively high mortality among people with XDR-TB as a substantial proportion of people with XDR-TB will be missed by treatment. As shown in Figure 5.7, high coverage with current drug regimens would moderately reduce the need for XDR-TB treatment by 2035, but the number of people in need of XDR-TB treatment would remain high at approximately 1,300 patients in 2035. With high coverage of new, more effective drug regimens, treatment completion would increase substantially. Patients covered by new drug-regimens are expected to be less likely to relapse or undergo re-treatment, ultimately decreasing the number of treatments needed. The Optima-TB model suggests that these benefits would accumulate over time and substantially reduce the number of people requiring XDR-TB treatment to approximately 300 in 2035.

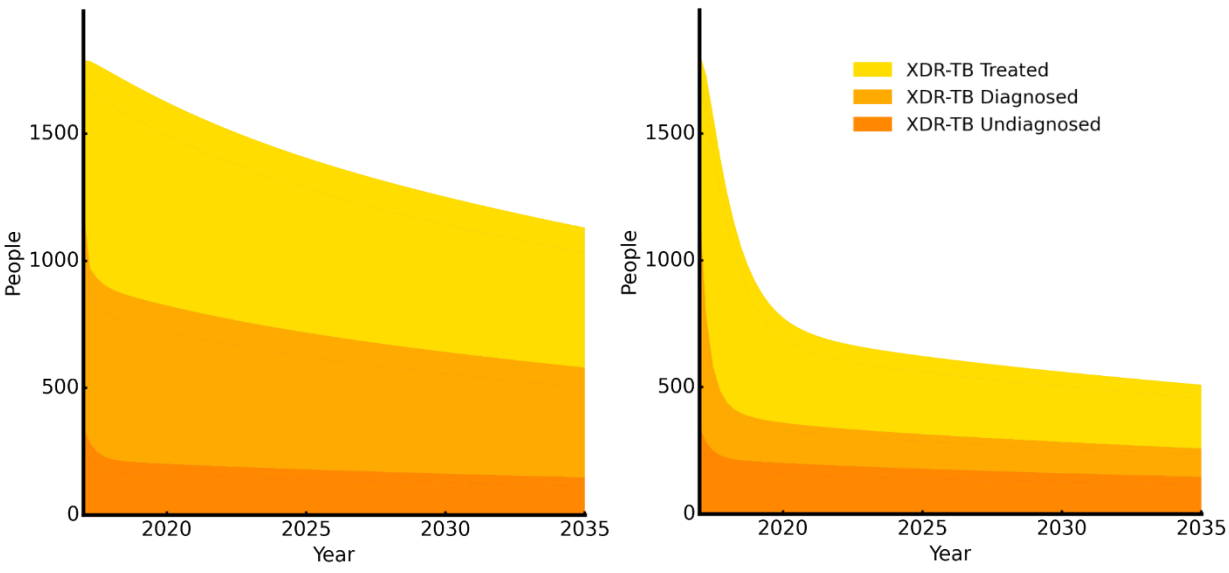
Figure 5.8 further illustrates that high coverage with new drug regimens has the potential to reduce the number of people with active XDR-TB by half by 2021 and sustain this reduction up to 2035.

Figure 5.7 Treatment outcomes among people treated with different XDR-TB treatment types



Source: Populated Optima model for Belarus.

Figure 5.8 People with active XDR-TB with different XDR-TB treatment types



Source:

Source: Populated Optima-TB model for Belarus.

In summary, the scenario analyses carried out in Optima-TB support the recommendation of the 2017 Green Light Commission (GLC) report, which calls for the improvement of MDR/XDR drug-regimens. (Gurbanova 2017) The GLC report estimated that there is need for 400 additional

regimens for MDR-TB patients, which include new and repurposed drugs (e.g. bedaquiline, linezolid, clofazimine), to meet demand in 2017-2018 – and an additional 250 courses to cover patients previously treated with other drugs for XDR-TB. (Gurbanova 2017)

There is evidence from studies assessing the efficacy of new and repurposed drugs, which supports the assumption of improved treatment outcomes made in the Optima-TB analysis. Linezolid results in significantly higher rates of sputum-smear conversion and overall treatment success for MDR-TB (Sotgiu 2012). Clofazimine and bedaquiline demonstrated promising outcomes for XDR-TB treatment despite the need for more evidence (Gualano 2016).

5.4 SCENARIO GROUP 4: EFFICIENT SCREENING AND DIAGNOSIS OF ACTIVE TB

As shown in chapter 4 of this report a substantial proportion of TB-related spending in Belarus is allocated to screening and diagnostic interventions. A scenario analysis was carried out to assess whether current rates of TB diagnoses could be achieved more cost-efficiently with a different mix of diagnostic interventions. The scenario analysis compares current screening and case finding practices with alternatives, including contact tracing, incentivized contact tracing, enhanced screening of key populations and a combination of enhanced contact tracing and screening of key populations. Table 5.5 summarizes the assumptions made for this scenario analysis.

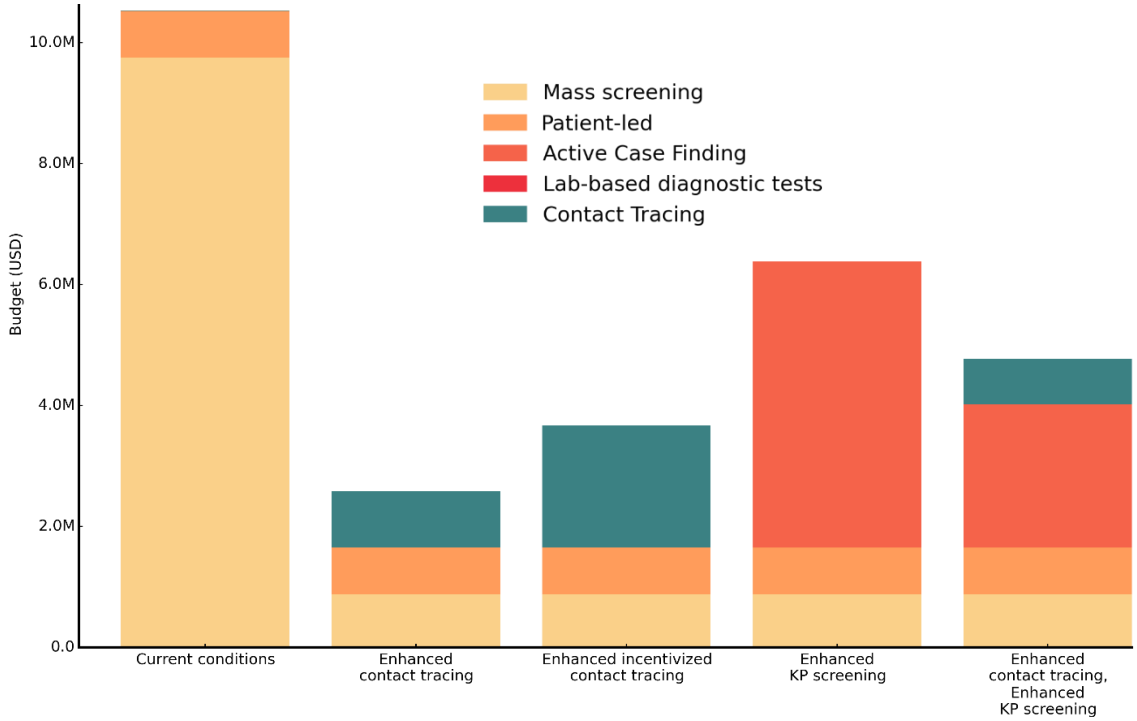
Table 5.5 Parameters for scenario group 4 - Efficient screening and case finding of active TB

	Percentage of new active TB cases found through each screening program				
	Current screening practice	**Enhanced contact tracing**	**Enhanced incentivized contact tracing**	**Enhanced KP screening**	**Enhanced KP, contact tracing**
Mass screening	12%	4%	4%	4%	4%
Passive case finding	88%	88%	88%	88%	88%
Contact tracing	<1%	8%	<1%	<1%	2%
Incentivized contact tracing	0%	0%	8%	0%	2%
Incentivized active case finding	0%	0%	0%	8%	4%

Source: Populated Optima-TB model for Belarus.

Figure 5.9 shows results of the scenario analysis on screening. The figure compares the cost required to identify an equal number of people using different diagnostic modalities.

Figure 5.9 Cost for same/equivalent/equal number of TB diagnoses using different diagnostic modalities



Source: Populated Optima model for Belarus.

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6. WHAT MIGHT BE GAINED FROM OPTIMIZED ALLOCATION OF CURRENTLY AVAILABLE FUNDING?

The analysis presented in this chapter answers the core questions of this allocative efficiency study. Previous chapters have identified the effects and costs of specific programmatic changes. This chapter analyzes the TB response holistically and answers the question of how resources need to be allocated to maximize health outcomes. The results presented in this chapter were obtained through the optimization algorithm mentioned earlier in this report and described in detail in Appendix A.

As outlined in chapter 4 of this report, the current allocation of resources in Belarus is projected to lead to continued moderate declines in TB incidence, prevalence and mortality. The scope of this chapter is to explore to what extent and how further reductions could be achieved.

6.1 OPTIMIZED ALLOCATION OF RESOURCES TO MINIMIZE INCIDENCE, PREVALENCE AND DEATHS

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

- Minimize the incidence of TB
- Minimize the prevalence of active TB
- Minimize TB-related deaths

In addition, optimizations for specific objectives were run to explore to what extent optimized allocations would differ for different sets of objectives.

How to reallocate resources?

The overall optimized allocation of resources to minimize TB incidence, prevalence and deaths is shown in Figure 6.1. In this analysis it was assumed that the same US$61.8 million that were available for TB-related programs in 2015 would remain available on an annual basis up to 2035. The optimized budget allocation differs from current allocations across several different areas. The allocation to the following program areas decreased by more than 50% each:

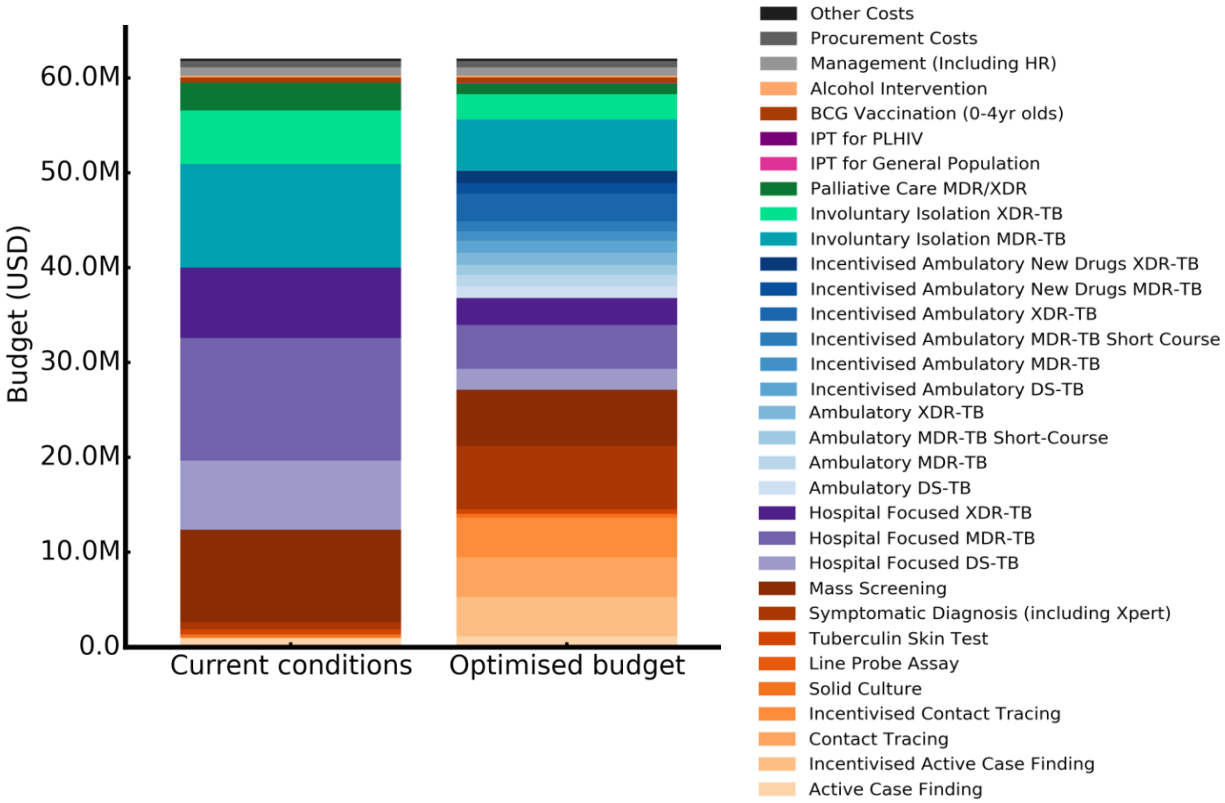
- Involuntary isolation department treatment;
- Hospital-based treatment modalities;
- Mass-screening;

- Palliative care.

In the optimized allocation, funds are reallocated to

- Incentivized ambulatory care;
- New TB drug regimens;
- Rapid-molecular testing;
- Enhanced /incentivized contact tracing and active case finding among key populations.

Figure 6.1 Current allocation of TB resources and optimized allocations to minimize cumulative TB incidence, prevalence and deaths from 2017-2030 in Belarus



Source: Populated Optima-TB model for the Belarus.
Notes: 2015=base year (current allocation); Optimized budget: It was assumed that the budget of US$61.8 million that were available for TB-related programs in 2015 would remain available on an annual basis up to 2035.

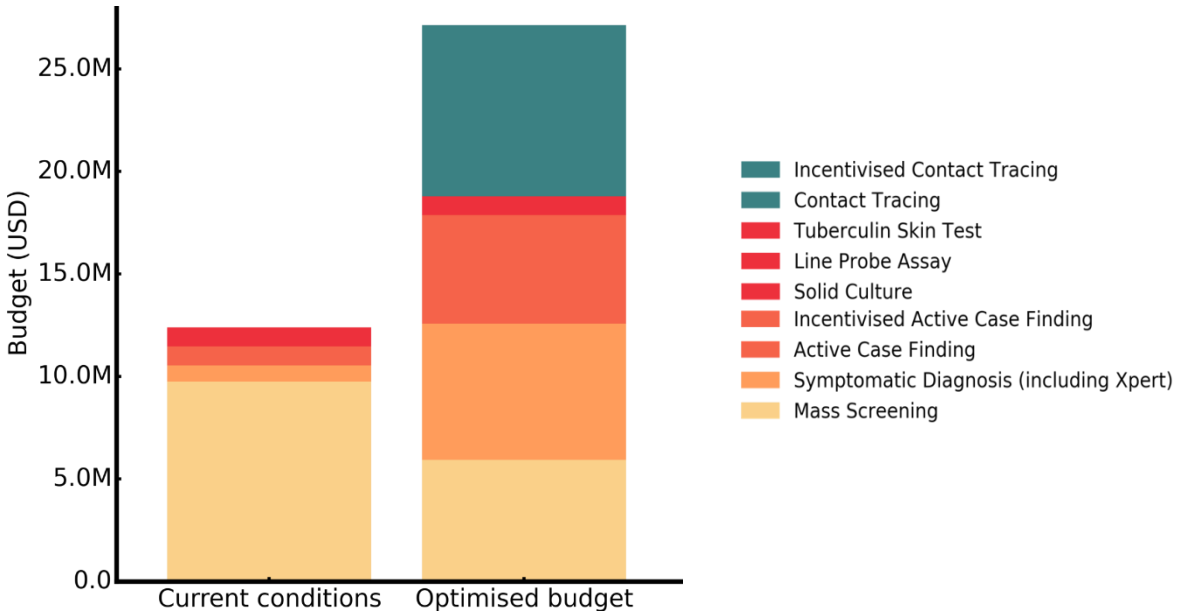
Shifts within testing and diagnosis programs

Gaps in diagnosis represent a major break point in the TB care cascade in most countries. In Belarus 3,765 new and relapse cases (72%) were notified in 2015 against an estimated 5,200 incident TB infections (WHO 2017b) as outlined in chapter 4 of this report. According to Optima-TB projections, optimized allocation of resources would imply an increase in diagnostic interventions. Figure 6.2 shows current and optimized investment into diagnostic interventions. Compared to the current diagnostic approach, which primarily builds on mass screening, optimized investment into screening and diagnosis would imply a mix of diagnostic interventions. In addition to currently available interventions, incentivized types of contact tracing and active case finding could absorb substantial investments as part of optimized allocations. Within currently available interventions, allocations to screening programs based on fluorography could be reduced substantially, while diagnosis including rapid molecular tests should be scaled up and provided to all people with presumptive TB. Overall, and considering

potential savings on hospital-care, optimized allocations imply doubling investment into case finding and diagnostic interventions to find the missing cases.

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

Figure 6.2 Current allocation and optimized allocations of resources for TB diagnosis to minimize TB incidence, prevalence and deaths

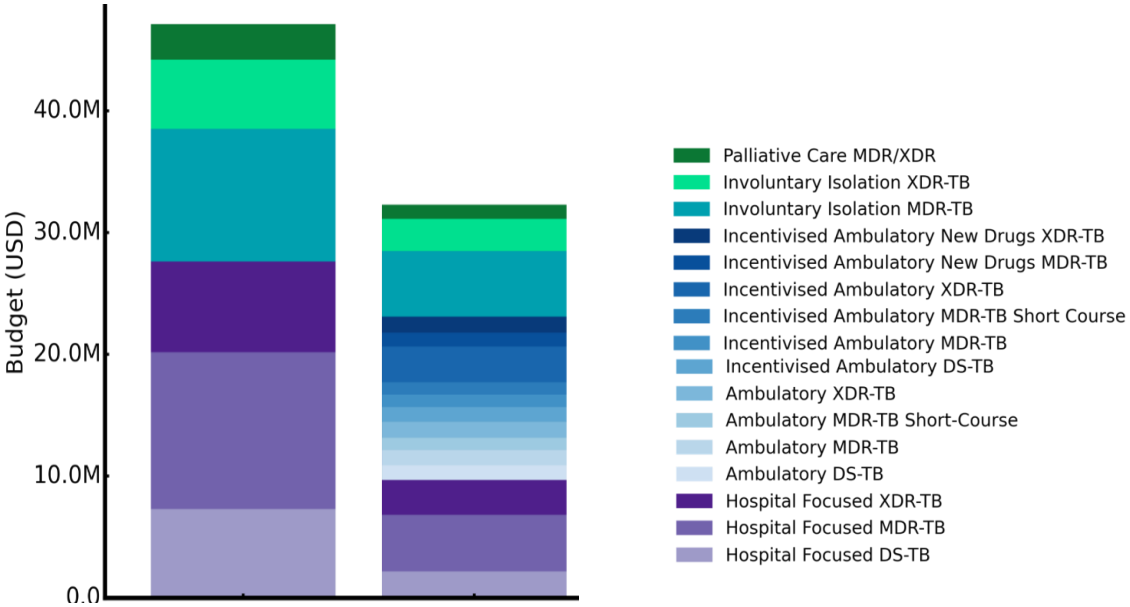


Source: Populated Optima-TB model for the Belarus.

Shifts within treatment and care programs

TB treatment and care (including hospital, ambulatory and palliative care as well as involuntary isolation) absorbed approximately three quarters of Belarus' TB spending in 2015. Optimization analysis suggests that large reallocations are possible within TB treatment and care programs. Optimized allocations imply that a combination of shortened hospital-based treatment, ambulatory care and incentivized ambulatory care would provide for approximately 90% of TB patients. Advice from national experts suggested that immediately closing involuntary isolation departments was not possible and that not all palliative care patients could be transitioned to new drug treatment regimens immediately. These treatment modalities, which were not cost-effective, were therefore constrained in the analysis, which means that investment into involuntary Isolation and palliative care in Figure 6.3 represents the minimum funding level that is needed to sustain the transition process from these modalities to more cost-effective types of treatment.

Figure 6.3 Current allocation and optimized allocations of TB treatment and care investments to minimize TB incidence, prevalence and deaths in Belarus



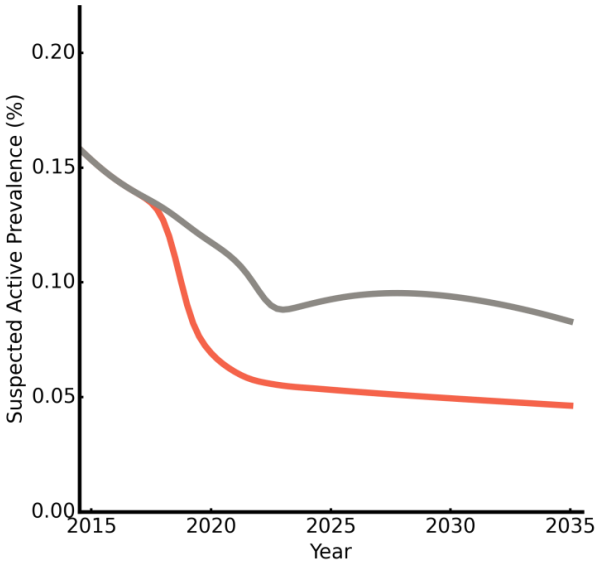
Source: Populated Optima-TB model for the Belarus.

Improved outcomes with optimized allocations

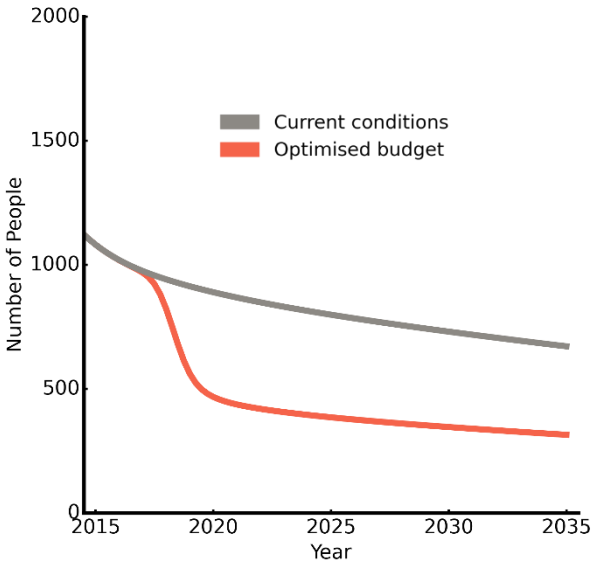
The optimized allocation of resources as shown in Figure 6.1 would have substantial effects. Figure 6.4 describes trends in TB prevalence and TB related deaths in the general population aged 15-64. Optimized allocation of resources would reduce adult TB prevalence by 45% by 2035 in comparison to current allocations. In addition, the optimized allocation would also reduce TB related deaths by 60% in comparison to current funding, and by 70% of 2015 levels, by 2035.

