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# Incorporating system dynamic modeling in infection transmission of tuberculosis

8D10139 – Public health

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**CONTENTS**

## NORMATIVE REFERENCES

The following normative references have been used in the thesis:

Concept of Healthcare System Development of the Republic of Kazakhstan until 2029.

Resolution A/RES/73/3 adopted by the United Nations General Assembly on October 10, 2018, following approval by the high-level meeting of the General Assembly on the fight against tuberculosis on September 26, 2018.

Resolution A/RES/70/3, Transforming our World: the 2030 Agenda for Sustainable Development adopted by the United Nations General Assembly on September 25, 2015.

Resolution EB134/SR/4, Global strategy and targets for tuberculosis prevention, care, and control after 2015 developed by the World Health Assembly on January 21, 2014.

## DEFINITIONS

The thesis involves the following terms with the corresponding definitions:

**Calibration** – a process by which model parameters are adjusted to bring model's outputs into agreement with data.

**Compartmental model** – a modeling approach where the population is divided into different compartments, representing their status of disease or other factors.

**Deterministic model** – a model which has only one possible output when all its parameters are fully specified.

**Optimization** – the process of finding the best input variable values from among all possibilities without explicitly evaluating each possibility.

**Parameter** – any quantity governing rates of change of different compartments.

**Simulation** – the representation of behavior or characteristics of one system using another system.

**System Dynamics** – an approach to understand the nonlinear behavior of a complex system over time using stock, flows, internal feedback loops.

**Validation** – the set of processes and activities intended to verify that models are performing as expected.

## LIST OF ABBREVIATIONS

| | |
|---|---|
| AR | – Autoregressive |
| ARMA | – Autoregressive moving average |
| ARIMA | – Autoregressive integrated moving average |
| CHE | – Current healthcare expenditure |
| CI | – Confidence Interval |
| DOTS | – Directly Observed Treatment Strategy |
| GDP | – Gross Domestic Product |
| GRNN | – Generalized regression neural network |
| KMO | – Kaiser-Meyer-Olkin |
| KZT | – Kazakhstan Tenge |
| MAE | – Mean Absolute Error |
| MAPE | – Mean Absolute Percentage Error |
| MDR TB | – Multidrug-resistant tuberculosis |
| MTB | – Mycobacterium tuberculosis |
| NNNAR | – Neural nonlinear autoregression |
| PC | – Principal Component |
| PCA | – Principal Component Analysis |
| RMSE | – Root Mean Square Error |
| SARIMA | – Seasonal autoregressive integrated moving average |
| SD | – System Dynamics |
| SDG | – Sustainable Development Goal |
| SDOH | – Social Determinants of Health |
| SIR | – Susceptible-Infected-Recovered |
| SEIR | – Susceptible-Exposed-Infected-Recovered |
| TB | – Tuberculosis |
| USD | – United States Dollar |
| VIF | – Variance Inflation Factor |
| WHO | – World Health Organization |
| XDR TB | – Extensively drug-resistant tuberculosis |

# INTRODUCTION

**Relevance of the research**

Tuberculosis (TB) is still a big global health problem. The World Health Organization (WHO) estimates that in 2024 around 10.7 million people developed TB and 1.3 million died from TB, making TB one of the top causes of death in the world [1].

This challenge closely relates to the United Nations Sustainable Development Goal (SDG) 3: «Good Health and Well-being», which aims to end the TB epidemic by 2030. Progress toward this goal, as outlined in the SDG monitoring framework, is mainly measures by tracking the rate of TB incident cases [2]. This goal is connected to the WHO's End TB strategy, which lays out clear milestones: reducing TB incidence rate by 80% and TB mortality by 90% by 2030 compared to 2015. By 2035, the targets rise to a 90% drop in TB incidence and a 95% decline in TB mortality, plus making sure no household faces catastrophic expenses because of TB [3].

Following year of gradual decline, global TB incidence. Stabilized and subsequently increased slightly during the period 2021-2023, primarily because of COVID-19-related disruptions to diagnostic, treatment, and healthcare services worldwide [4]. A similar pattern of stagnation was observed in Kazakhstan, where TB incidence rate exhibited a plateau from 2020 through 2024, following substantial reductions in previous years [5]. Consequently, overall progress toward reducing the TB burden continues to lag substantially behind the targets set for 2030 and 2035 under the WHO' End TB strategy [6].

TB incidence is profoundly influenced by a broad array of socioeconomic factors [7]. Since the WHO formally endorsed the concept of social determinants of health (SDOH) in 2008, the unequal distribution of these determinants has been recognized as a primary driver of health inequalities. This framework underscores that socioeconomic inequalities shape exposure to TB risk factors, vulnerability to progression from infection to active disease, and access to timely diagnosis and effective treatment, thereby perpetuating or exacerbating the TB burden in disadvantaged communities [8].

The Republic of Kazakhstan maintains a consistent policy focused on strengthening public health and advancing progress toward the United Nations SDGs, with particular emphasis on reducing TB incidence. The Concept for the Development of Healthcare in the Republic of Kazakhstan until 2029 establishes ambitious targets for TB incidence reduction. Furthermore, the Concept highlights a critical gap in the current forecasting system, specifically it largely lacks scientifically grounded methodologies, approaches, and tools for predicting and evaluating the epidemiological situation, as well as for analyzing and investigating the relationship between risk factors and population health status.

Thus, the epidemiological situation regarding TB us characterized by a persistently high incidence rate. Under these conditions, the need to develop and apply new approaches to assessing the epidemiological situation is increasing. Furthermore, particular importance is attached to taking in to account socioeconomic factors that determine the dynamics of TB spread and the effectiveness of control measures.

**Research aim**

Projecting TB incidence in the Republic of Kazakhstan through 2035 using System Dynamics modeling and assessment of the impact of socioeconomic factors on the dynamics of the epidemic process.

**Research objectives**

1. To study the dynamics of TB incidence and to evaluate the contribution of the healthcare system's activities and socioeconomic factors to changes in the indicator.
2. To develop a model of TB spread in Kazakhstan using the System Dynamics approach and to assess the predictive accuracy of the model.
3. To identify the most significant socioeconomic factors influencing TB incidence.
4. To conduct scenario modeling of the long-term impact of socioeconomic factors on TB incidence in Kazakhstan through 2035.
5. To determine optimal values of socioeconomic parameters in the model that contribute to achieving the WHO's target indicators for reducing TB incidence.

**Scientific novelty**

This study introduces significant scientific novelty by offering the following contributions:

1. An analytical linkage between the transmission coefficient of TB and key socioeconomic factors has been established for the first time.
2. A simulation model incorporating socioeconomic factors into the epidemiological framework of TB spread has been created for the first time.
3. Optimal target values for key socioeconomic indicators have been established and proposed for the first time, enabling the achievement of the WHO's targets for TB incidence reduction by 2030 and 2035.

**Theoretical significance of the research**

The theoretical significance of this work resides in its establishment of a robust methodological and conceptual foundation for an integrated modeling approach that merges epidemiological compartmental modeling with the systematic analysis of socioeconomic determinants. This contribution substantially enriches the theoretical underpinning of TB epidemiology and provides a reliable platform for future research in the field, allowing subsequent studies to build upon, refine, adapt, or extend the proposed hybrid frameworks across diverse epidemiological contents and geographic regions.

The results of the study provide empirical evidence supporting the SDH framework in the content of infectious disease epidemiology. This contributes to a more holistic theoretical approach for studying and controlling infectious disease in populations where socioeconomic conditions play a significant role in shaping health outcomes.

In addition, the work is closely aligned with both global initiatives such as the WHO's End TB Strategy and national TB control and healthcare development programs in Kazakhstan, and its findings and analytical approach can serve as a robust theoretical basis for the formulation and justification of evidence-based public health strategies and policy interventions.

**Practical significance of the research**

The results of the thesis were incorporated into the analytical and methodological work of the Regional Center of phthisiopulmonology in the form of a model designed as a user-friendly tool for assessing and projecting the epidemiological situation regarding TB (Appendix D). The adoption of the model in managerial practice allows healthcare administrators to distribute resources on an evidence-based basis and to strategically plan interventions aimed at controlling the epidemiological situation of TB.

The findings of the thesis were also integrated into the educational activities of the department of infectious diseases and phthisiology at Karaganda Medical University as an innovative educational tool (Appendix E). Implementation of the model supports the development of key competencies in analyzing the epidemiological patterns of the epidemic process of TB, as well as in evaluating and forecasting trends in the epidemiological indicators of TB.

A state certificate of copyright registration has been granted (Appendix C).

**The main finding to be defended**

1. In recent years, Kazakhstan has shown a tendency toward a slowdown in the rate of decline in TB incidence. Socioeconomic factors make the main contribution to the dynamics of TB incidence.
2. The developed model is a valid and reliable tool for projecting TB incidence.
3. The most sensitive parameters of the model are current health expenditure and unemployment rate.
4. Increasing the volume of social assistance to TB patients is the most effective measure for reducing TB incidence by 2035 in the long term.
5. To achieve the WHO' targets for reducing TB incidence, it is necessary to comprehensively improve the overall socioeconomic situation of the population, increase healthcare financing, and strengthen social support measures for TB patients.

**Publications**

The thesis findings resulted in the publication of 2 original articles in Scopus-indexed international peer-reviewed journals: Annali di Igiene Medicina Preventive e di Communita (55%) and International Journal of Environmental Research and Public Health (92%).

**Author's personal contribution**

The author's personal contribution to this thesis is comprehensive and spans the entire research process. The author developed the theoretical foundation and methodological framework of the study. The author formulated the study's aim, objectives; participated in all phases of the research from literature synthesis and data collection to computational implementation; and directly carried out the core investigated work. Furthermore, the author performed all statistical data processing, authored the thesis text across all sections, interpreted the findings, critically discussed their implications, and derived evidence-based conclusions together with practical recommendations. Through these extensive contributions, the author ensured the originality, scientific rigor, methodological consistency, and practical relevance of the work.

**The scope and structure of the thesis**

The present thesis is presented on 82 pages of Microsoft Word processing software and composed of the following sections: introduction, literature review, materials and methods, results, conclusions, references, and appendices. The thesis is illustrated with 19 tables and 10 figures. The bibliography includes 158 references in Kazakh, Russian, and English.

# 1 CURRENT TRENDS IN TUBERCULOSIS EPIDEMIOLOGY, APPROACHES TO CONTROL AND METHODS OF MATHEMATICAL MODELING (LITERATURE REVIEW)

## 1.1 Current trends in TB epidemiology

Over the nearly three-decade period from 1997 to 2020, the Republic of Kazakhstan has experienced a profound epidemiological transition in TB, evolving from one of the highest TB burdens in post-Soviet space to a situation of markedly reduced incidence and mortality [9].

The incidence rate of TB is primary measure of TB morbidity and the most direct indicator of ongoing transmission in a population, serving as a sensitive marker of the effectiveness of preventive measures, infection control strategies, and reduction in transmission risk factors [10]. Sustained declines in the number of incident cases are therefore a cornerstone of TB control and elimination efforts [11].

By the end of January 2020, the WHO recognized the COVID-19 outbreak as a global public health emergency and urged immediate actions to limit the spread of the virus. In response, extensive and large-scale prevention and control measures were implemented starting in February 2020 [12].

Pandemic-related interventions, such as lockdowns, reduced mobility, and the reallocation of healthcare resources led to substantial disruptions to TB diagnosis and treatment services. Importantly, these disruptions resulted in delayed case detection, reduced treatment initiation, and interruptions in patient follow-up. Consequently, this increased the risk of ongoing transmission of TB [13].

It was suggested that even relatively short disruptions to TB control measures could significantly increase TB burden worldwide. Furthermore, the increase in mortality would largely be driven by undiagnosed infectious individuals, who continue to transmit Mycobacterium tuberculosis (MTB) within communities [14].

Moreover, the COVID-19 pandemic has substantially set back global efforts to eliminate TB. Specifically, estimates from the Stop TB Partnership indicate that the disruptions caused by the pandemic wiped out nearly 12 years of progress in TB control within just one year [15].

A study conducted by researchers from China supports this statement. They analyzed monthly TB cases for the period of January to May in 2019 and 2020. It was found that newly registered TB cases in 2020 declined by 24%, 39%, 25%, 15, and 13%, respectively, relative to the corresponding months in 2019 [16].

In Kazakhstan, a retrospective analysis of TB epidemiology from 2018 to 2024 was conducted. The study encompassed the periods before, during, and after the COVID-19 pandemic. The findings indicate that the pandemic disrupted TB detection, which in turn contributed to a sharp incidence drop in 2020 mostly attributable to under-diagnosis rather than reduced transmission. However, it was followed by a partial rebound and subsequent recovery. The authors concluded that Kazakhstan achieved meaningful progress in TB control by 2024, despite the COVID-19 setbacks. It was also proposed that targeted public health strategies which address socioeconomic determinants and healthcare access are required [17].

In TB epidemiology, recurrence represents an important outcome for TB control and long-term patient prognosis. Recurrent cases can occur due to relapse, reinfection or reactivation. Recurrence remains a significant concern even after treatment success. The epidemiology of recurrence varies by underlying TB incidence [18].

A large retrospective study was conducted in Chine, which included more 10 million pulmonary TB patients. The authors assessed the incidence and temporal patterns of recurrence between 2005 and 2021. The results showed that the overall incidence rate of recurrent TB was 0.47 per 100,000 population. More importantly, 50% of recurrent cases occurred within the first two years after treatment completion. Moreover, the findings indicated that the proportion of recurrent cases doubled from 2015 to 2021. The author suggested that there is a need to strengthen post-treatment surveillance and follow-up strategies [19].

Regarding factors that influence on pulmonary TB recurrence, a comprehensive synthesis of the literature published over four decades was conducted. The findings highlight key determinants of TB recurrence. Among the factors, there are treatment adherence, previous TB history, as well as socioeconomic status. It was concluded that these factors increase the risk of recurrent disease [20]. Host genetics are also one of the factors that impact the risk of recurrent TB. A study demonstrated that specific HLA-DTB1 gene alleles in a Kazakh cohort were significantly associated with the likelihood of respiratory TB recurrent case [21].