Figure 6.4. Epidemiological outcomes for the general population aged 15-64, with current and optimized allocations, Belarus 2015–35

a. Prevalence of active TB



b. Number of TB related deaths,

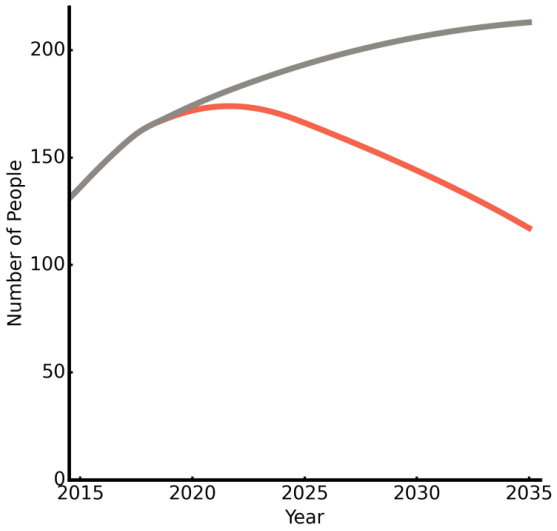


Source: Populated Optima-TB model for the Belarus.

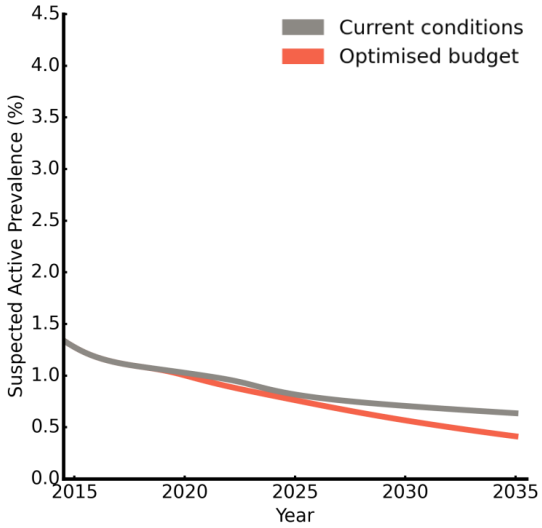
Figure 6.5 shows key outcomes of optimized allocations for PLHIV. The optimized allocation would reduce new infections by 45% by 2035 in comparison to current funding. TB prevalence among PLHIV is projected to decline by 30% through optimized allocations. Furthermore, optimized allocations were projected to avert 30% of TB-related deaths among PLHIV by 2035 in comparison to sustaining current allocations, and 15% of 2015 baseline levels.

Figure 6.5 Epidemiological outcomes for PLHIV, with current and optimized allocations, Belarus 2015–35

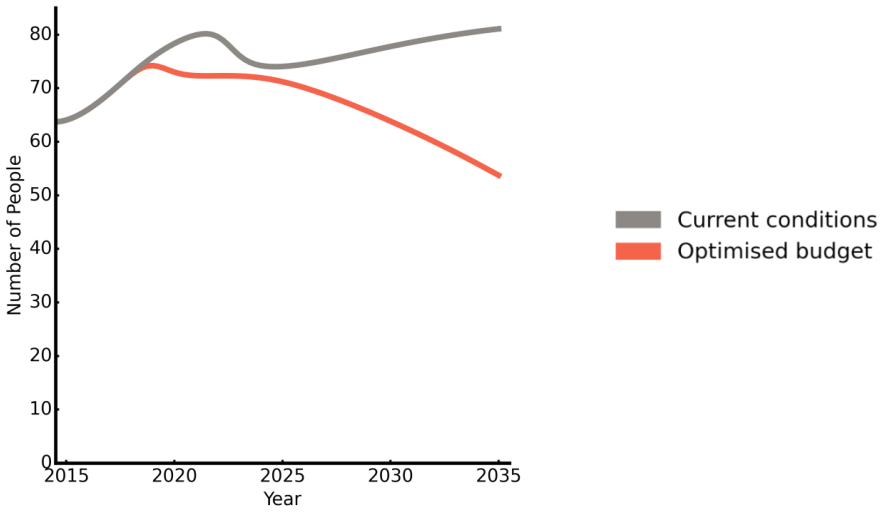
a. Number of new active TB infections



b. Prevalence of active TB, among PLHIV



c. TB-related deaths, PLHIV



Source: Populated Optima-TB model for the Belarus.

Other areas for optimizing the TB response, which were not analyzed in the model

The analyses represented in the optimized allocation do not include all possible dimensions of optimization in the TB response. A number of other areas could be considered in strengthening the TB response. For example, infection control is an area, in which additional investments could be made, particularly considering the high prevalence of MDR-TB and XDR-TB in Belarus.

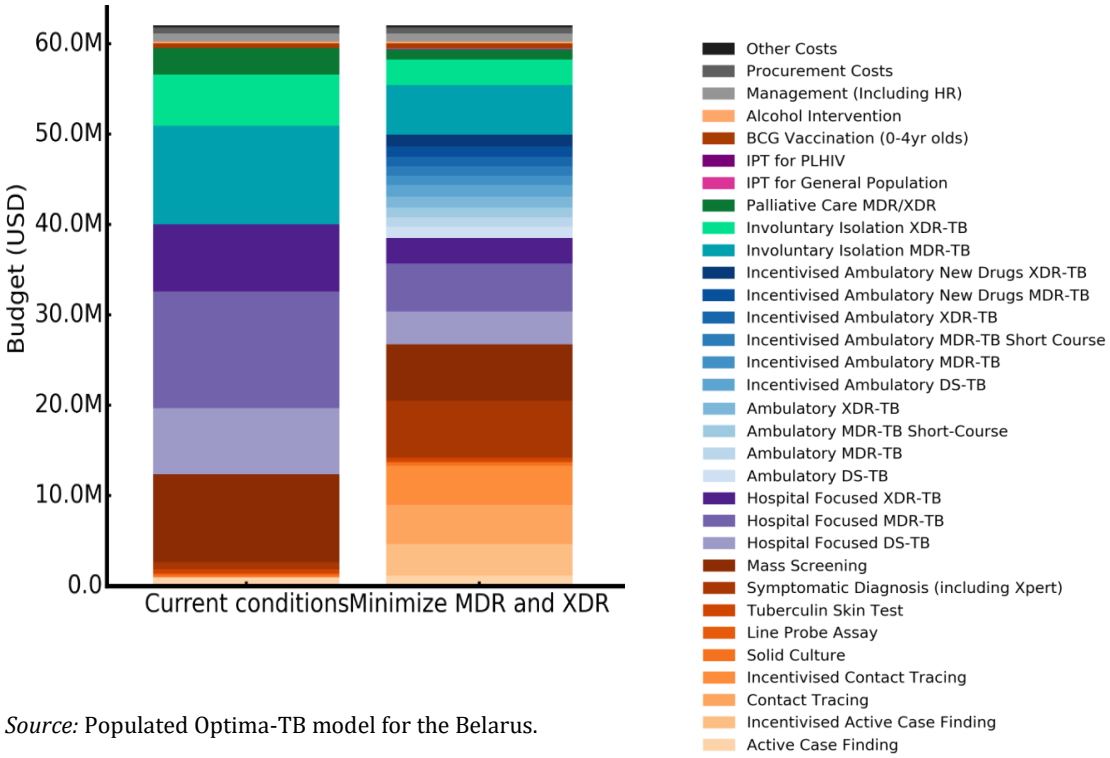
However, as part of this study it was not possible to conduct a detailed situation analysis of infection control measures, which would have been required to assess the extent of possible efficiency gains in this area. There may also be potential to enhance tobacco control in the population overall and supportive interventions to reduce smoking among TB patients. However, a detailed analysis of the effect of tobacco interventions on TB was not carried out due to limited availability of data to parametrize the model.

6.2 OPTIMIZED ALLOCATION OF RESOURCES TO MINIMIZE THE PREVALENCE OF MDR- AND XDR-TB

In addition to the overall optimization described in section 6.1, optimizations for specific objectives were run to explore to what extent optimized allocations would differ for different sets of objectives. This section summarizes findings from an optimization analysis to minimize prevalence of active MDR- and XDR-TB.

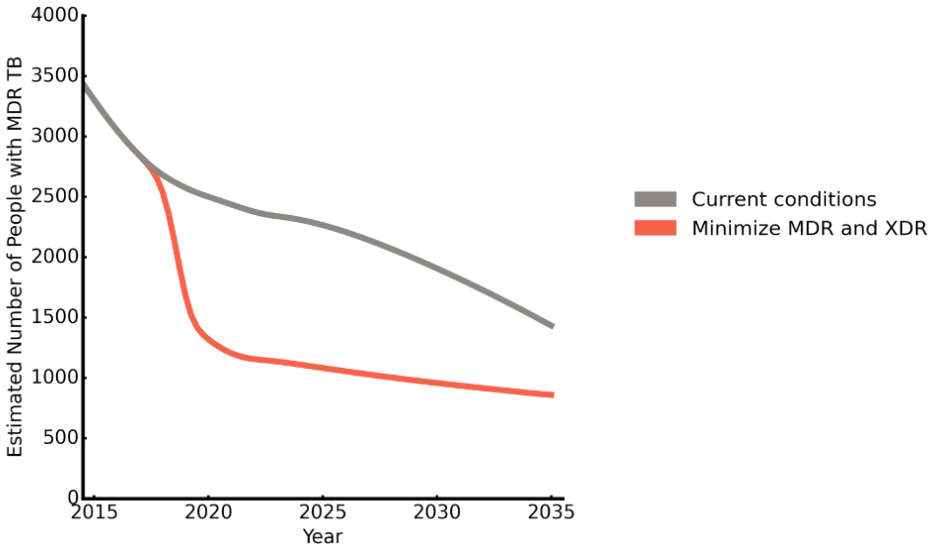
Figure 6.6. shows optimized allocations to minimize MDR- and XDR-TB. Figure 6.7 shows the effect of optimized allocations on the number of people with active MDR-TB.

Figure 6.6 Current allocation and optimized allocations of TB treatment and care investments to minimize TB incidence, prevalence and deaths



Source: Populated Optima-TB model for the Belarus.

Figure 6.7 Epidemiological outcomes for PLHIV, with current and optimized allocations, Belarus 2015–35



Source: Populated Optima-TB model for the Belarus.

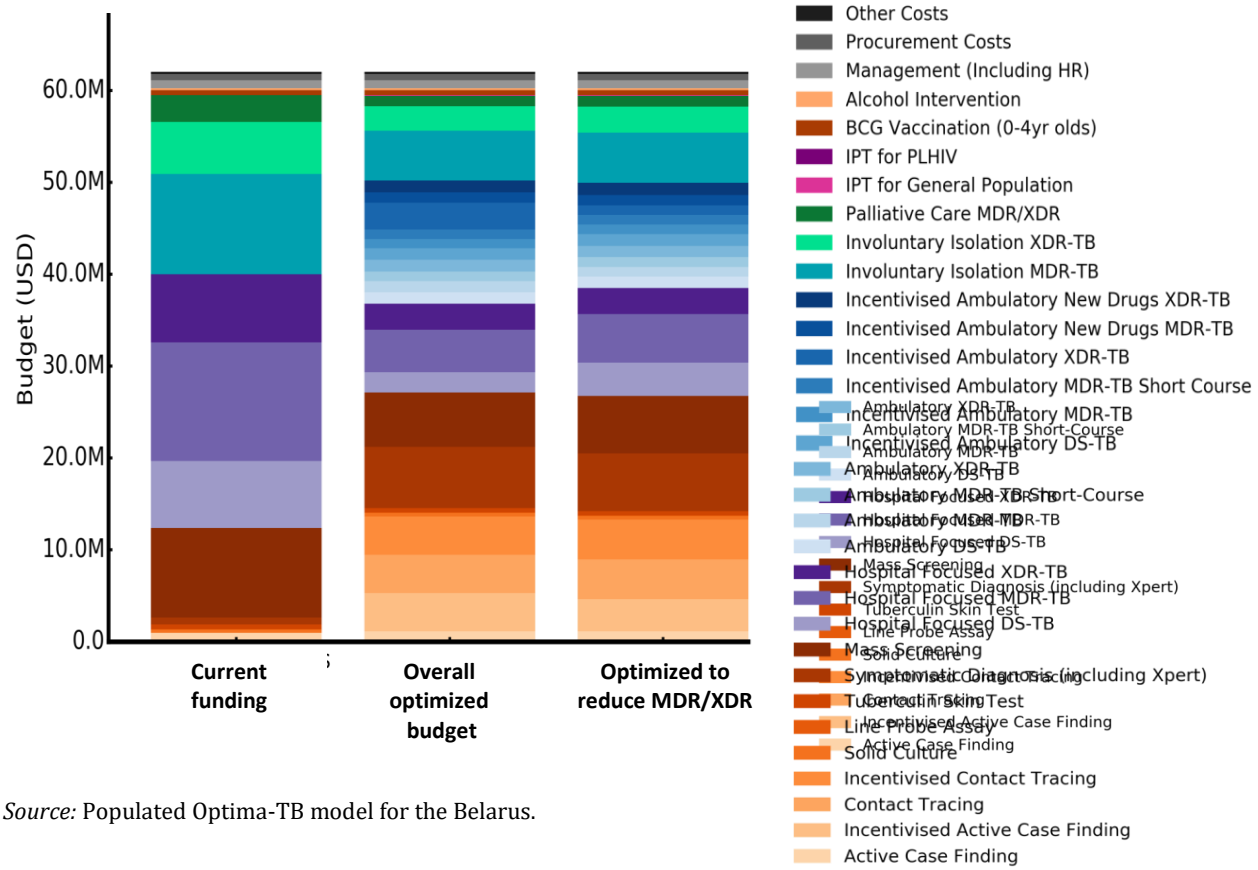
6.3 WILL OPTIMIZED ALLOCATIONS OF CURRENT RESOURCES ACHIEVE NATIONAL AND GLOBAL TARGETS?

This section explores to what extent the optimized allocations shown in previous chapters will achieve national and global targets (Table 2.2) with the level of resources available in 2015 (US$61.8 million).

Optimized allocations across different objectives have consistent findings

Figure 6.8 summarizes current allocations, overall optimized allocations (to minimize TB incidence, prevalence and deaths) and allocations to reduce prevalence of MDR-/XDR-TB. The comparison suggests that both optimized allocations require similar changes compared to current allocations. Optimized allocations to minimize MDR-/XDR TB require slightly higher levels of hospitalization than allocations to reduce all forms of TB. However, the difference is relatively minor and the core finding of this comparison is the similarity of investments required to maximize outcomes. This finding is not surprising, because given the high-level of drug resistant TB in Belarus, investments to reduce MDR-TB and XDR-TB are already reflected in the overall optimized budget to minimize all forms of TB.

Figure 6.8 Summary of current and optimized allocations



Source: Populated Optima-TB model for the Belarus.

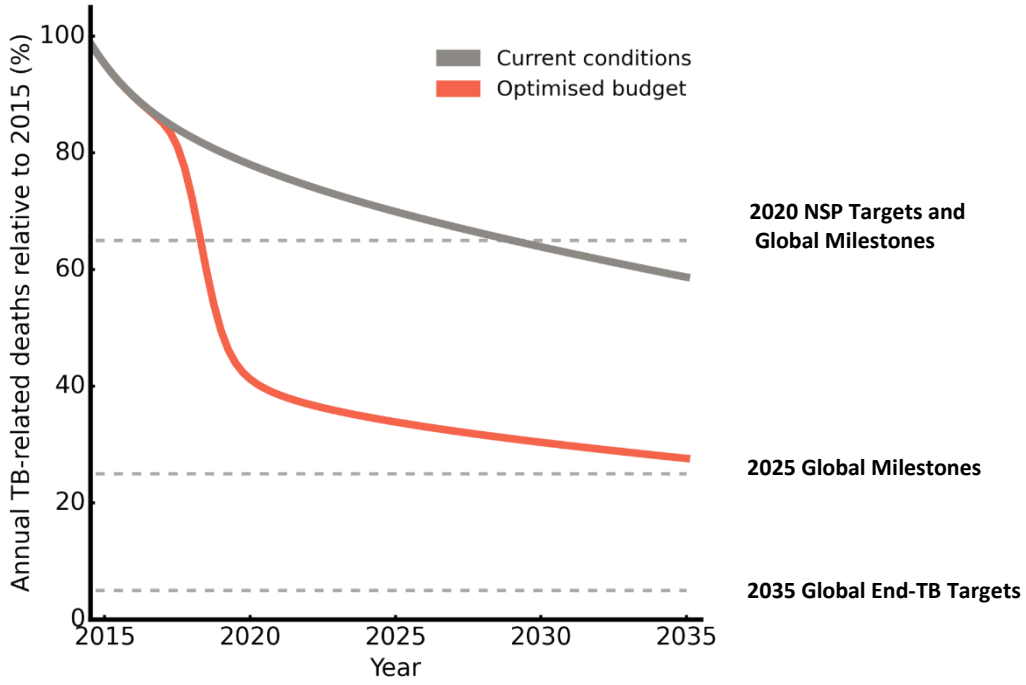
Progress towards targets with currently available resources optimized

Figure 6.9 illustrates the effect of the overall optimized allocation on TB-related deaths. The year 2015 is considered the baseline year and therefore 100%. Different key targets and milestones are represented by the dotted lines.

The Optima-TB analysis suggests that with current conditions, TB deaths would decline moderately, but all milestones and targets would be missed. The target of a 35% reduction of TB related deaths by 2020 will be missed, but a 35% reduction would be achieved by 2030. With optimized allocations, the 2020 target would be reached and progress towards 2025 milestones and 2035 End-TB targets would be made. By 2035, the optimized allocation of TB resources is projected to reduce TB related deaths by more than 70%.

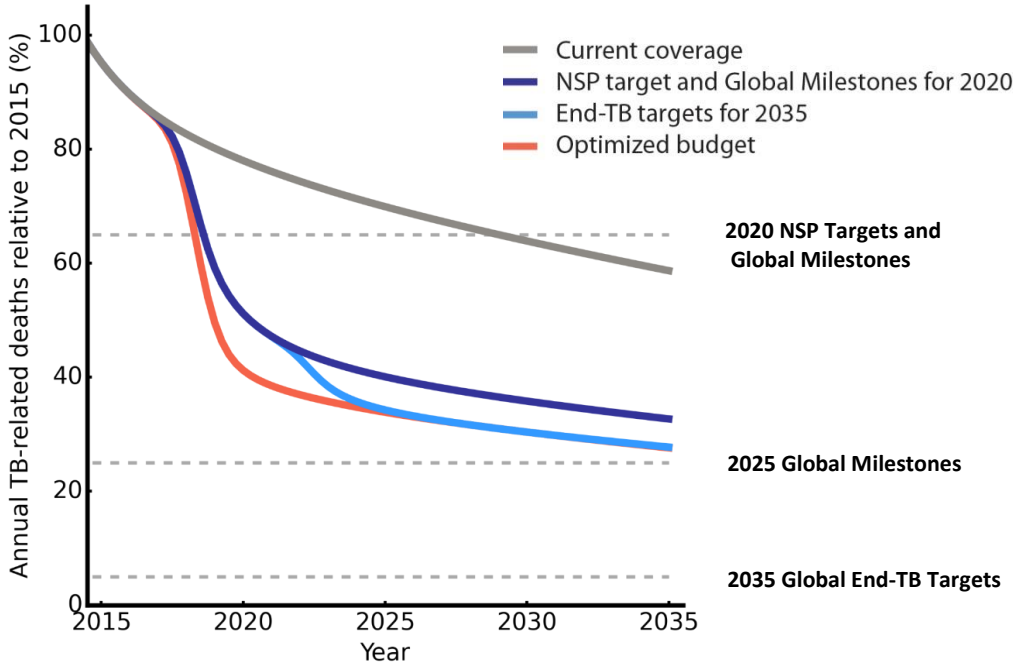
Figure 6.10 shows a comparison of TB deaths with the optimized allocation as shown in Figure 6.9 and the effect of parameter scenarios shown in chapter 5, namely the scenario to scale up diagnosis and treatment to achieve 2020 targets and the scenarios to scale up to achieve 2035 End-TB targets. As expected, the optimized allocation of resources would achieve similar death reductions as the scale up of diagnosis and treatment towards 2035 targets (scenario group 1 described in chapter 5 of this report).

Figure 6.9 Change in TB-related deaths between 2015 and 2035 with current and optimized allocations, Belarus 2015–35



Source: Populated Optima-TB model for the Belarus.

Figure 6.10 Change in TB-related deaths between 2015 and 2035 with current and optimized allocations as well as different TB care scale up scenarios, Belarus 2015–35



Source: Populated Optima-TB model for the Belarus.

While major reductions in mortality are possible with optimized allocations and scale up scenarios, the Optima-TB analysis suggests that reductions in mortality beyond 75% would be difficult to achieve. This is due to a combination of factors. The finding that the End-TB target of a 95% reduction in TB deaths is difficult to achieve is partially explained by the high prevalence of drug resistant types of TB. As long as efficacy of treatment with existing drugs remains at current levels, it is unlikely that mortality can be reduced by 95%. Another reason why it will be

difficult to end-TB by 2035 is the large number of people with latent TB infections, which under a number of circumstances can get activated (including immune compromised states, old age, malnutrition, diabetes, etc.). Diagnosis and treatment of latent TB were not modelled in detail and would require a separate analysis.