However, another recent genomic study from Kazakhstan revealed that 93% of genomic clusters indicative of recent active and ongoing transmission. These findings highlight the utility of genomic surveillance for understanding transmission dynamics [22].

Alongside recurrence of TB, prevalence rate is also a fundamental epidemiological measure. It captures the cumulative burden of TB disease in the population [23]. TB prevalence was also affected by the COVID-19 pandemic. It was supported by a global modeling study, which demonstrated that the pandemic significantly increased the global burden of TB. The results reflect the indirect health consequences of the pandemic-related disruptions to healthcare system [24].

Estimating the true burden of TB presents a burdensome task. In this regard, population-based prevalence surveys are taken and provide essential data. For example, a cross-sectional survey estimated the presence of undetected TB cases [25]. Similarly, a national prevalence survey provided estimates of confirmed pulmonary TB cases and demonstrated that a considerable proportion of TB cases remained undiagnosed [26]. Considering this, it was found that these undetected cases present a major contribution to TB-associated mortality rate [27].

TB-attributable mortality represents the most severe outcome of the disease. It also serves as one of the principal epidemiological indicators for assessing the impact of control programs [28]. Although global TB mortality rate continues to decline, reinforcing the downward trend, which started in 2022. The global statistics suggest that TB may once again be the leading cause of death from infectious disease [29].

TB-induced mortality is influenced by a broad array of factors. But, drug-resistance is the most significant factor, which increase the risk of death from TB [30,

31]. It was shown that the patterns of drug resistance have important important implications for both transmission dynamics and TB-induced mortality [32].

Socioeconomic status is also one of the factors, which impact TB-attributable mortality. A study examined the socioeconomic burden experienced by patients with multidrug-resistant TB in Ethiopia, Indonesia, and Kazakhstan. The results showed that multidrug resistance impose substantial direct and indirect costs on households. It potentially exacerbates poverty and hinders treatment access and adherence [33]

Therefore, the literature demonstrated that TB continues to represent a significant public health challenge. Despite the progress achieved in reducing TB incidence over decades, there is still a need for sustained and coordinated control measures. The current situation has been further complicated by the COVID-19 pandemic, which negatively affected TB prevention, diagnosis, and treatment services. As a result, the previously observed decline in TB epidemiology slowed. Furthermore, an increase in the risk of undiagnosed cases, which continue to transmit the infection in the population is decelerated.

Consequently, researchers around the world have emphasized the critical importance of maintaining essential TB services during and after global health emergencies. Ensuring uninterrupted access to TB preventive, diagnosis, and treatment interventions is necessary to avoid reversing the progress achieved in TB control over the past decades. It was also noted that enhancing the resilience of health systems and incorporating socioeconomic factors into response strategies are crucial measures for restoring pre-pandemic rate of decline in the TB burden and advancing glbal efforts toward TB elimination [34].

### 1.2 Interventions for TB transmission control

1.2.1 Vaccination as the primary measure for TB prevention

Current control measures for TB encompass a multifaced approach aligned with the WHO End TB strategy. They mainly focused on enhanced prevention, rapid diagnostics, effective treatment, and supportive interventions to address implementation berries and scale-up gaps.

It should be noted that prevention strategies form a cornerstone of contemporary TB control. Current prevention toolbox details Bacillus Calmette-Guérin (BCG) vaccination, screening and TB preventive treatment regimens. A comprehensive review emphasized the importance of infection control measure across various contexts, such as households, community, and congregate settings. It also highlighted ongoing challenges like limited TB preventive treatment uptake and the need for novel vaccines [35].

The BCG vaccine remains the only licensed vaccine against TB. However, its efficacy is variable, particularly among adults. In this regard, different measure are implemented to improve vaccine performance, including revaccination approaches to enhance immune responses. These approaches are considered essential for strengthening TB prevention and supporting broader public health control efforts [36].

It was indicated that efficacy of the BCG vaccine varies considerably. A study showed that, in newborns, vaccination offers a 90% reduction in the risk of severe forms of the disease and approximately 59% protection against pulmonary TB. Another

point presents higher levels of protection of 92% against severe disease and 74% against pulmonary TB [37]. More recent study has found that administering a repeat dose of the BCG vaccine to adolescents who were vaccinated at birth but remain uninfected provides 45% efficacy in preventing TB infection [38].

The WHO first recommended universal BCG vaccination for infants and children under 5-year-old in high TB incidence settings in 1974. In countries with low or declining TB rates, selective vaccination of newborns can be considered for those at increased risk of exposure [39].

### 1.2.2 Current approaches and advances in TB diagnosis

Early detection and accurate diagnosis of TB remain fundamental components of global TB control. The reason is that timely identification of infected individuals enables early treatment initiation and reduces transmission within communities [40].

Recent literature highlights substantial progress in diagnostic technologies and screening approaches. Overall, current trends reflect a shift toward faster, more sensitive, and decentralized diagnostic methods. Thus, a systematic review report that active case finding, improved laboratory capacity, and expanded screening programs are essential for identifying undiagnosed TB cases. This is especially relevant for high-burden settings [41].

Traditional diagnostic methods, such as sputum smear microscopy and mycobacterial culture, remain widely used due to their accessibility and established clinical value. However, according to a recent study, these methods have important limitations. Particularly, low sensitivity in cases with low bacterial load and longer turnaround times for culture-based detection. As a result, nowadays molecular diagnostic technologies have become increasingly important in modern TB diagnostics [42].

Multiple studies emphasized the development of innovative diagnostic technologies to improve sensitivity and enable rapid detection of TB in resource-limited settings. In particular, biosensor-based systems offer highly sensitive solutions. They reduce diagnostic delays and enhancing accessibility of testing [43,44].

Recent advances in molecular diagnostics further expand the capabilities of TB detection. For example, a study by Yong Chen et al. demonstrated the application of targeted next-generation sequencing for diagnosing paucibacillary TB cases, which are often difficult to detect using conventional diagnostic methods [45].

In Kazakhstan, recent studies highlight both progress in TB detection and diagnostic practices. National surveillance and clinical studies indicate that TB detection measures combine traditional methods with modern molecular diagnostics. For instance, Olga Prikhodchenko et al. reported improvements in detection and diagnostic coverage in pediatric TB cases. However, the study also emphasized the continued importance of early detection and screening in children due to the often-nonspecific clinical presentation of pediatric TB [46].

Eralieva et al. demonstrated the effectiveness of screening strategies performed among adolescents in Kazakhstan. The authors concluded that these approaches are essential to identify early-stage disease before the development of severe clinical symptoms [47].

Molecular diagnostics approaches are also increasingly used in Kazakhstan. Daniyarov et al. used whole genome sequencing to characterize drug-resistant MTB strains circulating in the country. Their finding highlights the importance of genomic diagnostics for identifying resistance mutations and understanding transmission patterns [48].

Overall, current literature demonstrates a clear trend toward integrating advanced molecular technologies into TB diagnosis framework. At the same time, traditional screening programs remain essential components of case detection strategies. Furthermore, combining modern diagnostic tools with established screening practices represents a key approach for improving early detection, reducing transmission, and strengthening national TB control programs.

### 1.2.3 Current treatment strategies in TB therapy

Effective treatment of TB remains a central component of global TB control strategies. It aims not only to cure individuals with active TB but also to interrupt transmission and prevent the emergence of drug resistance. Over the past decade, significant progress has been made in optimizing treatment regimens. In particular, it was made through shortening therapy duration and improving treatment outcomes for drug-resistant forms of the disease [49].

Traditionally, treatment of TB disease has required a standard sex-month regimen, which consists of a combination of first-line drugs. However, recent clinical trials have explored the feasibility of shorter treatment courses. For example, a randomized clinical trial demonstrated that four-month regimen could be non-inferior to the conventional six-month therapy for patients with drug-susceptible pulmonary TB. The authors concluded that this shortened regimen has the potential to improve patient adherence and reduce overall burden on healthcare system [50].

In addition to shortened regimens for drug-susceptible TB, substantial advances have been achieved in the treatment of drug-resistant TB. Multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB have historically required long and complex treatment regimens, often lasting 18-24 months. However, recent research has focused on the development of shorter regimens with improved efficacy profiles. A clinical study evaluated the shorter regimen for drug-resistant TB and demonstrated high treatment success rates among patients with XDR TB. The findings represent a significant advancement in the management of severe TB cases [51].

In parallel, a systematic review indicated that shorter regimens could achieve favorable treatment outcomes while reducing treatment duration. Such developments reflect a broader shift in TB treatment strategies toward more effective therapeutic approaches [52].

Similarly, several studies highlight the growing evidence supporting shorter and more simplified treatment strategies. The finding underscores the improved adherence to treatment, reduced cost, and effective treatment outcomes [53,54].

Studies conducted in Central Asia provide valuable insights into the implementation and outcomes of TB treatment programs [55]. In Kazakhstan specifically, recent epidemiological analysis highlights the progress in TB treatment. The study found that a majority of patients achieved successful treatment outcomes.

This reflects improvements in the national TB control program and the adoption of modern treatment regimens [56].

Under the WHO's End TB strategy, countries are encouraged to achieve a minimum treatment success rate of 90% and 80% for drug-susceptible and drug-resistant TB by 2025, respectively. Remarkedly, Kazakhstan successfully met these targets by 2023. It demonstrates substantial progress in both the management of TB treatment practice and country's commitment to strengthening national TB programs in line with the international goals [5].

Overall, contemporary research demonstrates a clear shift toward shorter and more effective treatment regimens for TB. Advances improved patient management strategies and strengthened national TB programs contribute to improved treatment outcomes worldwide.

### 1.2.4 Socioeconomic interventions for TB control

TB is widely recognized not only as a biomedical disease but also as a condition strongly influenced by social and economic determinants. Poverty, overcrowding, malnutrition, and limited access to healthcare significantly contribute to both the transmission of MTB and poor treatment outcomes. Consequently, current TB control strategies increasingly incorporate socioeconomic interventions alongside biomedical measures to address the underlying drivers of the epidemic [57].

Research literature has consistently shown that social determinants play a critical role in shaping TB incidence and distribution. Thus, a study, conducted in Central Asia settings, found that factors such as low income, undernutrition, population density, and limited healthcare access were strongly associated with increased TB incidence. Therefore, the authors emphasized that improving socioeconomic conditions and strengthening health system are essential components of effective TB control in the region [58].

Socioeconomic support interventions, which target TB-affected households, have received increasing attention in recent years. A scoping review evaluated various social protection strategies. They include financial assistance, nutritional support, and transportation subsidies. Therefore, the authors concluded that these measures can significantly reduce the economic burden of TB on affected households and improve adherence to treatment. Moreover, the study showed that alleviating financial stress and enabling patients to access healthcare services more consistently considerably contribute to better treatment outcomes and reduced transmission [59].

Evidence from large-scale population studies further supports the effectiveness of financial support programs in TB control. A study demonstrated that conditional financial support programs can substantially reduce TB incidence among socioeconomically disadvantaged populations. These programs improve living conditions and access to healthcare services and address key risk factors such as malnutrition and poverty [60]. Similarly, another study found that the conditional financial support was associated with significant improvements in TB outcomes. This illustrates the way social protection policies can indirectly reduce TB burden at the population level [61].

Interventions targeted at financial support of TB patients have also been shown to improve clinical outcomes. A systematic review analyzed the effect pf financial support on TB treatment outcomes. The authors found that financial incentives and direct cash transfers significantly improved treatment adherence and completion rates. Such interventions help mitigate the economic consequences of TB disease, which include lost income and healthcare expenses [62].

Overall, the current body of literature demonstrates that socioeconomic interventions play a critical role in TB control. Programs that address poverty, access to healthcare services, provide financial support, and reduce social inequalities can significantly reduce TB incidence and improve treatment outcomes. Integrating these measures into national TB control strategies is therefore essential for achieving global TB elimination goals and ensuring equitable access to care for vulnerable populations.

## 1.3 Mathematical modeling approaches for TB epidemiology

### 1.3.1 Mathematical models as a tool to analyze TB transmission

Mathematical modeling has become an important component of modern infectious disease research. Mathematical models can support the monitoring and projection of disease dynamics. Furthermore, they enable policymakers to forecast epidemiological trends and implement appropriate interventions [63].

In the field of epidemiology, projecting presents a rigorous, evidence-based methodology for predicting epidemiological events by extending observed historical trends into the future. This approach relies on the principle of trend extrapolation [64, 65].

Complementing the technique, scenario-based modeling adopts a more exploratory paradigm. Under this approach, multiple plausible future trajectories are constructed by developing a set of assumptions about potential divergences from current conditions. The scenario-based simulation enables the examination of «what-if» contingencies rather than a single projected continuation of existing trends [66, 67].

Multiple studies revealed a growing interest in predictive modeling. The analyses highlight a rise in applications of mathematical forecasting methods in epidemiology [68, 69].

As a part of a broader discussion on infectious disease epidemiology, a study emphasized the growing relevance of such methods in TB research. Modeling approaches have been used to explore transmission dynamics and the impact of control strategies [70].

Insights from the COVID-19 response underscore lessons for modeling infectious disease. Olesen et al. emphasize that epidemiological models are most useful when modelers and decision makers work in collaboration. This ensures that model structure, assumptions, and outputs align with public health priorities [71]. Similarly, Johnson et al. found that decision makers valued models that could provide projections and inform intervention choices. These insights underscore the importance of developing and communication models, which are tailored to specific epidemiological context [72].

In the commentary on infectious disease modeling, a study explored the strength and pitfalls of using mathematical models. The authors argue that while modeling can

provide valuable projections of disease spread and inform resource allocation, misinterpretation or overreliance on uncertain assumptions may lead to flawed policy choices. Therefore, they call for clearer communication of model assumptions, uncertainty, and limitations between modelers and policymakers [73]. Therefore, participatory engagement between modelers, policymakers. And stakeholders enhanced the utility of models for decision making [74, 75].