Our projections suggest that also other global targets presented in Table 2.2. will be missed, even with optimized allocations unless new technologies become available. Neither a TB incidence reduction to below 10/100,000 by 2035, 90% treatment success for MDR treatment and a 75% reduction in MDR-TB incidence were projected to achieve with optimized allocations under the assumptions made in our model in relation to epidemic trends and treatment efficacy.

7. CONCLUSIONS AND RECOMMENDATIONS

Optima-TB analyses identified and described a number of options to improve allocative efficiency of Belarus' TB response. The same budget available for TB-related activities in 2015 could, – if allocated differently – achieve the following changes by 2035:

- Reduce prevalence in the general adult population by up to 45%;
- Reduce the total number of TB deaths by up to 60%;
- Reduce TB incidence among PLHIV by up to 45% and TB prevalence among PLHIV by up to 30%.

Additional effects might be achieved with the roll-out of new and repurposed TB drugs up to 2035. The current budget, allocated optimally could achieve NSP 2020 targets and Global 2020 Milestones. The current budget, even allocated optimally, may not be sufficient to achieve Global End-TB Goals for 2035, with currently available technologies.

1 **Transition from hospital-focused to ambulatory treatment modalities could reduce the cost of TB treatment by up to 40% and free up resources for reallocation to high-impact interventions.** High and long hospitalization is the primary cost driver of the TB response in Belarus. Available evidence suggests that hospital-based treatment does not have clinical benefits over ambulatory treatment. The duration of hospitalization could be reduced substantially in line with WHO recommendations. (WHO 2017). This recommendation should not be implemented as a stand-alone measure, but in connection with enhanced support to basic ambulatory directly observed treatment (DOT) as described in Recommendation 2.

2 **Strengthening ambulatory care through incentives for health worker outreach support and for patients' adherence through a mix of delivery solutions is likely to improve treatment outcomes.** Available evidence suggests that enhanced ambulatory care can improve treatment outcomes by approximately 16% as suggested in a recent WHO review (Nguyen 2016). Belarus is already providing food packages and transport support for patients receiving outpatient care and these client incentives should be sustained. Given the substantial investment implied in providing drugs, particularly for MDR- and XDR-TB, additional incentives to support adherence could play an important role in an optimized TB response. Incentives to support providers of outpatient care in facilities and at patients' homes should be supported in line with the approach and lessons from the Mogilev pilot. The cost of video-observed treatment was estimated to be lower than the cost of incentivized outreach. Therefore video-observed treatment should be considered as an alternative for patients who were adherent in the initial phase of treatment and have the skills to use mobile technology (in line with WHO's conditional recommendation in the 2017 guidelines on TB treatment and patient care).

3 **Enhanced ambulatory care requires a reform of TB care financing to replace bed-based payment modalities by results-based modalities and single-source financing.** The current TB care financing system incentivizes facilities to sustain hospital beds and long hospitalization of patients, because financing is tied to beds. This implies that investments into ambulatory care are not made, because with a reduction of beds, units would lose their budgets. Based on the experiences from the Mogilev project and from other countries using results-based payment modalities, there is an opportunity for Belarus to explore applying a results-based financing system. Such a system might imply unifying all hospital and ambulatory TB services under a single TB budget code. In order to accelerate the expanded testing of the new financing system in Mogilev and Brest Oblasts, pragmatic choices may be required, such as the use of budget add-ons for incentivized ambulatory care based on the Mogilev pilot. National guidance for local authorities on how to operationalize changes in financing and delivery will be required. Since some patients will not be able to afford cost of care for co-morbidities related to TB, which are not provided for free in current out-patient services, there is need to ensure that care for such co-morbidities is taken into account in designing the financing model. Based on discussions during the Round Table on TB care held in May 2017 in Minsk, there is need to conduct a review of the regulatory frameworks relevant to TB care in Belarus and identify required amendments to these regulatory frameworks.

4 **Since involuntary isolation department treatment is the most expensive modality for delivering treatment, reducing and over time phasing out this delivery modality, would free up resources for other high-impact interventions.** Involuntary isolation department treatment absorbed 27% of TB response funding for 6% of TB patients (US$ ~45,600 per person/year). There is need for policy dialogue on how to transition from the current system to other types of support to patients who are currently served under this modality. One approach for transition considered by national experts is to reduce from one involuntary isolation department per Oblast to one national department at national level.

5 **Mass screening and screening of obligatory groups are the treatment modalities with the lowest testing yield and reducing their coverage in favor of more targeted screening approaches could increase diagnostic yield.** Although screening through fluorography absorbs an estimated 90% of TB related spending on diagnosis, it only contributed an estimated 12 % of all TB diagnoses, while the vast majority of new active TB was identified through passive case finding. Efforts to reduce mass screening require consideration of two specific challenges. Firstly, spending on screening is not part of TB program spending and therefore its reduction will not directly increase funding available for the TB response. Secondly, while yield of general population screening is low and cost per case identified high, simply abandoning it would increase the undiagnosed populations. Therefore the yield of scaling up alternative screening modalities (see following recommendations) should be continuously assessed. The reform of the TB screening and active case finding approach should be based on a detailed analysis of current TB testing yield (number needed to screen to identify one TB case) by sub-population and location to inform the new screening strategy.

6 **The contribution of contact tracing and active case finding among key populations to the total number of TB cases identified could be increased by introducing incentivized service delivery modalities.** Data available for the Optima-TB analysis

suggested that contact tracing currently accounts for less than 1% of new active TB cases identified. Since the yield of contact tracing is higher than for mass-screening, there is an opportunity to explore expanding contact tracing beyond current practice (and therefore improving compliance with global guidance on contact tracing of index cases). Providing provider-incentives per case identified and/or per person screened are one option to consider in expanding contact tracing. An expansion of contact tracing needs to be carefully monitored, and the 'number needed to screen' to identify one presumptive TB case and the cost per case identified need tracking. In addition, the undiagnosed population could be reduced by expanding active case finding among key populations (homeless, diabetics, alcohol, people who inject drugs, PLHIV) and exploring incentives for providers per TB case identified. Measuring yield of expanded active case finding in different sub-populations can inform decision-making on further expansion or reduction in active case finding in specific populations and locations.

7 **The scale up of rapid molecular diagnostics will be an important step towards reducing time from screening to treatment initiation and thereby reduce the infectious period.** Optima-TB analysis suggests that expanding rapid molecular (Xpert) testing towards reaching 100% of presumptive TB cases would accelerate diagnosis of rifampicin resistance and thereby accelerate initiation on MDR-TB treatment (in South Africa, the country with the largest Xpert testing program, Xpert improved the detection of rifampicin resistant TB and contributed to a reduction in treatment delay from a median of 44 days to 22 days over two years (Cox H 2017).

8 **Reallocating savings from palliative care and involuntary isolation department treatment to new drug regimens is projected to improve treatment outcomes, in particular for XDR-TB.** Current treatment success rates of 54% for MDR-TB and 38% for XDR-TB are below what has been achieved elsewhere with drug combinations involving new drugs. Optima-TB projections suggest that scaling-up XDR-treatment with current treatment success rates is not a viable pathway towards changing the trajectory of the XDR-TB epidemic. The use of drugs such as bedaquiline, clofazimine and linezolid for treatment of pre-XDR and XDR-TB patients would not only increase treatment success rates but was also projected to reduce future treatment need by more than half by 2035. Bedaquiline is currently procured through the Global Fund at no cost. The scale-up and sustained provision of effective treatment regimens will require financial and political commitment from the national government, in order to ensure that potential savings in other areas can be reallocated to treatment with more effective regimens.

9 **Introducing alcohol screening for all adult TB patients and provision of a brief alcohol intervention for TB patients with problematic alcohol use, are low-cost interventions with the potential to improve treatment adherence and outcomes.** Problematic alcohol use is very high in Belarus in international comparison (WHO 2014) and alcohol addiction and problematic alcohol use are likely the most prevalent comorbidity of TB in Belarus. Due to limited data available, the effect of alcohol interventions could not be tested in the mathematical optimization, but the cost of the intervention was estimated to be fairly low, at approximately US$0.2 million for covering all TB patients with alcohol screening and providing the brief alcohol intervention to all TB patients with problematic alcohol use. Although not analyzed in detail as part of this study, it would be worth considering to also introduce enhanced and regular counselling on tobacco use among TB patients during drug collection visits.

10 **The number of TB notifications in prisons has declined substantially, but enhanced TB care and screening for prisoners post-release remains a priority.** Optima-TB estimates suggest a more than five-fold reduction in TB prevalence in prisons in the past decade in line with a decline of a similar magnitude in TB notifications recorded in prisons. However, compared to the general population, the TB incidence rate in prisons remains high (>250/100,000 in 2015), which implies high testing yield, likely also after release. Retention of prisoners on TB treatment remain a priority post-release and should entail continued adherence support, which should be enhanced by incentivized ambulatory care.

11 **Considering the country's growing HIV epidemic, there is need for strengthened linkages between HIV and TB services.** While HIV testing for TB patients is near universal at 99% (WHO 2017b), ART coverage of 84% among TB patients could be further increased. There are major gaps in the HIV treatment cascade with less than half of the 35,000 estimated PLHIV diagnosed. Optima-HIV analysis recommended scaling up of ART and prevention programs for key populations. In addition to achieving 90-90-90 HIV testing and treatment targets, there is need to scale up IPT, which is currently only provided to 10% of PLHIV. Also, in addition to scaling up and linking clinical care, there is an opportunity in systematically integrating TB screening and IPT provision into routine care for PLHIV on ART, PLHIV pre-ART, and key population outreach services, in particular for people who inject drugs.

12 **Reaching the 2035 target of a reduction in TB incidence to less than 10/100,000 will require addressing latent TB.** Optima-TB analyses suggest that even very high coverage of active TB-treatment is unlikely to result in the targeted TB incidence reduction to less than 10/100,000. Interventions to reduce latent TB were not specifically analyzed as part of this study, however, the analysis did suggest a large number of latent TB infections in the general population as well as PLHIV. In order to inform future strategic planning processes post 2020, it will be useful to consider incorporating operational research needs on latent TB into the current national strategic plan.

13 **Closing strategic information gaps through operational research, will be essential in informing Belarus' TB care reform.** As Belarus' engages in a process of TB care reform, continued generation of evidence to inform policy choices will be critical. The operational research agenda could include (but not be limited to) specific strategic information gaps that emerged as part of this allocative efficiency study such as enhanced understanding of TB transmission by sub-population, evolvement of antimicrobial resistance patterns, yield of different screening approaches and break points in the TB care cascades for different sub-populations.

APPENDIXES

APPENDIX A TECHNICAL SUMMARY OF OPTIMA

Appendix A provides a brief technical overview of Optima. The Optima mathematical modelling suite was designed to support decision-makers in prioritization, resource allocation and planning to maximize impact of health interventions. 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 (Kerr 2016).