Contemporary epidemiological practice draws upon a diverse repertoire of modeling paradigms. The following categories proving particularly prevalent: time-series models, machine-learning techniques, compartmental models. These approaches are frequently combined in hybrid to leverage complementary strength [76, 77].

### 1.3.2 Application of time-series models in TB epidemiology

Time-series modeling plays a crucial role in understanding how infectious diseases spread. The main goal of time-series models is to systematically collect and analyze historical data over time to build a model that accurately reflects the underlying patterns of the series. This type of model can be used to predict future trends based on past behavior to project upcoming disease dynamics.

The foundation approach within this family of models is the autoregressive (AR) model. In this framework, each observation is modeled as a linear weighted combination of a fixed number of preceding values from the same series. This structure captures the dependence of the current value on its own historical trajectory. This makes the AR model well-suited to processes that exhibit clear serial autocorrelation [78].

Over time, successive refinements have produced a hierarchy of flexible extensions. Building upon the AR foundation, the autoregressive moving average (ARMA) model incorporates an additional moving average component. Thus, a study shows a case, in which ARMA model was developed to forecast TB incidence [79].

To accommodate non-stationary processes, the autoregressive integrated moving average (ARIMA) model extends the ARMA framework. This innovation has rendered ARIMA on of the most versatile and widely implemented tools for modeling real-world time series [80-82].

Time-series models have been widely applied to project TB incidence and support surveillance systems. For instance, a modeling study developed an ARIMA-based model in Malaysia. The study identified ARIMA as the best-fit model for TB incidence. The authors highlighted that such models could serve as early-warning systems for predicting disease trends [83]. Another study, conducted in China, supports the usefulness of time-series models for TB surveillance systems [84].

Time-series models remain critical, especially during the COVID-19 pandemic. Li et al. applied the ARIMA model to TB data for 2021-2022 in China. The results demonstrated that the model could accurately capture short-term trends [85].

Further adoptions have addressed specific structural features. The seasonal ARIMA (SARIMA) model augments the standard ARIMA specification with additional seasonal parameters. This extension allows the model to simultaneously capture both non-seasonal and seasonal trends. This feature is especially valuable for

epidemiological time-series, which displays pronounced annual and intra-annual cycles [86-88].

SARIMA models have been utilized in the TB epidemiology of Kazakhstan. Kalizhanova et al. investigated TB transmission dynamics by integrating the SARIMA model. The authors indicated that SARIMA models were effective in identifying seasonal patterns and provide accurate short-term forecasts [89].

Recent studies have applied time-series modeling to analyze and forecast drug-resistant TB. Thus, a study conducted in Brazil provided evidence for areas that require targeted interventions. Similarly, Chinese researchers applied the SARIMA model to capture seasonal fluctuations and regional variations in TB incidence. Collectively, these studies underscore the value of robust SARIMA models to understand the dynamics of drug-resistant TB [90-92].

It is important to recognize that time-series models impose certain methodological constrains. They can limit their effectiveness in epidemiological applications. A primary requirement is the availability of a sufficiently extensive historical dataset. Since inadequate sample size can lead to unstable parameter estimates, poor identification of underlying patterns, and unreliable projections. In many real-world surveillance contexts, consistently reported retrospective data may not always be accessible. This may lead to constraining applicability of the time-series approach [93].

Moreover, while effective for short-term horizons, time-series projections tend to deteriorate markedly over longer periods. Cumulative errors and the influence of past observations fades, which in turn renders the approach less suitable for projecting long-tern trends [94].

Despite this dependency on substantial data volume, time-series models offer a notable advantage in terms of conceptual and operational simplicity [95].

### 1.3.3 Machine learning approaches for epidemiological modeling

The increasing use of machine learning approaches in infectious disease research highlights new opportunities for improving predictive models [96]. A scoping review demonstrated that machine leaning techniques are increasingly applied to analyze communicable disease data. Such methods may also strengthen TB modeling frameworks by enabling the analysis of complex epidemiological patterns and enhancing the predictive accuracy of disease forecasting models [97, 98].

In a comparative modeling study, the performance of traditional statistical methods and machine learning techniques were assessed in the context of TB epidemiology. The authors concluded that machine learning models can improve forecasting performance by identifying complex patterns within epidemiological data. This may not be fully captured by classical statistical methods. The findings also show the potential of integrating advanced techniques with traditional modeling to enhance the projection of infectious disease dynamics [99].

Thus, in a recent study from South Africa, Azeez et al. applied a random forest algorithm to project TB cases among children. The authors argued that such approaches can serve as a valuable tool for public health planning, especially in populations where true burden of TB is underreported [100].

Compared with single statistical models, machine learning models improved prediction accuracy. This indicates the benefit of incorporating machine learning techniques into TB forecasting frameworks [101].

Therefore, recent advances in TB forecasting emphasize the integration of machine learning into traditional epidemiological modeling. Multiple studies demonstrated how various machine learning models can be adapted to predict TB incidence more effectively. This offers alternatives to classical models. Such approaches are increasingly viewed as valuable tools for capturing complex patterns in disease data and supporting evidence-based decision making in public health planning [102-104].

### 1.3.4 Hybrid modeling techniques for epidemiological prediction

Advances in forecasting techniques increasingly rely on hybrid modeling approaches. They usually combine statistical and machine learning methods. According to Sina et al., hybrid modeling frameworks often outperform individual models. The reason is that they capture both linear and nonlinear patterns within data. Such approaches are usually used in epidemiological settings, where complex patterns of transmission require flexible and robust forecasting models [105].

In recent years, hybrid modeling approaches have been increasingly applied to improve accuracy of TB incidence projections. Several studies from Chine have demonstrated the advantages of integrating linear statistical models with nonlinear computational methods. For example, hybrid model combining SARIMA with neural networks have been developed. Also, Guo et al. proposed an ARIMA-GRNN hybrid model that significantly improve prediction accuracy [106]. Similarly, Zhang et al. developed a SARIMA-NNNAR model to forecast TB incidence. The finding demonstrated superior performance over conventional models [107].

Other studies have incorporated decomposition techniques to further enhance model performance. Thus, a study applied a hybrid model to TB incidence data in Tibet [108]. More recent research has combined empirical decomposition with additional machine learning frameworks. Some studies incorporated advanced neural network structures to analyzed long-term temporal trends in TB morbidity [109, 110].

Therefore, hybrid modeling approaches can effectively capture complex temporal patterns in TB data. They also provide more accurate forecasts than traditional time-series models alone. This highlights their potential utility for public health surveillance and decision making [111-113].

### 1.3.5 Compartmental models for TB epidemiology

Compartmental models have been widely applied to examine TB transmission dynamics. This approach divides the population into epidemiological compartments, such as susceptible, infectious, and recovered individuals. This feature allows researchers to analyze transitions between disease states [114, 115].

Compartmental models have been used to evaluate the potential impact of vaccination strategies on disease transmission. Modeling studies demonstrated that vaccination plays an important role in reducing TB incidence. However, its impact depends on vaccine efficacy and coverage rate. In addition, some studies evaluated

different vaccination scenarios. They include mass immunization and targeted vaccination of high-risk groups. Such applications provide valuable insights into how vaccination strategies can contribute to reducing TB transmission [116-118].

More advanced models have incorporated age-specific vaccination. They highlight the importance of integrating demographic structure into modeling framework to better understand TB dynamics [119-121].

Furthermore, in recent years, compartmental models have been increasingly applied to evaluate interventions aimed at case detection and diagnosis of TB. These models allow researchers to explicitly incorporate parameters related to detection rates, diagnostic delays, screening strategies. Thus, it quantifies the effect of such measures on TB transmission dynamics. For example, Shrestha et al. employed a compartmental model to simulate active case finding via chest X-ray screening, as well as confirmatory testing with Xpert MTB. The analysis projected significant reductions in TB incidence and burden. The authors highlighted the way that intensified detection efforts could achieve a rapid change in epidemic control [122].

Similarly, another study developed a compartmental model to compare technologies for active TB finding among homeless populations. The model assessed their relative impacts on case detection rates and transmission interruption. The authors underscore the value of targeted screening in hard-to-reach groups [123].

More recent studies have extended these frameworks to include additional detection compartments. These works utilized a modified SEIR model. It incorporated compartments for diagnosed and undiagnosed infectious individuals. The results provided insights into how improved diagnosis influences overall TB transmission dynamics [124, 125].

Other investigations have focused on diagnostic accuracy. These works explored the impacts of different case detection measures like epidemiological consequences of false-positive diagnosis. The results quantified trade-offs in sensitivity and specificity of diagnostic tools within mathematical model [126, 127].

Collectively, these studies show that compartmental models offer a powerful tool for assessing TB diagnosis and case detection interventions.

Treatment evaluation is also widely modeled topic in the current modeling literature. Cho et al. evaluated improvements in TB treatment success rates with a deterministic compartmental model. The analysis projected substantial reductions in TB burden. It demonstrates that better treatment outcomes can interrupt transmission chains [128].

Compartmental model has been used to focus on the improvements of TB treatment quality and completion. By incorporating parameters for diagnostic delays, treatment adherence, and high-quality regimens. The model quantified reduction in mortality and transmission intensity [129]. For drug-resistant TB, a compartmental model was used to project the population-level impact of expanded treatment. The study simulated increased diagnosis and treatment success. The results showed significant reductions from treated cases and emphasizing treatment scale-up as an effective preventive tool against TB spread [130].

Another study constructed a dynamic model which incorporated MDR TB strains. The model assessed treatment interventions for both drug-susceptible and

resistant forms. The study provided insights into epidemic progression and the role of regimen efficacy in controlling resistance amplification [131].

Country-specific analyses have further illustrated treatment strategies. Such, a transmission model was employed in high-burden settings to evaluate enhancements in treatment protocols, success rates, and DOTS expansion. Projections indicated that aligning treatment performance in India and Indonesia to China's levels could reduce incidence by over 65% by 2035. This underscores the need for complementary interventions to meet global targets [132].

Recent work has addressed recurrence and regimen innovation. An SEIR model was developed to study recurrent TB in China. The study simulates scenarios with novel treatments reducing recurrence by up tp 90%. The analysis projected long-term burden reductions toward End TB goals from 2025 to 2035. This emphasizes key treatment's role in breaking reinfection cycles [133].

Agbata et al. presented a compartmental model that incorporates treatment interventions. The model captures memory effects in TB transmission. This approach examined treatment's influence on control and offered nuanced insights into non-integer order effects relevant to chronic diseases like TB [134].

The review literature collectively illustrates that compartmental models serve as a powerful and reliable framework for evaluating treatment interventions in TB. These applications deliver clear, interpretable forecasts of how advancements in treatment regimens, enhanced adherence measures, strategies for managing drug resistance, and efforts to minimize recurrence can significantly speed up progress toward TB elimination.

Despite the substantial body of literature that predominantly concentrates on biomedical interventions for TB control, a growing number of studies have begun to direct attention toward social and economic determinants of the disease. Compartmental models are increasingly employed in this emerging line of research to examine how factors such as poverty, undernutrition, income disparities, and social protection mechanisms shape TB transmission dynamics. By incorporating these elements as dynamics modifiers of core epidemiological parameters, the models enable researchers to simulate and quantify the potential epidemiological benefits of targeted poverty alleviation, nutritional supplementation, financial support, and broader social welfare policies. This shift is limited in scale, however, underscores the value of mechanistic approaches in bridging social equity and infection control to achieve more sustainable reductions in TB burden.

Nutritional interventions have received particular attention as a key social level. Thus, an age-stratified compartmental model incorporated body mass index strata to link undernutrition with accelerated disease progression and poorer treatment outcomes. The model evaluated household-level nutritional support. The results projected substantial reductions in annual TB incidence and mortality. This highlights the preventive potential of targeted nutritional care in high-burden settings [135].

Similarly, a deterministic model for the WHO's South-East Asia region captures the excess risk which is conferred by undernutrition. The results showed meaningful declines in TB incidence across the region. It emphasizes undernutrition as a modifiable upstream determinant of TB [136].

Broader socioeconomic dynamics, such as income and poverty, have also been modeled mechanistically. A compartmental model where transmission, recovery and mortality rates were explicitly functions of income and nutritional status. Simulations of improvements in these factors demonstrated significant reductions in transmission and overall disease burden. This underscores the synergic benefits of holistic socioeconomic enhancements for TB control [137].

In settings marked by social inequality and economic hardship, Rubio et al. applied a compartmental model to TB in Brazil. The study simulated economic crisis followed by social protection policies of differing coverage. The results indicated that strengthened poverty reduction measures could avert tens of thousands of TB cases and deaths through 2030. This illustrates social protection's role in buffering economic shocks and mitigating disease resurgence [138].

Conceptual and review literature further supports this modeling paradigm. Pedrazzoli et al. reviewed mathematical approaches to social and structural determinants of TB. The review identified opportunities to expand compartmental models for simulating poverty reductions and social protection interventions. It also notes persistent gaps in integration [139]. Boccia et al. advocated for compartmental models to quantify the epidemiological effects of social protection mechanisms. The authors argued that such tools are critical to evidence-informed, multisectoral strategies [140].

Therefore, although the body of literature remains relatively limited, the reviewed studies collectively demonstrate that compartmental models offer a robust and dependable framework for assessing socioeconomic interventions in TB. These models provide clear and interpretable projections of how targeted improvements in nutritional support, income levels, poverty reduction, and social protection policies can substantially accelerate progress toward TB control and long-term elimination.

In summary, compartmental models stand out from statistical and time-series approaches because they do not demand a large volume of historical data. This property becomes especially valuable when deep retrospective records simply do not exist. At the same time, these models remain relatively straightforward from a technical standpoint [141].

The strength of compartmental models lies in being mechanistic rather than purely statistical. They explicitly represent the underlying epidemiological processes. Because of the structure, the model parameters carry clear real-world meaning, which makes it natural to use the model for exploring hypothetical scenarios [142, 143].

Public health interventions can be directly incorporated and their likely impact simulated. Most classical statistical and time-series models struggle to evaluate such interventions without introducing strong extra assumptions [144, 145].

Furthermore, the dynamics produced by the model are comparatively easy to explain to public health officials and policy makers. This interpretability often proves more persuasive than coefficients coming from complex models [146].

Finally, the framework is highly extensible by nature. Starting from the classic SIR or SEIR skeleton, it is easy to add compartments and flows that reflect new feature, as they become relevant, without needing to rebuild the entire modeling approach from scratch [147-149].

All these features together explain why compartmental models continue to be one of the central tools in mathematical epidemiology whenever rapid insight is needed and detailed long-term datasets are not available.

In conclusion, TB continue to pose a significant public health challenge, and global progress in controlling the disease was disrupted by the COVID-19 pandemic. In Kazakhstan, the pre-pandemic decline in TB incidence and prevalence has slowed. It reflects the broader interruptions in healthcare services and disease monitoring.

Today, the country benefits from high diagnostic coverage, treatment success rate, and ongoing innovation in TB care. Nevertheless, sustained investments are needed to reverse the current stagnation and achieve the targets outlined in the End TB strategy. Globally, despite modest gains in recent years, most regions remain off-track due to persistent funding shortfalls and social inequalities.

Scaling up social protection interventions is widely recommended to address these gaps, yet significant challenges remain, such as limited prioritization of social and financial support [150]. An urgent review of current socioeconomic measures, with a focus on equity and impact, is essential to accelerate progress and meet the milestones of the End TB strategy.

Furthermore, the WHO has emphasized the importance of incorporating social determinants of health into infectious disease response strategies. This need has become increasingly pressing as the COVID-19 pandemic has intensified existing health inequalities and disproportionately affected marginalized populations. Consequently, interest in social determinants has grown within the infectious disease modeling community.

Considering that TB is widely recognized as a socially determined disease, relatively few modeling studies have incorporated social determinants into TB transmission models. One key obstacle to advancing this area of research is the lack of clear methodological guidance in how such determinants should be systematically integrated into modeling frameworks. By mechanistically linking social factors to core epidemiological processes, compartmental models equip policymakers with robust evidence for integrated approaches that promote both infection control and socioeconomic equity to accelerate TB burden reduction. The present study seeks to address this limitation by incorporating social determinants into the modeling approach, thereby contributing to efforts aimed at bridging this methodological gap.

# 2 MATERIALS AND METHODS

## 2.1 Study design and procedures

The present study adopted a hybrid methodological framework, which integrates mathematical modeling with correlational analysis. The study design is multistage and sequential, comprising a series of interrelated analytical phases.

In the first stage, a temporal trend analysis of TB incidence was performed over the period from 2000 through 2024. It was followed by the assessment of relative contribution of healthcare and socioeconomic factors to TB incidence dynamics.

In the second step, a compartmental model structured on the SIR framework was developed and parameterized with demographic and TB-specific epidemiological data. Furthermore, model validity and predictive performance were evaluated through systematic comparison of simulated and observed TB incidence.

In the third stage, sensitivity analysis was conducted to quantify the contribution of variability of socioeconomic factors to the overall uncertainty surrounding the projected TB incidence estimates.

In the fifth phase, an ensemble of prognostic scenarios was developed, which was followed by the simulation of the scenarios and assessment of the cumulative impact of socioeconomic interventions on future TB incidence.

Finally, an inverse optimization procedure was employed to identify the optimal values of socioeconomic determinants needed to attain the milestones outlined in the WHO's End TB strategy for 2030 and 2035. These optimal values serve as illustrative and target benchmarks to inform policy formulation and decision making.

## 2.2 Study settings

The study was conducted within the epidemiological and socioeconomic context of the Republic of Kazakhstan, which is the largest landlocked country in the world. Kazakhstan spans a vast territory with a relatively low population density of 7 individuals per square kilometer, reflecting its extensive steppe, desert, and mountainous landscape. As of the estimates of 2024, the country's total population stands at around 20.4 million people with a youthful demographic profile: roughly 28% of the population is aged 0-14 years, 63% is of working age (15-64 years), and about 9% is 65 years or older [151]. Socioeconomically, Kazakhstan is classified as an upper-middle-income country.

## 2.3 Data sources and collection

### 2.3.1 Sources of demographic, socioeconomic, and epidemiological data

The study draws on nationally representative data sources. The settings provide a realistic backdrop for modeling TB transmission dynamics, calibrating model parameters to observed data, and projecting future TB trends.

In this research, a comprehensive set of demographic, socioeconomic, and epidemiological variables was compiled for the time frame 1997-2024. Demographic and socioeconomic indicators were derived from the Bureau of National Statistics of the Republic of Kazakhstan [151]. Epidemiological data on TB was obtained from the National Scientific Center of Phthisiopulmonology of the Republic of Kazakhstan [5].

The demographic data was presented by net population growth, while socioeconomic data was presented by Gross Domestic Product (GDP) per capita, which was expressed in United States dollars (USD), current health expenditure (CHE) as a percentage of GDP, poverty and unemployment rates (%), the volume of social assistance provided to TB patients, measured in millions of Kazakhstan tenge (KZT).

2.3.2 Adjustments for COVID-19-related disruptions in TB incidence

A significant interruption in TB surveillance was observed in Kazakhstan and globally during 2020 and 2021. This was characterized by a marked reduction in notified TB incidence cases. The observed decrease primarily resulted from the COVID-19 pandemic, which triggered widespread under detection and under reporting.

Therefore, consistent with the WHO recommendations, which acknowledge systematic under detection of TB cases during the initial pandemic years, incidence estimates for 2020 and 2021 were revised and adjusted upward to more accurately reflect the underlying disease burden. Thus, according to the recommendations, the adjusted incidence estimates was calculated by applying the following increase coefficients to the official reported data: 1.25 in 2020 and 1.10 in 2021 [152].

$$\text{Incidence}_{2020}^{\text{Adjusted}} = \text{Incidence}_{2020}^{\text{Observed}} \times 1.25 \quad (1)$$

$$\text{Incidence}_{2021}^{\text{Adjusted}} = \text{Incidence}_{2021}^{\text{Observed}} \times 1.10 \quad (2)$$

No analogous corrections were applied to the data from other years, as national notification system had largely regained pre-pandemic functionality by 2022. All subsequent stages of model calibration, parameters estimation, model validation, scenario-based simulations relied exclusively on this adjusted incidence data. This approach mitigates potential bias in the analysis of long-term trends and strengthens the validity of the model's projections.

**2.4 Trend analysis of TB incidence rate**

To study the temporal trend of TB incidence rate for the period 2000-2024, a trend analysis was conducted. Initially, the data was visually assessed using a line plot. The period was then divided into two subperiods: 2000-2020 and 2021-2024. This division allowed to test the hypothesis that the rate of decline in TB incidence may have slowed in recent years.

A linear regression was conducted for each subperiod. To calculate the annual percentage change, a log-linear model was additionally used. The statistical significance of trends was determined using p-value of the slope coefficient. To objectively assess whether the rate of decline changed significantly after 2020, an extended model was constructed with a dummy variable and an interaction term.

The analysis was conducted in Python 3.12.

### 2.5 Evaluation of contribution of healthcare and socioeconomic factors to TB incidence

The first stage involved descriptive statistical analysis and assessment of correlations between TB incidence and predictor variables. Furthermore, an inspection of the correlation matrix was performed to quantitatively assess multicollinearity.

The principal component analysis (PCA) was used to eliminate the influence of multicollinearity. The use of principal components allowed us to reduce the dimensionality of the data and avoid distortions in the estimates of the regression coefficients. A multiple linear regression was then employed to quantitatively assess the influence of the predictors on the incidence rate of TB.

Partial and semi-partial correlation were obtained to assess the contribution of factors in more detail. Partial correlations were used to assess the strength of the relation between TB incidence and each predictor, while holding the other variables constant. Semi-partial correlations were utilized to determine the unique contribution of each factor to explaining the variance in TB incidence dynamics. The squared semi-partial correlations were interpreted. As the proportion of unique variance explained in TB incidence.

The analysis was conducted in Python, version 3.12.

### 2.6 Compartmental model of TB transmission

The Susceptible-Infectious-Recovered (SIR) compartmental model for TB transmission can be fully described and interpreted through the lens of System Dynamics (SD), which is a methodology that emphasizes stocks and flows, feedback loops, rates of change, and non-linear interactions to understand complex system behavior over time [153].

The developed model is a modified SIR structure specifically adapted to describe the epidemic dynamics of TB in the population of Kazakhstan.

Within this model, the population is divided into three main compartments. The first compartment includes *susceptible individuals* (S), who do not have active TB and lack protective immunity against MTB. The second compartment accumulates *infectious individuals* (I), those with active pulmonary TB who can excrete MTB and transmitting the infection to others. The third compartment include *recovered individuals* (R), who have successfully completed treatment and achieved clinical recovery. The stock-and-flow diagram of the model is presented in Figure 1.

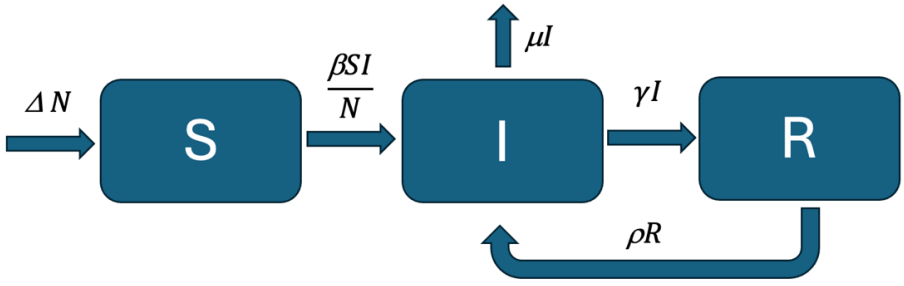


Figure 1 – Stock-and flow diagram of the SIR model

The SIR model is deterministic. The deterministic nature facilitates clear scenario analysis, policy experimentation, as well as making it well0suited for strategic planning and evaluation of TB control interventions.

The model relies on ordinary differential equations solved numerically. It is formulated as a following system of ordinary differential equations.

$$\frac{dS}{dt} = \Delta N + \mu I - \frac{\beta SI}{N} \quad (3)$$

$$\frac{dI}{dt} = \rho R + \frac{\beta SI}{N} - \mu I - \gamma I \quad (4)$$

$$\frac{dR}{dt} = \gamma I - \rho R \quad (5)$$

Notes:

1 $\Delta N$ – the rate of net population growth

2 $\mu$ – the rate of TB death

3 $\beta$ – the transmission coefficient

4 $\gamma$ – the rate of recovery

5 $\rho$ – the rate of recurrence

The total population size is maintained through a balanced system of flows, which ensure that the model remains consistent with real demographic data throughout the simulation period.

$$N(t) = S(t) + I(t) + R(t) \quad (6)$$

At the start of the simulation, the entire population is placed in the S compartment. It assumes uniform susceptibility and no prior immunity to MTB. The introduction of one or more infectious individuals initiates transmission, moving newly infected persons from the S compartment to the I compartment. Following successful treatment, individuals transition from the I compartment to the R compartment. However, due to the relapsing nature of TB, recovered individuals remain at risk of recurrent disease and can return to the I compartment. Furthermore, individuals may exit the I compartment due to TB-attributable mortality. This outflow removes people from the I compartment and reflects deaths directly caused by active TB disease.

The model incorporates several distinctive features tailored to the epidemiology of TB in Kazakhstan. A key modification is the inclusion of recurrence, represented by the flow from the R compartment to the I compartment, which denotes the rate at which recovered individuals transition back to the infection state due to reactivation or reinfection.

It should be emphasized that the parameter of net population growth accounts for all natural demographic processes. They include births, non-TB-related deaths, as

well as net migration, but explicitly excludes TB-attributable mortality. In other words, this parameter captures the overall change in population size that would occur in the absence of TB-specific deaths.

TB-induced morality is modeled as an outflow exclusively from the I compartment. Importantly, to maintain strict conservation of the total population and to align the model's demographic behavior with the real population accounting practices, the TB-specific deaths are not simply removed from the system. Instead, they are mathematically reintroduced as an equivalent inflow into the S compartment. This adjustment ensures that the sum of individuals across all the compartments remains consistent with independently observed demographic trajectories reported in official statistics.

It is also worth noting that the developed model is the utilization of the classical SIR structure without an explicit latent compartment. This simplification does not fully capture the prolonged latent period of TB. Contemporary global-scale models typically incorporate a latent compartment and offer more granular projections. However, within the epidemiological context of the Republic of Kazakhstan, this simplification is warranted and substantiated by recent molecular-genetic evidence. Specifically, the study by Takenov et al., based on the whole-genome sequencing of 272 MTB isolates, identified that 93% of new TB cases were linked to recent active transmission. The authors explicitly conclude that in Kazakhstan active community transmission serves as the primary driver of the TB epidemic [22, p. 6-7].

Furthermore, the SIR model's emphasis on the transmission parameter, infectious period reduction, and recurrence mirrors the core mechanisms of Kazakhstan's epidemiological situation regarding TB. Notably, the model captures the observed increase in the recovery rate, which reflects the substantial improvements in diagnosis and treatment achieved in Kazakhstan between 2006 and 2024. Faster case detection and more effective treatment regimens have shortened the average infectious period, thereby reducing the relative contribution of the latent reservoir. It means that individuals are identified and treated more rapidly, limiting both prolonged infectiousness and the buildup of intreated latent infectious that could later reactivate. In such conditions, where recent active transmission overwhelmingly predominates over reactivation, the omission of an explicit latent compartment does not substantially distort the model's projections or key epidemiological insights.

The construction of the SIR model was performed using Python, version 3.12.

### 2.7 Model parameterization

2.7.1 Initial values for the SIR model compartments

The calculation of the initial values of the SIR model compartments and demographic changes constitutes a fundamental preparatory step for simulation. These values define the model's starting state and ensure population balance throughout the entire modeling period. In the study, initial values were determined based on the official demographic and epidemiological data for the baseline year of 1997. It precedes the main analysis period of 1998-2024, in order to avoid artificial distortion of the dynamics in the first year of simulation.