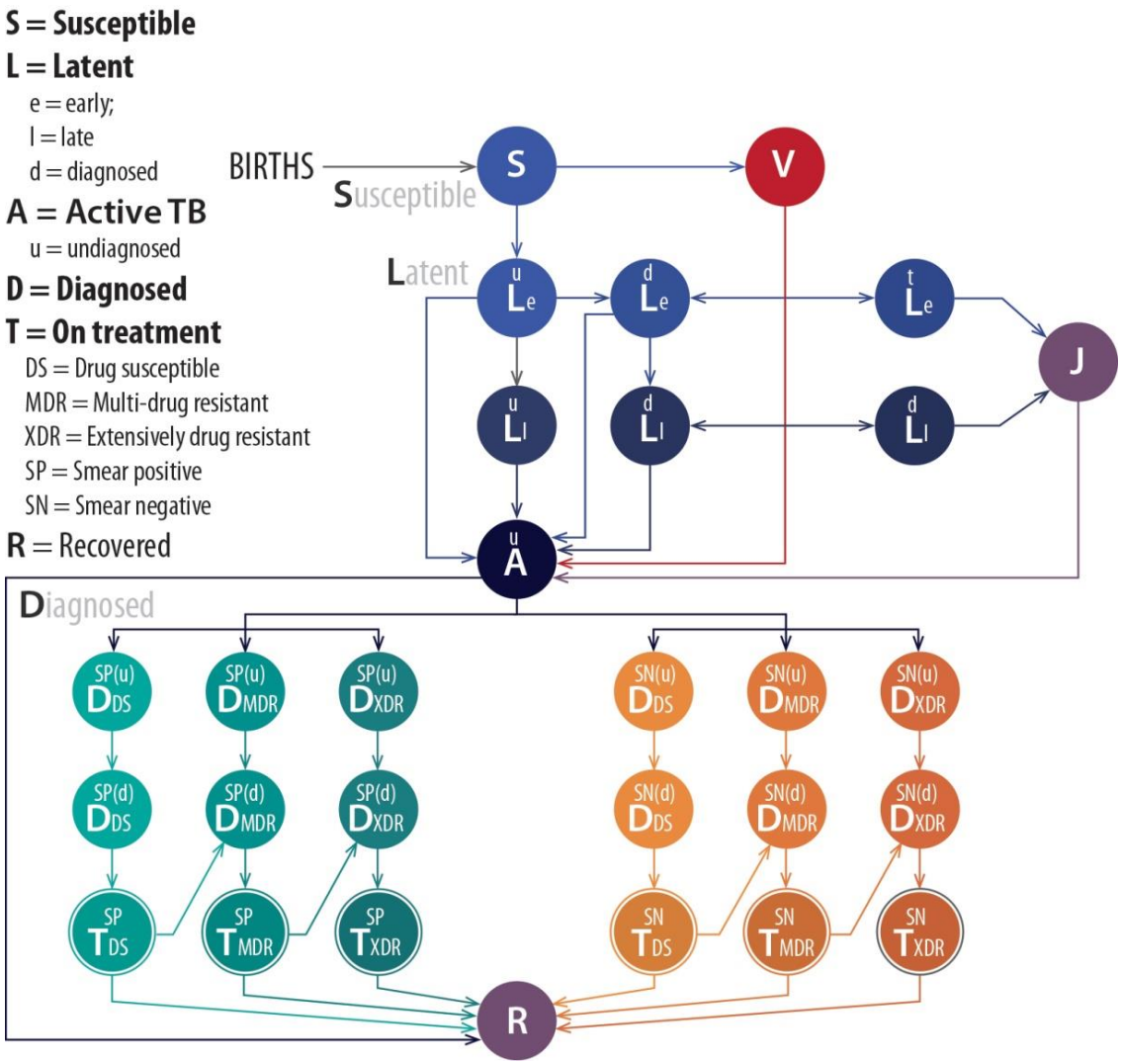
Optima-TB is a mathematical model of TB transmission and disease progression integrated with an economic and program analysis framework. Optima uses TB epidemic modeling techniques and incorporates evidence on biological transmission probabilities, detailed infection progression and population mixing patterns. Optima-TB is a compartmental 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 type into drug susceptible (DS), multi-drug resistant (MDR) and extensively drug resistant (XDR).

Optima-TB is based on a dynamic, population-based TB model. Figure A.1 shows the basic disease progression implemented in the model at the time it was applied in Belarus.

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.1, disks) corresponds to a single differential equation in the model, and each rate (Figure A.1, arrows) corresponds to a single term in that equation. Table A.1 lists the parameters used in Optima; most of these are used to calculate the force of infection. The analysts interpret 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 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.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 among 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 Optimization and Program Coverage Targets

A novel component of Optima is its ability 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 can be used to inform TB strategic planning and the determination of program coverage levels.

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

To perform the optimization, Optima uses a global parameter search algorithm, which is an adaptive stochastic descent algorithm. (Kerr C. 2017) 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 optimization problems, the team has shown that the algorithm can determine optimized solutions with fewer function evaluations than traditional optimization methods, including gradient descent and simulated annealing.

Uncertainty Analyses

Optima uses a Markov chain Monte Carlo (MCMC) 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.[3]

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

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

APPENDIX B FITTING PROCESS FOR OPTIMA-TB IN BELARUS

This appendix describes the fitting process during the application of Optima-TB to Belarus, and specific modification that had to be included while fitting the model to the TB epidemic in Belarus.

Demographics

Country demographics within the Optima-TB framework are calculated for each key population within the model by considering:

- initial population size;
- annual birth rates or numbers;
- annual mortality rates;
- transfers in and out of population, due to aging;
- other transfers in and out of the population, due to non-aging effects such as migration or incarceration.

Population size, number of births and mortality rates are reported directly from the country, while transfers between populations can either be at rates that are calculated using values similarly specified following known data, or due to aging, where a proportion of a key population is moved to the next population and assuming that there is a uniform distribution of ages within a key population. As these values are directly reported by the country with considerable confidence, the model output is usually consistent with the known data values for country demographics and no modifications are required.

In the case of Belarus, it was found that the simulated population sizes using the reported values did not follow the reported demographic values (Fig 1a). The discrepancy between the reported and simulated population sizes was especially significant for two populations: the “0-4 Years” and the “5-14 Years”, reaching differences in population sizes that were in the order of 10,000’s and 100,000’s, respectively. These discrepancies were causing related challenges in fitting the prevalence and incidence values for the disease.

It was found that the underlying cause for this discrepancy between known demographic data and model output was due to an abrupt increase in the birth rate during the mid-2000s in Belarus, following a change in its socioeconomic situation. (National Statistical Committee of the Republic of Belarus 2012) This is reflected in the age proportions for each age as recorded for 2011. As a result, although aging transfers were applied as a proportional value (for example, in the case of the “0-4 Years”, one fifth of the population was aged out to the “5-14 Years” key population), the actual aging structure should have assumed a non-uniform proportion.

This was able to be addressed in Optima-TB by including a non-linear aging transfer that reflected the reality of the trends within each age bracket. The resulting fit when using this updated term alone was able to reduce the discrepancies originally observed (Figure B1. B).

The inclusion of non-uniform aging was a new feature that had not been required for previous country applications in other disease areas, such as HIV, malaria or nutrition.

Disease progression using epidemiological model

Progression rates for TB were obtained for natural progression of the disease and in response to treatment for values such as disease duration and fatality. The model was setup to replicate

these experiments by considering a population that all started in the same disease state, and examining how quickly people progressed into subsequent disease states or death.

Using this process, we found generally a good agreement with the values for case fatality and disease duration, for both the natural progression of the disease and when on treatment (Table B.1; Figure B.2).

Prevalence estimates from notified cases for total Active TB

Data provided by Belarus included the yearly numbers of registered notified new TB cases, but not estimates in absolute numbers for TB prevalence. The most recent WHO Global Tuberculosis Report 2016 did not publish country-level prevalence estimates in the Global TB Database supplements and as a result, two options were suggested to estimate prevalence for Belarus.

The first involved using the WHO report on TB Estimation (Glaziou 2016), and following the method outlined to calculate prevalence from the notified cases shared by the country. After consulting a TB expert however, we were advised to use WHO prevalence estimates, because trying to calculate prevalence from notified cases would almost always result in an underestimation compared to the widely recognized and accepted WHO prevalence estimates. Attempts using this method did result in underestimations (around 2000 cases lower than expected for a given year), partly because notified cases reported by the WHO differed slightly compared to those supplied by Belarus, and likely due to some additional assumptions made by the WHO that are not published within the WHO report (Glaziou 2016).

Given the underestimation, the suggestion of using country-level prevalence rates published by the WHO 2015 Global TB Programme (sourced from supplement section of a journal article (Houben 2016)) was followed. The prevalence for a given year was multiplied by the total population of that year (reported in the country sheet provided by Belarus), in order to generate a prevalence estimate as a number for the total population.

To disaggregate total TB prevalence by age, an assumption that 5-10% of the total TB-prevalence is accounted for by the 0-14 population was used. Using the assumption therefore apportioned 7.5% of the total prevalence to the 0-14 population and the remaining 92.5% to the rest (15+). There are however four age-groups in the model (0-4, 5-14, 15-64, and 65+), and the 0-14/15+ estimates calculated were further split into these four groups by using proportions calculated from the notified cases reported by the country. For example to estimate prevalence in the 0-4 age-group, the proportion of 0-4 notified TB cases as a fraction of the total number of notified TB cases in the 0-4 and 5-14 age-groups combined, was multiplied by the prevalence number calculated for the 0-14 age grouping using the 7.5% assumption. Similarly, for the remaining 5-14 age-group, and in the cases of 15-64/65+ the denominator of proportions was the combined number of notified cases recorded for both groups 15+.

The need to disaggregate prevalence according to smear-status or type of resistance was addressed by using proportions based on the numbers of notified cases reported by the country. The respective age-group estimates were multiplied by the proportions of smear+ and smear-out of the total number of recorded notified cases by age-group. Similarly, in order to disaggregate by resistance-type, the proportions of DS-TB, MDR-TB, or XDR-TB as fraction of the total notified cases of a given smear-status in an age-group, was multiplied by the smear-status prevalence estimates of their respective age group.

The second method involved only the data provided by Belarus and three carefully selected assumptions. The prevalence of TB each year was calculated as an iterative process by adding incidence of new cases to the prevalence in the previous year and subtracting deaths and recoveries. The model was firstly built to study the value of prevalence for the whole TB

population, results were compatible with estimates from WHO 2015 Global TB Programme. Afterward we disaggregated the equations to study age-specific values for 0-4, 5-14, 15-64 and 65+ age groups. In the end we finally disaggregated for smear status and strain (i.e. drug sensitive, drug resistant and extreme drug resistant TB).

The assumptions used to initialize the model were: (i) the prevalence value describing the starting year which came from the WHO 2015 Global TB Programme, (ii) the rate describing children (0-14) cases selected accordingly to another report (Hovhannesyan 2015) and (iii) incidence detection rate from WHO Surveillance Report 2014.

To study the data of notified cases, deaths and recovery cases polynomial regression analysis was applied. The method also allows to infer prevalence of undiagnosed TB cases, both as a total yearly values and also as disaggregated values by age, smear status and strain.

Disaggregation of by diagnosis and treatment status

Assumed values for diagnosis and treatment were taken from Global Fund reporting, with diagnosis rate of 0.68 and treatment rate of 0.97 respectively. Assuming steady-state equilibrium, this corresponds for a given population that 32% are undiagnosed, 2% are diagnosed and 66% are in treatment. This was independently verified, using the case notifications.