The S compartment represents individuals without active TB who remain at risk of infection. The initial value was calculated using the balance equation.

$$S(0) = N(0) - I(0) - R(0) \quad (7)$$

In subsequent years, the S compartment was updated dynamically during simulation through infection outflows and demographic inflows.

The I compartment includes individuals with active pulmonary TB capable of transmitting the pathogen. The initial value of the I compartment was taken directly from official data as the absolute prevalence of active TB cases registered the end of 1997. This figure represents bacteriologically confirmed and clinically active cases. In the model, the I compartment was updated through inflows from new infections and recurrences, and outflows due to successful treatment and TB-specific mortality.

The R compartment comprises individuals who have successfully completed treatment but remain at risk of recurrence. The initial value was set at 0. This simplifying assumption is justified by the structure of available historical data, which primarily tracked active cases and did not provide separate, reliable counts of previously treated individuals. Latent infection and accumulated immunity were not explicitly modeled. The potential return of recovered individuals to the infectious state is instead captured through the recurrence flow in subsequent year. This approach is common in TB modeling literature when focusing on active disease dynamics, as well as detailed recovery compartment data are unavailable. In later years, the R compartment accumulates via recovery inflows and decreases via recurrences.

These empirically derived initial states provide a consistent, data-grounded foundation for model calibration, validation, sensitivity analysis, and all forecast scenarios, thereby enhancing the reliability and policy relevance of the results in the context of the epidemiological situation regarding TB in Kazakhstan.

2.7.2 Parameterization of demographic inflow

The demographic inflow represents the annual net population growth and is added directly to the S compartment to maintain the total population balance. The values of the net population growth for the historical period 1998-2024 were derived from official data.

$$\Delta N_1 = N_{t+1} - N_t \quad (8)$$

For the forecast period 2025-2035, the net population growth was obtained through linear interpolation of the medium-variant projections from the United Nations World Population Prospects 2024 [154]. The projections for Kazakhstan's expected annual population growth of 1.2%. The inclusion of realistic net population growth ensures that long-term projections remain demographically plausible and isolates epidemiological dynamics from confounding population trends.

2.7.3 Estimation of TB transmission coefficient

The transmission coefficient of TB serves as a pivotal parameter in the SIR model. It governs the rate at which susceptible individuals transition to the I compartment upon effective contact with infectious sources. In the current study, the transmission coefficient was estimated empirically for each year of observation from 1998 through 2024. This approach yielded a time series that accurately captures the real dynamics of TB transmissibility in Kazakhstan over a 27-year period.

$$\beta(t) = \frac{\text{Prevalence}(t) \times N(t)}{I(t) \times S(t)} \quad (9)$$

Notes:

1 Prevalence (t) – the absolute number of TB prevalent cases at the end of year *t*

2 N (t) – the total population size in year *t*

3 I (t) – the absolute number of infectious individuals in year *t*

4 S (t) – the number of susceptible individuals in year *t*

By deriving the transmission coefficient from observed epidemiological data, the method ensures close alignment with actual disease patterns and enables the identification of long-term trends in TB transmission intensity. Such an empirically grounded estimation provides a robust foundation for understanding the evolving epidemiology of TB in the Kazakhstan context.

2.7.4 Estimation of TB mortality rate

The TB mortality rate serves as a critical parameter in the Sir model. It governs the rate at which infected individuals exit the I compartment due to TB-induced mortality. The parameter captures the intrinsic biological lethality of TB combined with the real effectiveness of case management and therapy within the Kazakhstan population.

In the present study, the mortality rate was estimated empirically for each year from 1998 through 2024 based on the official data. The mortality rate is a weighted average considering the proportions of drug-susceptible and drug-resistant forms of TB. This approach ensures the closest possible alignment with the actual epidemiological situation in the country, incorporating both long-term secular trends and period-specific perturbations.

$$\mu(t) = \frac{\text{Mortality rate}(t)}{\text{Prevalence}(t)} \quad (10)$$

Notes:

1 Mortality rate (t) – the absolute number of TB deaths in year *t*

2 Prevalence (t) – the absolute number of TB prevalent cases at the end of year *t*

The empirical calculation enabled the model to reflect historical reductions in TB mortality. By grounding the parameter directly in observed death-to-prevalence ratios, the model avoids reliance on generic international estimates and instead incorporates Kazakhstan-specific factors. This data-driven estimation enhances the model's fidelity to local reality and strengthening its validity for long-term forecasting, scenario analysis, and evaluation of control interventions in the Kazakhstan context.

2.7.5 Calibration of recovery and recurrence rates of TB

Although the model includes many parameters estimated from the relevant datasets, there are still some parameters which cannot be retrieved or easily estimated. To improve the validity and reliability of the model, it is highly valuable to calibrate the model to best match historically observed values between 1997 and 2024.

The recovery and recurrence rates were calibrated in the model. They are both critical parameters in the epidemiology of TB. Each parameter plays a distinct yet complementary role in capturing the unique dynamics of TB as a chronic, relapsing infection.

The recovery rate determines the intensity of the transition from the I compartment to the R compartment. It directly reflects the inverse of the average duration of the infectious period. In the context of TB, the recovery rate holds epidemiological significance. Thus, accelerating recovery represents one of the most effective mechanisms for reducing the infectious reservoir and interrupting further transmission.

The recurrence parameter, in turn, governs the rate of return from the R compartment back to the I compartment. It captures the risk of relapse or reinfection after successful treatment. Since TB is a chronic infection, even individuals who complete therapy remains at elevated risk of developing active disease. In the model, the recurrence rate quantifies the annual proportion of recovered individuals who transition back to active TB, thereby directly influencing the size of the infectious reservoir.

Calibration of the recovery and recurrence parameters were performed using the Nelder-Mead simplex algorithm to adjust several parameter values to find the best observed match to the historic data. The objective function minimized the mean absolute percentage error (MAPE) between the observed and simulated incidence. Each calibration is simulated for 1,000 times to optimize a weighted sum of square about the discrepancies between the historical data and simulated results.

$$\mathrm{MAPE} = \frac{1}{n}\sum_{t=1}^{n}\left|\frac{\mathrm{Incidence}_{sim,t} - \mathrm{Incidence}_{obs,t}}{\mathrm{Incidence}_{obs,t}}\right| \times 100\% \qquad (11)$$

Note – n is the number of years in the calibration period.

To account for substantial structural changes in the national TB control system, calibration was conducted separately for two distinct time periods.

The first interval is the period from 1998 through 2005. This period corresponded to the initial establishment and partial rollout of the DOTS strategy in Kazakhstan, which started nationwide implementation in 1998. During these years, treatment coverage remained limited, standardized short-course chemotherapy was not universally applied, and patient adherence was generally low. It resulted in longer infectious periods and lower overall treatment success.

The second period ranges from 2006 through 2024. This interval reflected the full-scale expansion and consolidation of the DOTS course across the country. This was accompanied by a shift toward predominantly outpatient-based treatment, widespread adoption of molecular diagnostics, introduction of second-line drugs, and strengthened adherence monitoring. These advancements led to treatment success rates reaching 90%, and a marked reduction in the average duration of infectiousness.

The division into 2 timeframes is presented in Figure 2.

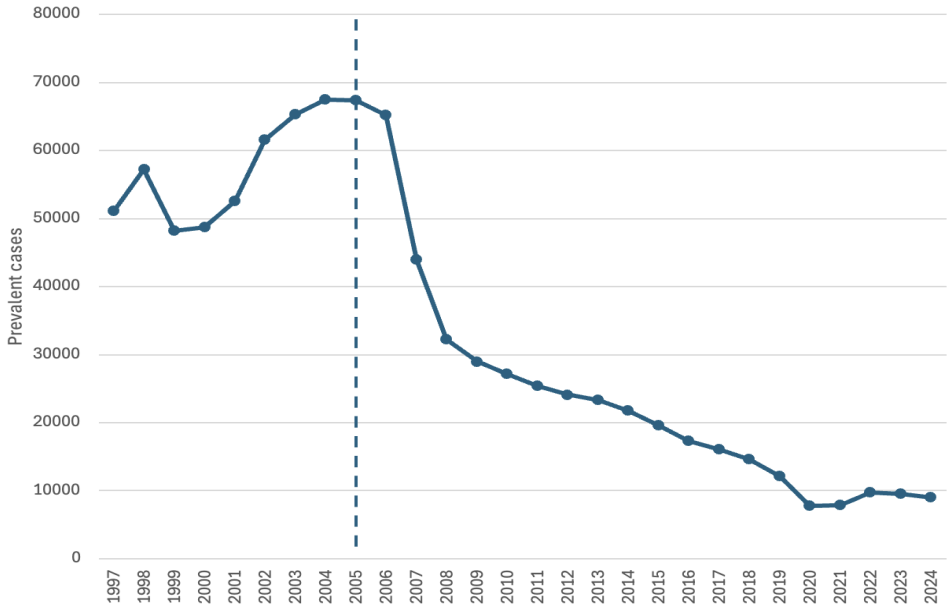


Figure 2 – The division into 2 timeframes for calibration

The period-specific calibration approach ensured that the model parameters reflected the evolving effectiveness of TB control. By optimizing the recovery and recurrence rates independently for each period, the model captured the historical transition from fragmented early-phase implementation to a high-performance national program. Thus, it improves the accuracy of simulated incidence trajectories and enhancing the reliability of long-term projections under varying control scenarios in the epidemiological context of Kazakhstan.

The calibration of the SIR model parameters was performed using Python, version 3.12.

### 2.8 The predictive accuracy of the SIR model

To evaluate the predictive accuracy and generalizability of the developed model, a hold-out validation procedure was implemented. The dataset was partitioned into two

non-overlapping subsets. A training set spans the years from 1998 through 2019. A test set covers the period from 2020 through 2024.

The division into training and testing datasets is presented in Figure 3.

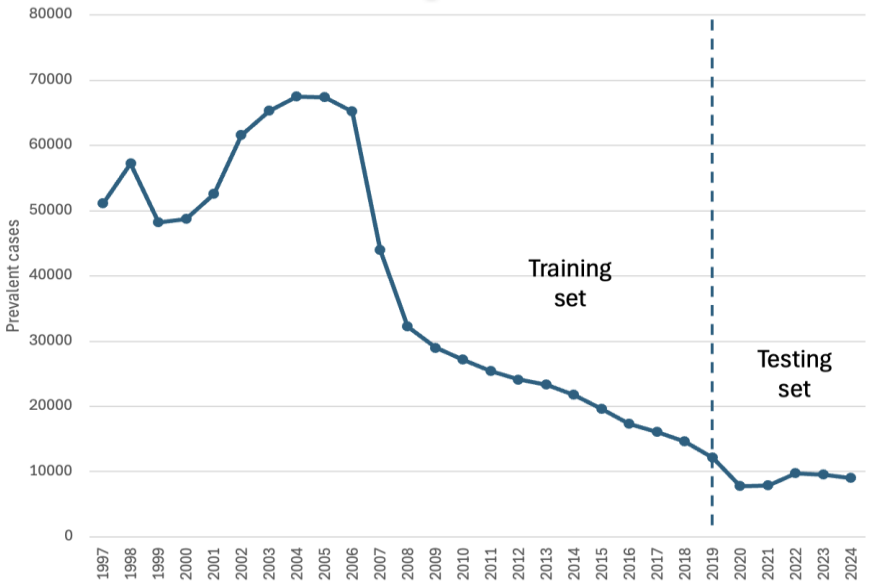


Figure 3 – The division into training and testing periods

Model performance was assessed by computing the MAPE between the model simulated incidence values and the corresponding observed incidence values exclusively on the test set.

$$\text{MAPE} = \frac{1}{n}\sum_{t=1}^{n}\left|\frac{\text{Incidence}_{sim,t} - \text{Incidence}_{obs,t}}{\text{Incidence}_{obs,t}}\right| \times 100\% \qquad (12)$$

Note – n is the number of years in the testing period.

2.8.1 The transmission coefficient in the SIR model validation

To prevent data leakage in the context of hold-out validation, the transmission coefficient for the period 2020-2024 was not predicted using a quadratic regression model fitted exclusively to the empirically estimated values from the training period. The resulting quadratic function was then employed to extrapolate the parameter forward in time. In thus generates a conservative projection of future transmission dynamics.

$$\beta(t) = at^2 + bt + c \qquad (13)$$

Similarly, the recovery rate and recurrence rate were calibrated using only the training data. Consistent with the structural break identified in the epidemiological time series, these parameters were estimated separately for the sub-periods 1998-2005 and 2006-2019 within the training set. Once calibrated, the obtained parameter values were

held fixed, and the model was subsequently run forward in time to simulate TB dynamics over the entire test period (2020-2024) within any additional parameter tuning or re-optimization.

This hold-out design ensures an unbiased evaluation of the model's ability to extrapolate beyond the calibration window and provides a robust test of its suitability for long-term forecasting under changing epidemiological and socioeconomic conditions.

The validation of the developed SIR model was performed using Python, version 3.12.

### 2.9 Incorporating of socioeconomic factors into the SIR model

For forecasting purpose over the period 2025-2035, the transmission coefficient was modeled as a function of key socioeconomic determinants through quadratic polynomial regression. The quadratic polynomial regression was chosen to accommodate and capture potential nonlinear association between the transmission coefficient and socioeconomic characteristics. In this framework, the annually estimated values of the transmission coefficient served as the dependent variable. The selected socioeconomic variables were incorporated as independent variables.

To address the issue of multicollinearity among the socioeconomic predictors, which could otherwise compromise model stability and interpretability. All candidate variables retained after preliminary screening underwent PCA. An oblique rotation method was applied to allow for correlated components. It yields a more realistic and interpretable representation of the underlying data structure. Prior to the components extraction, the suitability of the data for the PCA was assessed using the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy and Barlett's test of sphericity. The number of components to retain was determined by a combination of criteria. They include inspection of the scree plot employing the elbow criterion, and adherence to Kaiser's rule retaining. Components with eigenvalues greater than 1.

The resulting principal components, which effectively summarized the shared variance among the original socioeconomic determinants while mitigating multicollinearity, were then used as predictors in the quadratic polynomial regression model to estimate the transmission coefficient. This approach enabled the derivation of a robust predictive equation that links key socioeconomic factors to TB transmission coefficient, without the instability introduced by high correlations among the raw predictors.

The final model specification was selected based on comprehensive evaluation metrics, including adjusted coefficient of determination for explanatory power, residual diagnostics, and predictive accuracy indicators such as mean absolute error (MAE) and MAPE.

The validated regression equation was subsequently applied to projected future values of the socioeconomic factors to generate forecasted values of the transmission coefficient across the period 2025-2035.

The statistical analysis of the data was performed using Python, version 3.12.

### 2.10 Sensitivity analysis

To evaluate both the independent effect and the interaction influences of the socioeconomic predictors on the uncertainty surrounding projected TB incidence, a global sensitivity analysis was conducted. Each predictor was systematically perturbed within a 10% interval centered on the baseline value of 2024. This range was selected to reflect standard, realistic variation of the socioeconomic parameters. A total of 1,000 parameter combinations were generated using Latin Hypercube Sampling, as well as Monte Carlo technique that ensures efficient, near-uniform coverage of the input space dined by the predictors while minimizing correlation among sampled points.

For each of the 1,000 sampled configurations, the model was executed to produce corresponding incidence projections for a target year or cumulative outcome over the forecast horizon. From the resulting distribution of 1,000 incidence values, Sobol's sensitivity indices were calculated to quantify the relative importance of each predictor.

The First-order index represents the proportion of the total variance in the incidence of TB that is attributable solely to the variation of a socioeconomic predictor when considered in isolation, excluding any interaction with other predictors.

While the total-order index captures the full proportion of the predictor to the incidence of TB variance, including both its main independent effect and all higher-order interactions involving that predictor with anu combination of the remaining predictors.

The computation of the Sobol's indices this provides a robust decomposition of forecast uncertainty, enabling identification of the most influential drivers of the variability of the TB incidence and highlighting the extent to which predictor effects are mediated through interactions rather than acting additively.

The sensitivity analysis of the model parameters was performed using Python, version 3.12.

### 2.11 Development and description of simulation scenarios

In the present study, the development of forecast scenarios is treated as an essential methodological requirement, ensuring that the calibrated modified SIR model serves not only as a tool for reproducing past dynamics but also as a robust framework for informing long-tern TB control strategies in Kazakhstan. To determine the potential long-term effects of targeted socioeconomic interventions on lowering TB incidence, a scenario-based analysis was performed using the established SIR model.

#### 2.11.1 Baseline scenario

The baseline scenario served as the reference path. It represents the continuation of current trends without additional interventions or policy accelerations.

The baseline scenario assumes no changes to any of the socioeconomic predictors, resulting in the transmission coefficient fixed at its 2024 value. The other parameters of the SIR model were also fixed at their levels of 2024.

The baseline scenario provides a benchmark against which the incremental effect of each alternative scenario could be measured.

2.11.2 Alternative scenarios

The alternative scenarios were constructed with a strong emphasis on practical applicability and alignment with the realistic possibilities of socioeconomic policy in the Republic of Kazakhstan. All assumed rate of change for the socioeconomic factors is firmly grounded in official and historical data. It enables the scenarios to be regarded as achievable and credible under conditions of continuation or moderate acceleration of existing development trends (Table 1).

Table 1 - Description of simulation scenarios for TB incidence

| Scenario | Key assumption | Source |
|---|---|---|
| Baseline scenario | No changes to socioeconomic predictors | Assumed |
| Scenario 1. Sustained economic growth | Annual 3% increase in GDP per capita | Data [156] |
| Scenario 2. Poverty alleviation | Annual 0.1% reduction in poverty rate | Data [156] |
| Scenario 3. Unemployment alleviation | Annual 0.1% reduction in unemployment rate | Data [156] |
| Scenario 4. Enhanced healthcare investment | Annual 0.1% increase in CHE | Historical trend |
| Scenario 5. Improved social support for TB patients | Annual 5% increase in social assistance for TB patients | Historical trend |

Scenario 1, which constitutes 3% annual growth in per-capita GDP, is based on the official forecast issued by the Ministry of National Economy of the Republic of Kazakhstan. According to the forecast, real GDP growth is projected at 4-5% per annum in 2025-2029, while per-capita GDP growth is expected to range between 3.0% and 3.8% annually [156]. The value of 3% was deliberately selected as the lower bound of the official forecast range. It ensures that the scenario remains plausible even under adverse external conditions.

Scenario 2, which is a 0.1% annual reduction in the poverty rate, corresponds closely to the actual trends observed in Kazakhstan in recent years and to the projections of the Ministry of National Economy of the Republic of Kazakhstan [156]. The official forecast shows an average annual decrease of 0.1% in poverty rate. The chosen rate of 0.1% per year represents a realistic trajectory.

Scenario 3, which is a 0.1% annual reduction in the unemployment rate, is likewise anchored in the official projections from the Ministry of National Economy of the Republic of Kazakhstan [156]. The official forecast shows an average annual decrease of 0.1% in unemployment rate. The chosen rate of 0.1% per year represents a realistic trajectory.

Scenario 4, which presents a 0.1% annual increase in current health expenditure as a share of GDP, is informed by historical trends. Recent years have shown a gradual

upward trend in budgetary allocations for healthcare. The rate of 0.1% per year was chosen as a moderate and sustainable increment, consistent with past dynamics and the potential for further prioritization of healthcare funding in the national budget.

Scenario 5, which reflects 5% annual growth in social support to TB patients, is derived from the analysis of historical trends of the indicator. Over the period 2015-2024, the volume of the social assistance to TB patients increased at an average annual rate of 4.5-6.5% [5]. The value of 5% was selected as a balanced, realistic estimate, achievable under continuation of current trends, including payments during treatment and compensation for lost earnings.

All the scenarios are designed so that changes in the predictors follow linear or exponential trajectories over time and remain firmly within historically observed and officially projected ranges. This ensures their practical relevance for strategic planning and positions the results as actionable benchmarks for national TB control programs and broader socioeconomic development strategies in Kazakhstan.

2.11.3 Comparison with the baseline scenario

To quantitatively assess the contribution of each socioeconomic factor to the reduction in TB incidence, the results of the alternative scenarios were compared against the baseline scenario. All comparative analyses were calculated with respect to this no-change reference path. This approach enables clear quantification of the incremental epidemiological benefit attributable to specific improvements in socioeconomic conditions, thereby providing a structured framework for assessing the sensitivity of future TB burden to realistic policy levers in Kazakhstan.

The relative effect of each scenario was evaluated through the percentage change in incidence relative to the baseline scenario.

$$\Delta\%_t = \frac{\text{Incidence}_{\text{scenario,t}} - \text{Incidence}_{\text{baseline,t}}}{\text{Incidence}_{\text{baseline,t}}} \times 100\% \quad (14)$$

Note – t is the forecast year

Negative values of the percentage change indicate and additional reduction in TB incidence compared to the baseline. It implies a positive effect of the scenario. Positive values signify a worsening of the situation meaning a negative effect. The metric was computed annually across the entire forecast horizon, enabling the tracking of the temporal dynamics of each scenario's impact.

In addition to year-by-year absolute incidence values, cumulative relative changes were calculated at key milestones of 2030 and 2035 to quantify the long-term contribution of each scenario to TB burden reduction.

This comparative framework provides a clear, standardized measure of the marginal benefit attributable to improvements in individual predictors, after accounting for the baseline epidemiological trends. By expressing outcomes as percentage deviations from the baseline reference, the analysis isolates the incremental epidemiological returns associated with realistic policy adjustments in socioeconomic domains, thereby offering actionable insights for prioritization of interventions within

the constraints of Kazakhstan's national TB control strategy and socioeconomic development plans.

The 95% confidence intervals (CI) for all main outputs were calculated via Monte Carlo simulation. The projection of future incidence of TB under the prognostic scenarios as well as the quantitative assessment of socioeconomic factors' contribution were performed using Python, version 3.12.

### 2.12 Optimization of socioeconomic parameters

To determine the minimum improvements in the socioeconomic predictors necessary to achieve the WHO's End TB strategy targets of reduction in TB incidence by 2030 and 2035, an inverse optimization framework was implemented.

The optimization process sought to identify the smallest feasible changes in the socioeconomic variables that would enable the calibrated compartmental model to reproduce these incidence reduction milestones. The Nelder-Mead simplex method was employed for this purpose. Initial parameter guesses were deliberately positioned close to the empirically observed 2024 baseline values to ensure rapid convergence and to anchor the search within a realistic region of the predictor space.

$$f(x) = \sum_{t=2025}^{t} \left( \frac{\text{Incidence}_{\text{simulated},t}(x) - \text{Target}_t}{\text{Target}_t} \right)^2 \quad (15)$$

The objective function was formulated to minimize a minimize the deviations from the target incidence trajectories while simultaneously discouraging excessively large deviations from the 2024 baseline values for each socioeconomic predictor. This formulation effectively identifies the most parsimonious set of socioeconomic improvements required to meet the End TB benchmarks under the dynamics of the calibrated transmission model.

The resulting optimal values of the socioeconomic predictors represent the threshold levels of socioeconomic progress deemed necessary and sufficient to place Kazakhstan on track to eliminate TB. These optimized trajectories provide actionable benchmarks for policymakers, highlighting the scale and direction of socioeconomic interventions required to complement existing TB control efforts.

The optimization procedure was performed using Python, version 3.12.

### 2.13 Ethical consideration

The Bioethics Committee of Karaganda Medical University review the study and granted ethical approval through Protocol №18 dated on 12.04.2021. The ethical approval process involves the review of the study design, potential risks and benefits, confidentiality of data, and the overall ethical implications of the study. Ethnical approval ensures that the study is conducted in an ethical and responsible manner.

# 3 COMPARTMENTAL MODEL OF TUBERCULOSIS TRANSMISSION IN KAZAKHSTAN

## 3.1 Trends and determinants of TB incidence in Kazakhstan

3.1.1 Trend analysis of TB incidence in Kazakhstan in the period of 2000-2024

The incidence rate of TB in Kazakhstan from 2000 through 2024 is presented in Figure 4.

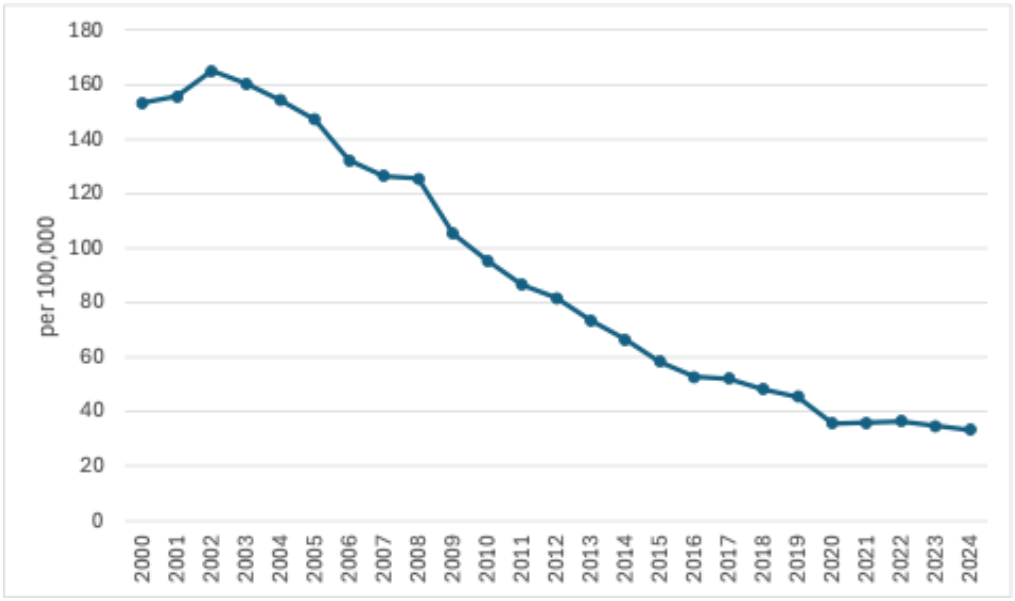


Figure 4 – The incidence rate of TB in Kazakhstan from 2000 through 2024

As can be seen from the long-term dynamics of TB incidence, the overall picture for the period of 2000-2024 shows a significant decline in TB incidence. However, the rate of this decline varies significantly between periods.

The results of the trend analysis are presented in Table 2.

Table 2 – Trend analysis of TB incidence

| Period | B | p-values | Annual percentage change | R-squared |
|---|---|---|---|---|
| 2000-2020 | -5.91 | < 0.001 | -6.85 | 0.978 |
| 2021-2024 | -0.85 | 0.312 | -2.38 | 0.412 |

The results showed a steady and rapid decline in TB incidence between 2000 and 2020. Each year, the rate decreased by an average of approximately 5.91 cases per 100,000 population (B=-5.91, $p < 0.001$). The annual percentage change was 6.85% per year. The model explains the variability of TB incidence well ($R^2 = 0.978$).

However, between 2021 and 2024, the situation changed dramatically. The decline almost stopped. The rate of decline was only 0.85 cases per 100,000 and this

change was not statistically significant (B=-0.85, p = 0.312). Furthermore, the annual percentage change slowed to 2.38% per year.

In addition, a structural break test confirmed that the change in the rate of decline after 2020 is statistically significant ($p < 0.05$). This means that the slowdown in the trend cannot be explained by random fluctuations.

The results show that the long period of steady decline in TB incidence, which lasted for over 20 years, has noticeably lost momentum in the last four years. While it was previously recorded that an annual decline was roughly 7%, but after 2020, the decline became minimal and statistically insignificant.

3.1.2 Contribution of healthcare and socioeconomic factors to TB incidence dynamics

The temporal dynamics in the BCG vaccination coverage in Kazakhstan from 2000 to 2024 is presented in Figure 5.