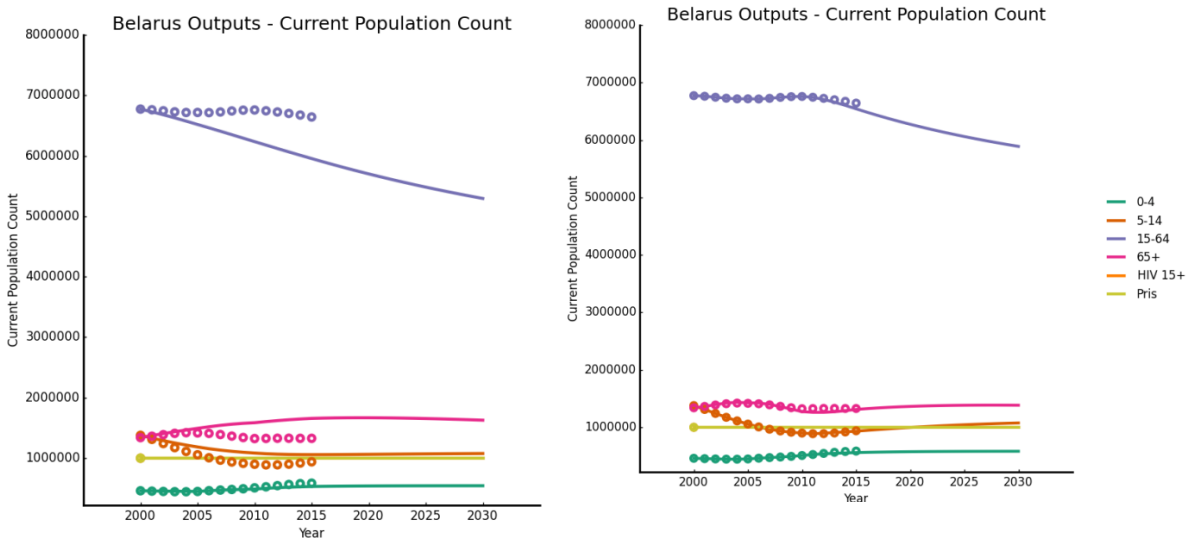
Progression from Latent to Active TB

To evaluate the outflow of people moving from the early latent compartment to both the late latent and active TB compartments we based our analysis on a review paper. (Andrews 2012) In this work, several studies from the pre-chemotherapy era were analysed where healthy individuals got in contact with active infected individuals. Subjects were followed up for a variable amount of time and the number of new active cases was recorded. After assuming, due to the high level of exposure, that all people in contact with the active patients entered the latent status, using statistical analysis (survival model) we were able to infer the probability of developing active TB during the first five years after infection (early latent timeframe).

We applied the same methodology to devise the probability of not developing active TB after 5 years and, combining the two values, we were able to estimate the early latent progression rate.

Figure B.11 Demographics fit. (A) Using original aging transfers that assumed a uniform distribution of ages; (B) improved fitting, using a non-uniform distribution of ages within each key population.

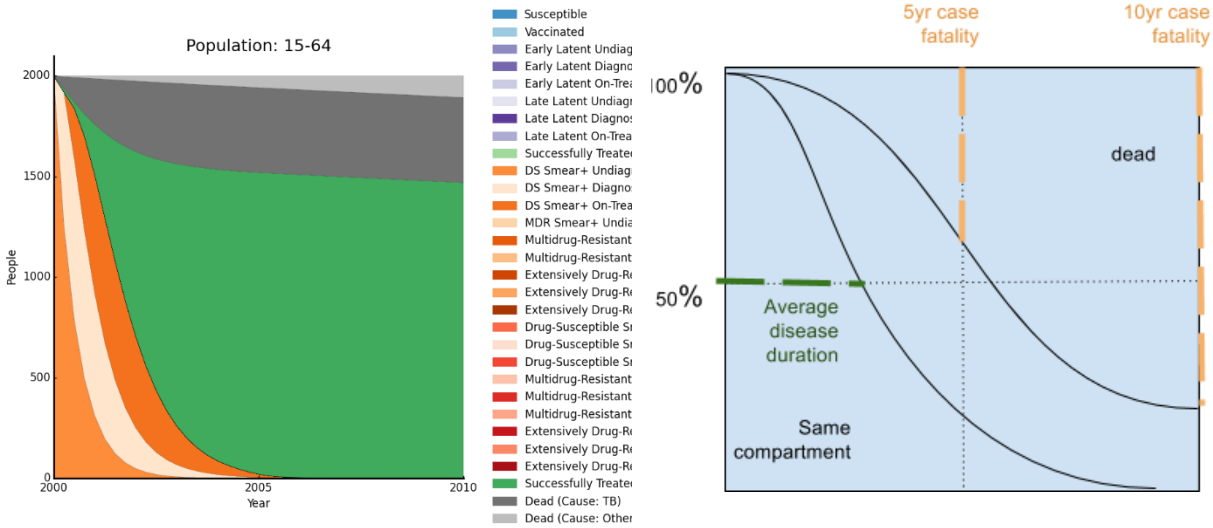
Figure B.1(A) **Figure B.1(B)**



Source: Authors.

Figure B.12: Disease progression.

Figure B.1(A) **Figure B.1(B)**



Source: Authors.
Notes: (A)=Determining disease states, following progression from an initial state. Here, births and population migrations in and out of the population were disallowed. Depending on the investigation, testing and treatment rates were disabled to represent the natural progression of the disease, or set as the calibrated version if treatment was included. This specific example shows Treated, HIV; (B)=Disease progressions were used to obtain average disease duration and case fatality rates, as well as other characteristics such as percentage of people who spontaneously self-heal.

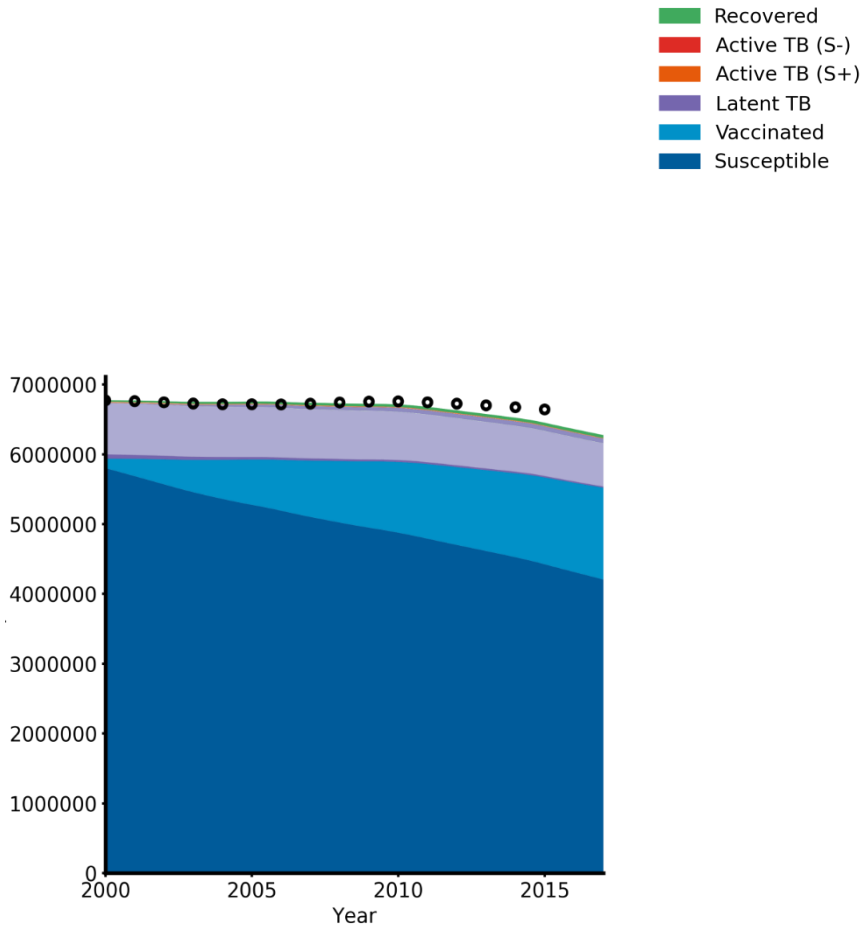
Table B.6 Disease progression values

Natural progression			**Model output**	**Reference**
Untreated, HIV negative	**Disease duration:**		3.25–3.5 years	
	1–4 years			WHO
	3 years			Tiemersma 2011
	Smear positive case fatality			
	Case fatality rate	70%		WHO
	5 year case fatality	55%	46% at 5 years	Tiemersma 2011
	10 year case fatality	72%	66% at 10 years	Tiemersma 2011
	Smear negative case fatality			
	Case fatality rate:	20%		WHO
	10 year[4] case fatality	20%	15% at 10years	Tiemersma 2011
Untreated, HIV positive	Disease duration		0.01–0.2 years	WHO
	SP Case fatality rate	83%		WHO
	SN Case fatality rate	74%		WHO
Disease progression on treatment			Model output	Reference
Treated, HIV-	Disease duration: 0.2–2 years		0.25–2 years	WHO
Treated, HIV+	Disease duration: 0.01–1 year			WHO

Source: Authors

[4] Reported as 'lifetime case fatality', although in the same study the authors refer to a maximum window of 10 years.

Figure B.3 Sample calibration figure: General population 15–64



Source: Authors.

APPENDIX C KEY DATA INPUTS INTO THE MODEL

Demographic inputs

Table C.7 Population sizes

	2000	2005	2010	2015	2020	2025	2030	Assumption
0–4	460,895	449,370	509,391	586,330	545,506	496,739	441,386	–
5–14	1,378,121	1,056,221	899,809	939,479	1,082,908	1,130,785	1,041,454	–
15–64	6,772,442	6,717,244	6,758,057	6,642,413	6,300,537	5,966,079	5,751,617	–
65+	1,340,065	1,417,309	1,324,413	1,327,604	1,435,637	1,600,268	1,743,031	–
Prisoners	–	–	–	–	–	–	–	29,000

Source: Prepared by authors based on UN World Population Prospects (United Nations, Department of Economic and Social Affairs, Population Division. 2015).

Table C.2 Background mortality (percentage of people who die annually)

	2000	2005	2010	2011	2012	2013	2014	2015
0–4	0.24%	0.18%	0.12%	0.12%	0.11%	0.11%	0.11%	0.09%
5–14	0.03%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%
15–64	0.70%	0.66%	0.65%	0.66%	0.66%	0.66%	0.67%	0.68%
65+	7.57%	6.95%	6.69%	6.68%	6.67%	6.67%	6.68%	6.90%
Prisoners	**1.40%**	**1.31%**	**1.31%**	**1.31%**	**1.32%**	**1.33%**	**1.34%**	**1.35%**

Source: Prepared by authors based on UN World Population Prospects (United Nations, Department of Economic and Social Affairs, Population Division. 2015).