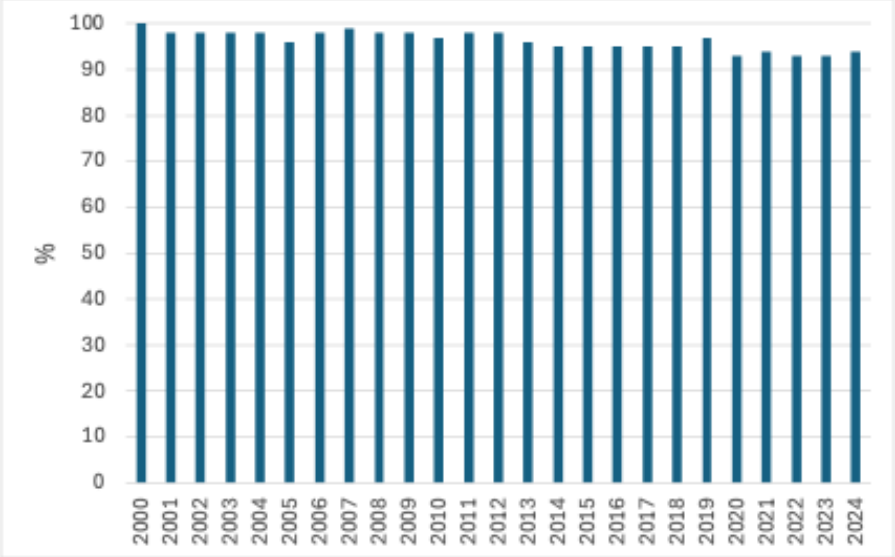


Figure 5 – BCG vaccination coverage in Kazakhstan from 2000 through 2024

BCG vaccination rates have stayed high throughout the period from 2000 through 2024. They alternated between 92% and 99%. Also, in most years, the rate stayed above 95%. Both rates showed high levels over the 20 years which indicates the BCG immunization program performed well in the country.

The changing patterns of TB case detection in Kazakhstan from 2010 through 2024 are shown in Figure 6. Between. 2000 and 2019, the TB case detection rate was very high and stable, maintaining at 99% consistently. This means all estimated TB cases were found and treated during this period. But in 2020, there was a sharp fall to around 80%. This large drop shows the negative effects of the COVID-19 pandemic on TB services. From 2021 onward, a steady recovery took place. By 2024, the rate got back to 99%. Though there was a big drop in 2020. Kazakhstan's TB control program showed strong resilience. TB case detection was back to its pre-pandemic high levels by 2024.

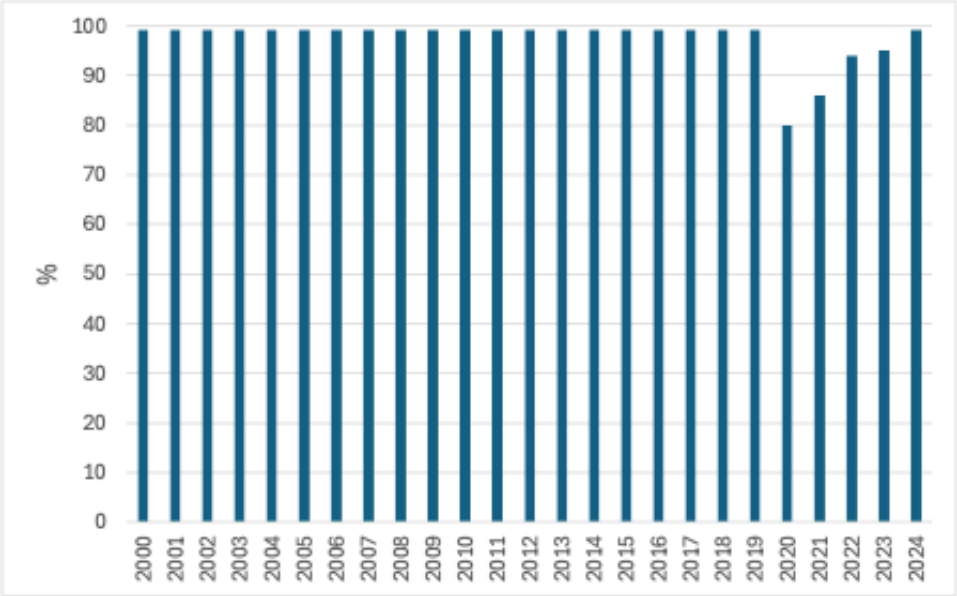


Figure 6 – TB case detection rate in Kazakhstan from 2000 through 2024

The study analyzed the influence of healthcare system and socioeconomic determinants on the incidence of TB using multiple linear regression and partial and semi-partial correlation analysis.

To overcome the problem of multicollinearity caused by the high interrelationship o socioeconomic factors, the PCA was applied (Table A.1). This resulted in formation of two integral principal components (Table A.3). The first principal component reflects the combined influence of social protection, while the second represents the joint impact of financial protection (Table A.2).

The results of the multiple linear regression, where the outcome variable was TB incidence and the predictors were healthcare indicators, together with the principal components obtained from the PCA, are summarized in Table 3.

Table 3 – Multiple linear regression predicting TB incidence

| Variable | B | Standard error | t | p-value |
|---|---|---|---|---|
| Intercept | -288.85 | 114.31 | -2.53 | 0.024 |
| BCG vaccine coverage | 2.84 | 1.15 | 2.48 | 0.027 |
| TB case detection rate | 1.16 | 0.53 | 2.21 | 0.045 |
| Social protection | 47.09 | 7.57 | 6.22 | < 0.001 |
| Financial protection | -8.40 | 3.02 | -2.78 | 0.015 |

To test the adequacy of the constructed regression model, an analysis of variance was conducted. The results showed that the overall model was statistically significant

(F=45.49, $p < 0.001$), indicating a significant impact of the combined factors on TB incidence.

The coefficient of determination ($R^2 = 0.929$) indicated the model's high explanatory power approximately 92.9% of the variation in TB incidence is explained by the included predictors.

The results of the partial and semi-partial correlation analysis are presented in Table 4. The strongest correlation with TB incidence rate was observed for the principal components. As for the component of social protection, the partial correlation value was 0.857, while for the component of financial protection, the partial correlation coefficient was -0.796. These coefficients indicate a strong direct and inverse relationship, respectively. Meanwhile, the healthcare factors were characterized by a weak correlation for vaccination coverage, the partial correlation was 0.352, and for the TB case detection rate, it was 0.308.

Table 4 – Partial and semi-partial correlation with TB incidence

| **Predictor** | **Partial correlation** | **Semi-partial correlation** |
|---|---|---|
| BCG vaccination coverage | 0.352 | 0.177 |
| TB case detection rate | 0.308 | 0.157 |
| Social protection | 0.857 | 0.444 |
| Financial protection | -0.796 | -0.398 |

More informative in assessing the contribution of the factors is the analysis of semi-partial correlations. They allow us to determine the unique contribution of each predictor to explaining the variation of outcome variable. It was found that the social protection component explains 19.7% of the unique variance of the TB incidence, while the financial protection explains 15.8%. Thus, the total contribution of socioeconomic factors, presented by the principal components, is 35.5%

The contribution of medical factors is significantly smaller. For the BCG vaccination rate, it is 3.1%, and for the TB case detection rate, it was 2.5%, which in total equals 5.6%. The obtained results indicate that the influence of healthcare system on the variation in TB incidence is limited compared to the socioeconomic determinants.

Overall, the findings suggest the dominant role of socioeconomic factors in shaping the dynamics of TB incidence. Integrated principal components reflecting the level of socioeconomic development have a significantly greater impact on TB incidence than healthcare factors, confirming the socially determined nature of TB.

### 3.2 Model parameters estimation and calibration

3.2.1 Initialization of the SIR model's compartment

The initial values of the SIR model compartments were established as of the end of 1997 immediately preceding the primary observation period of 1998-2024. This choice ensured an appropriate starting state for the model and maintained demographic consistency in the total population balance throughout the entire simulation horizon.

The S compartment was initialized with 15,283,280 individuals. The I compartment was set to 51,125 individuals, corresponding to the absolute TB prevalence at the end of 1997. The R compartment was assigned a value of 0 individuals, following a simplifying assumption consistent with the structure of the available data (Table 5).

Table 5 – Initial values of the SIR model's compartments

| Initial state | Description | Value | Source |
|---|---|---|---|
| S (0) | Initial number of susceptible individuals | 15,283,280 | Calculated |
| I (0) | Initial number of infectious individuals | 51,125 | Data [5] |
| R (0) | Initial number of recovered individuals | 0 | Assumed |

3.2.2 Identification of demographic inflow

The historical annual net growth exhibited considerable variation, reflecting Kazakhstan's demographic trajectory. Spcifically, negative values in the late 1990s and early 2000s transitioned to sustained growth in subsequent decades by 2024.

In the projection period of 2025-2035, the expected annual net increase stabilizes at 0.26 million individuals per year [154].

This empirically grounded initialization and demographic inflow mechanism ensure that the model reproduces realistic population dynamics. Furthermore, the approach enhances the validity of both historical calibration and forward-looking scenario projections in the context of Kazakhstan.

3.2.3 Estimation of the transmission coefficient of the SIR model

The transmission coefficient exhibits a consistent nonlinear upward trend from 0.310 in 1998 to 0.749 in 2024. This long-term increase reflects the actual dynamics of TB transmissibility in Kazakhstan, driven by a combination of structural and epidemiological factors.

The resulting values of the transmission coefficient served as the foundation input for the subsequent stages. By anchoring the transmission parameter to historical observations, the approach achieved high fidelity in reproducing past incidence and prevalence trajectories while enabling realistic simulation of how future changes in

socioeconomic predictors could modify transmissibility and TB burden over the 2025-2035 horizon. This empirical grounding of the transmission coefficient enhances the model's credibility for policy-relevant forecasting and underscores the critical interplay between diagnostic advancements, social determinants, and epidemiological outcomes in shaping long-term TB control in Kazakhstan.

The temporal trend in the estimated transmission coefficient is presented in Figure 7.

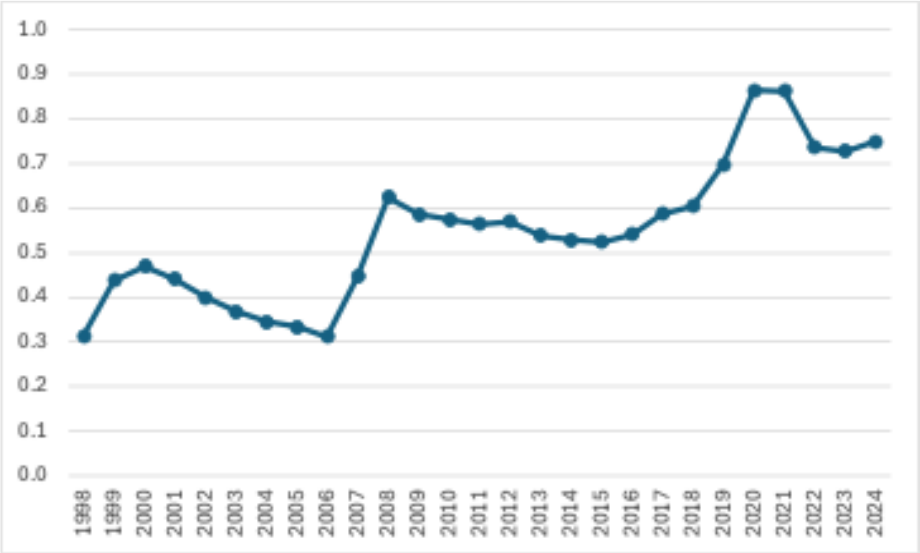


Figure 7 – Temporal trend in the estimated transmission coefficient

The observed increase in the empirically estimated transmission coefficient may at first appear to contradict the expected decline in transmissibility associated with improved TB control. This apparent rise is an artifact of the estimation methodology amid substantial advances in Kazakhstan's national TB program. Enhanced case detection, diagnostic and treatment improvements, together with a shortened infectious period has caused prevalence to fall more rapidly than TB incidence. The recovery rate increased from 1.39 to 2.8, reducing the average infectious deration from 8.6 to 4.3 months. Consequently, the apparent transmission coefficient increases even if the true per-contact transmission probability remains stable or decrease [157].

To ensure the model still accurately reproduces observed incidence trends fitting procedures often require a compensatory upward adjustment of the transmission coefficient. This does not reflect a true rise in biological transmissibility but rather a mathematical artifact. The model compensates for the reduced opportunity for transmission per infectious case by elevating the per-contact transmission probability.

Therefore, confirming the success of control efforts in rapidly identifying and treating cases, which in turn diminishes reliance on the latent reservoir for sustaining the epidemic.

### 3.2.4 Estimation of the TB-induced mortality rate of the SIR model

The mortality rate is a key parameter of the SIR model. It determines the rate at which individual with active TB leave the I compartment due to death from the disease.

Empirical estimation of the parameter was based on the ratio of combined TB deaths of drug-susceptible and drug-resistant TB to prevalence rate.

The value of 0.0228 across the entire forecasting period was adopted in the model as a realistic estimate. This value reflects the current epidemiological situation in Kazakhstan. These calculation results confirm the model's adequacy and its ability to account for the real TB mortality under conditions of evolving treatment effectiveness.

3.2.5 Calibration results of recovery and recurrence parameters

The calibration of the recovery rate and recurrence probability revealed a clear division of the model's dynamics into two distinct periods. It mirrors the real advancements in Kazakhstan's national TB control program.

During the period 1998-2005, the calibrated recovery parameter was estimated at 1.39, which corresponding to an average infectious period of 8.6 months. For the same period, the recurrence parameter was determined to be 0.35.

These values accurately reflect the epidemiological conditions of that period, which was characterized by limited coverage of the DOTS strategy during its initial implementation phase, incomplete patient adherence to treatment, sand relatively high proportion of chronic and relapsing forms of TB. Therefore, the longer infectious duration and elevated recurrence risk contributed to sustained transmission pressure and slower epidemiological progress during the transitional stage.