Table C.3 Number of newly notified TB infections

	2000	2005	2010	2011	2012	2013	2014	2015
0–4	–	1	–	–	–	–	–	–
5–14	–	–	1	–	–	–	–	–
15–64	595	1071	696	**667**	577	481	392	348
65+	131	114	79	**70**	72	66	53	36
Prisoners	–	–	–	–	–	–	–	–

Source: Vital registration system

TB notifications (new active TB)

Table C.4 Number of newly notified TB infections

			2005	2010	2011	2012	2013	2014	2015
0–4	**Total**	All strains	35	7	5	2	2	6	3
		DS-TB	–	7	3	2	2	4	1
		MDR-TB	–	0	2	0	0	2	1
		XDR-TB	–	–	–	–	–	0	1
5–14	**Total**	All strains	124	19	17	13	11	14	9
		DS-TB	–	19	14	13	11	11	5
		MDR-TB	–	0	3	0	0	2	1
		XDR-TB	–	0	0	0	0	1	3
15–64	**Total**	All strains	4301	3621	3438	3214	2983	2669	2419
		DS-TB	–	3151	2802	2471	2260	2050	1850
		MDR-TB	–	470	636	743	723	493	361
		XDR-TB	–	–	–	–	–	126	208
	Smear +	All strains	–	2401	2632	2939	2848	2429	1827
		DS-TB	–	2092	2153	2264	2168	1854	1285
		MDR-TB	–	309	479	675	680	449	334
		XDR-TB	–	–	–	–	–	126	208
	Smear -	All strains	–	1220	806	275	135	240	592
		DS-TB	–	1059	649	207	92	196	565
		MDR-TB	–	161	157	68	43	44	27
		XDR-TB	–	–	–	–	–	0	0
65+	**Total**	All strains	–	542	450	523	525	469	532
		DS-TB	–	505	407	419	433	419	424
		MDR-TB	–	37	43	104	92	23	87
		XDR-TB	–	–	–	–	–	27	21
	Smear +	All strains	–	315	246	337	329	292	379
		DS-TB	–	293	222	270	271	242	277
		MDR-TB	–	22	24	67	58	23	81
		XDR-TB	–	–	–	–	–	27	21
	Smear -	All strains	–	227	204	186	196	177	153
		DS-TB	–	212	185	149	162	177	147
		MDR-TB	–	15	19	37	34	0	6
		XDR-TB	–	–	–	–	–	0	0
Prisoners	**Total**	All strains	364	151	139	159	106	105	83
		DS-TB	–	0	122	127	79	66	42
		MDR-TB	–	–	17	32	27	12	3
		XDR-TB	–	–	–	–	–	27	38

Source: National TB program database (Republican Scientific and Practical Centre on Pulmonology and Tuberculosis 2017)

Cost data

Table C.5 Unit costs for TB prevention and diagnosis in Belarus

Diagnosis & preventive programs	Unit cost (per test or person-year), 2015, US$
BCG vaccination	1.32
Tuberculin skin test	4.32
LPA testing	16.16
Solid culture testing	1.43
Liquid culture testing	12.97
Microscopy	0.50
Xpert testing	16.80
General population screening X-ray /fluorography	1.00
Preventive therapy for latent individuals	11.52
IPT/ART for HIV positive individuals	11.52
Costs for management (totals)	
Management including HR	892,061
Other costs	255,055
Procurement cost	649,349

Source: WHO NHA, procurement records, expert opinion.
Note: Assumptions: Commodity cost plus 20% for delivery for all tests and preventative therapy, except Xpert where 25% is added to the commodity cost.

Table C.6 Treatment duration and cost of care by modality and resistance type

		Duration (in days)			Unit cost per day US$		Cost of care
Modality	**Regimen**	**Inpatient**	**Outpatient**	**Total**	**Inpatient**	**Outpatient**	**Total US$**
Current practice							
Hospital-based	DS treatment	60	120	180	24.80	8	2492
Hospital-based	MDR	210	390	600	32.90	8	10170
Hospital-based	XDR	270	450	720	32.90	8	12646
Involuntary isolation	MDR	600	_	600	29.50	_	17700
Involuntary isolation	XDR	720	_	720	29.50	_	21240
Alternative modalities							
Standard ambulatory	DS treatment	14	166	180	24.80	8	1735
Standard ambulatory	MDR - long	45	555	600	32.90	8	6122
Standard ambulatory	MDR - short	30	285	315	32.90	8	3370
Standard ambulatory	XDR	60	660	720	32.90	8	7493
Incentivized ambulatory	DS treatment	14	166	180	24.80	8	1735
Incentivized ambulatory	MDR - long	45	555	600	32.90	8	6122
Incentivized ambulatory	MDR - short	30	285	315	32.90	8	3370
Incentivized ambulatory	XDR	60	660	720	32.90	8	7493

Source: Prepared by authors based on national program records

Table C.7 Treatment costs by modality and resistance type

		Costs of care	Other costs		Total non-drug costs	Drug costs	Total costs	
Modality	**Treatment regimen group**	**Total**	**Food packages**	**Incentives**		**Full course**	**Full course**	**Annualized**
Current practice								
Hospital-based	DS	2491.52	63	_	2,555	55	**2,610**	2609.7
Hospital-based	MDR	10170.43	205	_	10,376	3,782	**14,158**	8612.8
Hospital-based	XDR	12646.19	237	_	12,883	7,600	**20,483**	10383.8
Involuntary isolation	MDR	17700.00	0	_	17,700	3,782	**21,482**	13068.4
Involuntary isolation	XDR	21240.00	0	_	21,240	7,600	**28,840**	14620.3
Alternative modalities								
Standard ambulatory	DS	1735.40	87	_	1,823	55	**1,878**	1877.8
Standard ambulatory	MDR - long	6121.77	292	_	6,414	3,782	**10,196**	6202.7
Standard ambulatory	MDR - short	3370.36	150	_	3,520	1,000	**4,520**	4520.5
Standard ambulatory	XDR	7493.35	348	_	7,841	7,600	**15,441**	7827.7
Incentivized ambulatory	DS	1735.40	87	338	2,160	55	**2,215**	2215.4
Incentivized ambulatory	MDR - long	6121.77	292	1129	7,543	3,782	**11,325**	6889.2
Incentivized ambulatory	MDR - short	3370.36	150	580	4,100	1,000	**5,100**	5100.0
Incentivized ambulatory	XDR	7493.35	348	1342	9,183	7,600	**16,783**	8508.0

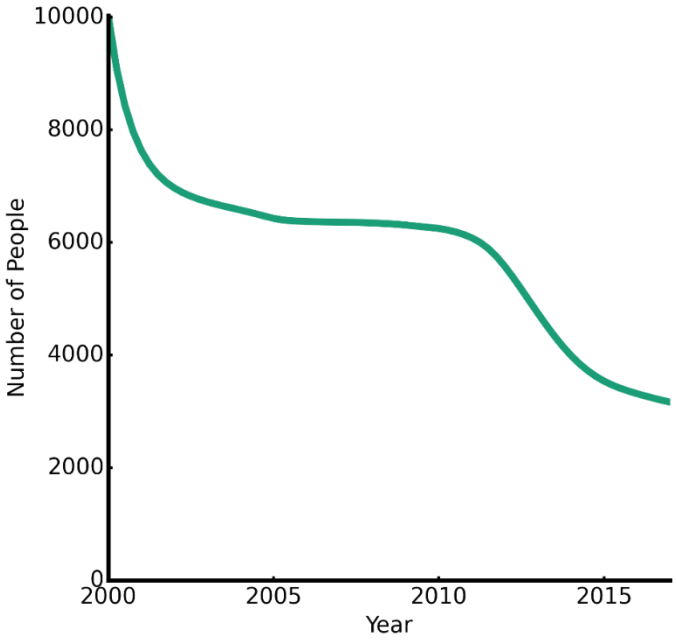
Source: Prepared by authors based on national program records

APPENDIX D ADDITIONAL RESULTS NOT INCLUDED IN THE BODY OF THE REPORT

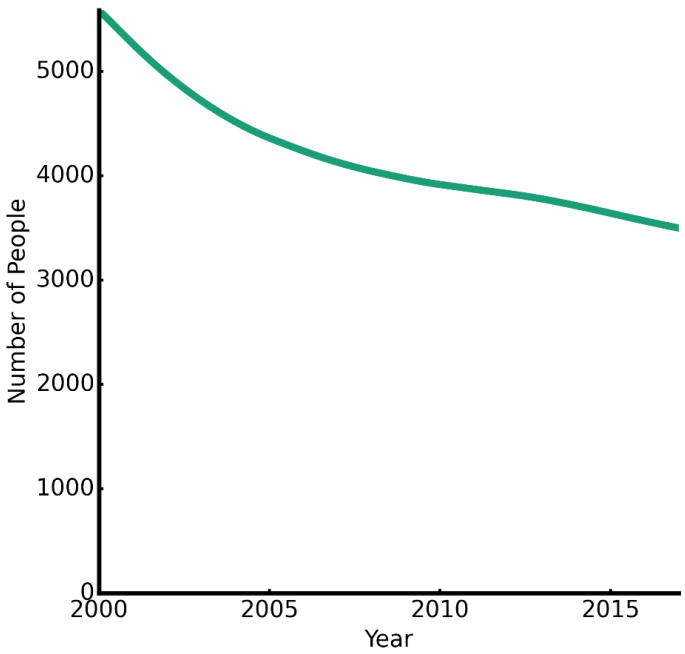
New latent and active TB infections

Figure C.1 Model-predicted new TB infections

a. New latent TB infections



b. New active TB infections



Source: Populated Optima-TB model for Belarus.

APPENDIX E GLOSSARY

Allocative efficiency (AE)	Within a defined resource envelope, AE of health or HIV-specific interventions provides the right intervention to the right people at the right place in the correct way to maximize targeted health outcomes.
Effectiveness	Degree of achievement of a (health) outcome in a real-world implementation setting.
Efficiency	Achievement of an output with the lowest possible input without compromising quality.
Financial sustainability	Ability of government and its partners to continue spending on a health or HIV outcome for the required duration and to meet any cost of borrowing without compromising the government's, household's, or other funding partner's financial position.
TB incidence	Estimated total number (or rate) of new (total number of diagnosed and undiagnosed) HIV infections in a given period.
TB prevalence	Percentage of people who are infected with HIV at a given point in time.
Implementation efficiency	Set of measures to ensure that programs are implemented in a way that achieves outputs with the lowest input of resources. In practical terms, improving implementation efficiency means identifying better delivery solutions. Doing so requires improving planning, designing service delivery models, and assessing and addressing service delivery "roadblocks." Implementation efficiency will improve the scale, coverage, and quality of programs.
Model	Computer system designed to demonstrate the probable effect of two or more variables that might be brought to bear on an outcome. Such models can reduce the effort required to manipulate these factors and present the results in an accessible format.
Program effectiveness	Program effectiveness incorporates evaluations to establish what works and impacts disease and/or transmission intensity, disseminating proven practice, and improving the public health results of programs.
Program sustainability	Ability to maintain the institutions, management, human resources, service delivery, and demand generation components of a national response until impact goals have been achieved and maintained over time as intended by the strategy.
Saturation	Maximum level of coverage that a program can achieve.
Technical efficiency	Delivery of a (health) service in a way that produces maximum output at the lowest possible unit cost while according with operational quality standards.
Universal health coverage (UHC)	Universal health coverage (UHC), is defined as ensuring that all people have access to the promotive, preventive, curative, rehabilitative, and palliative health services that they need, of sufficient quality to be effective, while ensuring that the use of these services does not expose the user to financial hardship.

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