In the subsequent period of 2006-2024, the calibrated parameters shower marked improvement. The recovery rate increased to 2.8. This means that the average infectious period reduced to 4.3 months. The recurrence probability decreased to 0.105.

The significant rise in the recovery parameter and more than threefold reduction in the recurrence parameter provide quantitative confirmation of the effectiveness of major programmatic reforms implemented during this period.

Model fitting to the observed TB incidence is presented in Figure 8.

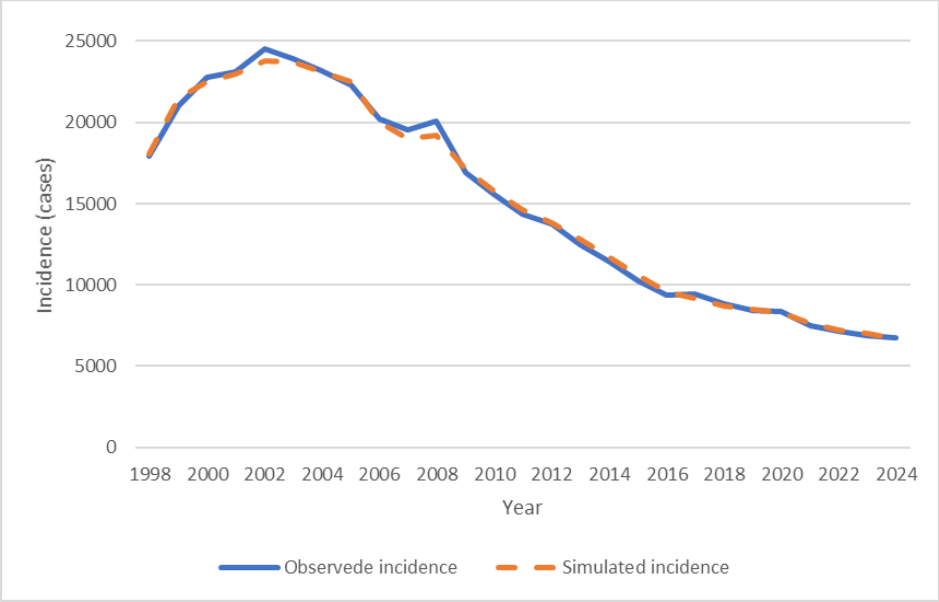


Figure 8 – Model fitting to the observed TB incidence

The substantially lower MAPE of 2.9% in the earlier period (1998-2005) indicates excellent model fit. The higher MAPE of 9.8% in the later period (2006-2024) reflects greater year-to-year variability in the data, particularly during the COVID-19 pandemic years. The overall MAPE, weighted across the entire historical period from 1998 through 2024, amounted to 7.6%. This value indicates a high degree of adequacy in the model's performance and confirms its capacity to reproduce the observed epidemiological dynamics of TB in Kazakhstan.

In the forecast scenarios for the period of 2025-2035, the calibrated parameters served as fixed epidemiological constants. It allows the analysis to isolate the marginal impact of socioeconomic improvements on the transmission coefficient and resulting incidence trajectories.

The calibrated parameters for the recovery and recurrence rates were applied consistently across all the subsequent stage of the model analysis. This uniform use of the period-specific values ensured internal consistency, enhanced the model's ability to reproduce historical patterns with high fidelity, and provided a robust foundation for projecting future TB dynamics under varying socioeconomic conditions. The period-specific calibration also offered direct, measurable evidence of the epidemiological benefit derived from sustained investments in TB control infrastructure, diagnostic capacity, and treatment quality.

### 3.3 Predictive accuracy of the SIR model

3.3.1 Projection of the transmission coefficient for the test period

The transmission coefficient for the test period was forecasted using a polynomial quadratic regression fitted exclusively on the training period to prevent data leakage and ensure unbiased out-of-sample evaluation.

$$\beta(t) = 0.0002t^2 + 0.0091t + 0.3675 \quad (16)$$

The comparison of the forecasted and empirically calculated values of the transmission coefficient values for the test period is presented in Table 6. The findings show that, in 2020 and 2021, the model significantly underestimated the transmission coefficient. It resulted in large relative errors of 23.6% and 21.5%. These substantial discrepancies are attributable to the severe impact of the COVID-19 pandemic on TB control.

From 2022 onward, the agreement improved markedly. The forecasted transmission coefficient values aligned closely with the real values, with relative errors dropping to 5.7% in 2022, and further to 2.2% and 2.4% in 2023 and 2024, respectively. Overall, the results demonstrate the model's robustness for capturing transmission trends under normal conditions. At the same time, it highlights its limitations during major external shocks like the COVID-19, followed by rapid recovery to high accuracy in the post-pandemic years.

Forecasting the transmission coefficient demonstrated satisfactory overall accuracy on the test period, with an average MAPE of 11.1% across the period 2020-2024.

Table 6 – Comparison of forecasted and observed values of the transmission coefficient

| Year | Forecasted β | Observed β | Absolute percentage error (%) |
|---|---|---|---|
| 2020 | 0.659 | 0.863 | 23.6 |
| 2021 | 0.676 | 0.861 | 21.5 |
| 2022 | 0.694 | 0.736 | 5.7 |
| 2023 | 0.712 | 0.728 | 2.2 |
| 2024 | 0.731 | 0.749 | 2.4 |

The quality of the quadratic regression model's fit on the training set is characterized by several key goodness-of-fit metrics. The sum of square residuals is 0.167. It reflects a relatively low level of unexplained variance in the data. This value suggests that the model explains the most of systematic variation in the transmission coefficient over the 22-year training period. The MAE is 0.066, meaning that, on average, the model's predicted values of the transmission coefficient deviate from the empirically estimated values by 0.066 units. This absolute error is considered small in the context of the overall range and scale of the transmission coefficient. The MAPE stands at 12.5%, which represents a reasonably good relative accuracy for modeling a non-linear, gradually accelerating trend with some year-to-year fluctuations.

Overall, these metrics confirm that the quadratic function provides a solid and interpretable approximation of the long-term upward trend in TB transmission during the training period. The fit is sufficiently accurate to justify its use for extrapolation into the test period.

3.3.2 Evaluation of the predictive performance of the SIR model

The predictive performance of the model was evaluated by comparing the simulated incidence values against the observed TB incidence data. This was conducted exclusively on the testing set (2020-2024).

The comparison of the model-predicted and observed TB incidence cases is presented in Table 7.

Table 7 – Comparison of simulated and observed TB incidence cases with MAPE

| Year | Observed incidence cases | Simulated incidence cases | MAPE (%) |
|---|---|---|---|
| 2020 | 8,370 | 8,150 | 2.6 |
| 2021 | 7,500 | 7,720 | 2.9 |
| 2022 | 7,167 | 7,350 | 2.6 |
| 2023 | 6,905 | 6,980 | 1.1 |
| 2024 | 6,733 | 6,650 | 1.2 |

The SIR model demonstrates outstanding predictive performance, with the MAPE values ranging from 1.1% to 2.9% across the years. The errors show no systematic bias confirming balanced, unbiased forecasts. The particularly low errors in 2023 and 2024 suggest that the model captures post-pandemic recovery trends very accurately. Overall, these results provide strong validation of the model's ability to generate to unseen years, making it reliable for forecasting of TB dynamics.

Error metric confirms strong model performance during the test period. The MAPE averaged 2.1% across 2020-2024. This low MAPE value indicates excellent agreement between the model's simulated outputs and the observed TB incidence data. It demonstrates high predictive accuracy and reliability of the adapted compartmental SIR model for capturing long-term TB trends in Kazakhstan.

### 3.4 Relationship between the transmission coefficient of TB and socioeconomic factors

The correlation matrix presents Spearman's correlation coefficients for the transmission coefficient and socioeconomic determinants (Table B.1).

The transmission coefficient shows a very strong negative correlation with per-capita GDP (r = -0.838). This indication that higher economic wealth per person is very strong linked to a lower TB transmission coefficient in this dataset. The transmission coefficient also has a strong negative correlation with CHE (r = -0.955). It suggests that settings with higher health spending as a share of GDP tend to have lower TB transmission intensity. The transmission coefficient exhibits a strong negative correlation with poverty rate (r = -0.929) and a strong negative relation with unemployment rate (r = -0.970). Additionally, there is a strong negative correlation with the volume of social support (r = -0.991). It implies that greater social assistance for TB patients is associated with lower transmission rates.

Regarding the relation between the socioeconomic characteristic, per-capita GDP displays very strong positive correlations with social support (r = 0.960) and CHE (r = 0.991). In contrast, it has very strong negative correlations with poverty (r = -0.957) and unemployment (r = -0.960) rates.

CHE shows strong negative correlation with poverty rate (r = -0.912) and unemployment rate (r = -0.934), but a strong positive correlation with social support (r = 0.945). This pattern suggests that higher CHE co-occurs with stronger social support mechanisms and lower levels of poverty and unemployment.

The poverty and unemployment rates demonstrate an extremely tight positive correlation with each other (r = 0.978). It forms a core cluster of socioeconomic disadvantage indicators. Both variables have strong negative associations with social support to TB patients (r = -0.813 and r = -0.855, respectively).

In summary, the TB transmission coefficient aligns inversely with the socioeconomic variables. This pattern is consistent with global and regional TB epidemiology, where higher-income settings typically achieve better case detection, treatment success, and control measures that reduce effective transmission, while also enabling more social support programs and higher CHE due to greater healthcare investments. In contrast, poorer settings often face under-detection and higher transmission burdens.

The results of the multiple linear regression analysis that investigated multivariate associations of the TB transmission coefficient with socioeconomic determinants (Table B.2). The results show that the coefficient of determination was 0.998. This implies that the model explains 99.8% of the variance of the transmission coefficient. The result for the Durbin-Watson test was 1.493, implying that the model did not show residuals autocorrelation. Regarding multicollinearity aspects, the tolerance statistics and VIFs of all variables were less than 0.1 and greater than 10. This implies that the model showed multicollinearity of the predictors.

PCA was performed to reduce multicollinearity among the socioeconomic factors, which are used to approximate the transmission coefficient. Two principal components were extracted with eigenvalues above 1 (Table 8). The KMO measure verified the sampling adequacy for the PCA (KMO = 0.682). Barlet's test of sphericity indicated that correlation between items were sufficiently large for the PCA ($\chi^2$ (10) = 128.5, $p < 0.001$). Two principal components have eigenvalues over Kaiser's criterion 1 and in combination explained 89.2% of the variance.

Table 8 – Eigenvalues and proportion of variance explained by principal components

| **Principal component** | **Eigenvalues** | **Variance explained (%)** | **Cumulative variance explained (%)** |
|---|---|---|---|
| PC1 | 3.125 | 62.5 | 62.5 |
| PC2 | 1.335 | 26.7 | 89.2 |
| PC3 | 0.312 | 6.2 | 95.4 |
| PC4 | 0.152 | 3.0 | 98.4 |
| PC5 | 0.076 | 1.5 | 100.0 |

Principal component 1 (PC 1) is interpreted as an integral factor representing economic and social stability with high loadings from per-capita GDP, poverty and unemployment rates. PC 2 is interpreted as an integral factor capturing financial and social assistance with high loadings from CHE and social support to TB patients. The factor loadings after rotation indicate how the original predictors relate to each component (Table 9). Loading greater than 0.7 are considered significant for interpretation.

Table 9 – Factor loadings of the principal components after rotation

| **Predictor** | **PC1** | **PC2** | **Communality** | **Uniqueness** |
|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 |
| Per-capita GDP | 0.92 | 0.12 | 0.85 | 0.15 |
| CHE | 0.15 | 0.89 | 0.81 | 0.19 |
| Poverty rate | -0.88 | 0.10 | 0.78 | 0.22 |

Continuation of Table 9

| 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|
| Unemployment rate | -0.85 | 0.14 | 0.74 | 0.26 |
| Volume of social support | 0.18 | 0.85 | 0.76 | 0.24 |

The communalities for the original predictors range from 0.74 to 0.85. This means that the two retained components collectively account for a substantial share of the variance in each variable between 74% and 85%. This strong explanatory coverage underscores the suitability of extracting two components, which together capture 89.2% of the overall data variance and demonstrate that the PCA solution is highly effective.

Furthermore, the uniqueness values are relatively low, falling between 0.15 and 0.26, which indicates that only a small proportion of each variable's variance remains unexplained by the model. Such low uniqueness is a characteristic of datasets exhibiting strong inter-correlations among the predictors, where most of the information is successfully condensed into the PCs.

The results of the quadratic multiple regression model investigated multivariate associations of the transmission coefficient with the two retained PC as predictors (Table 10).

Table 10 – Quadratic multiple regression for the transmission coefficient regressed on the PC1 and PC2

| **Coefficient** | **Value** | **Standard error** | **t** | **p-value** |
|---|---|---|---|---|
| Intercept | 0.699 | 0.012 | 58.27 | <0.001 |
| PC1 | 0.003 | 0.001 | 2.74 | 0.011 |
| PC2 | 0.110 | 0.009 | 12.22 | < 0.001 |
| $PC1^2$ | -0.029 | 0.005 | -5.72 | < 0.001 |
| PC1*PC2 | -0.014 | 0.003 | -4.57 | < 0.001 |
| $PC2^2$ | 0.004 | 0.001 | 3.97 | 0.001 |

The results show that the coefficient of determination was 0.931. It implies that the model explained 93.1% of the variance of the transmission coefficient. With respect to collinearity aspects, the tolerance statistics and VIFs of all variables were greater than 0.1 and less than 10. This implies that the model did not show collinearity of the predictors.

The intercept of the quadratic regression model, estimated at 0.699, represents the baseline value of the TB transmission coefficient when both PC 1 and PC 2 are at their standardized mean of zero. This highly significant constant indicates a substantial

average level of transmission. It also serves as the reference point from which the effects of the predictors are measured.

The linear coefficient for PC 1 is positive but modest at 0.003. This result suggests that, holding all other terms constant, settings, which are characterized by higher per-capita GDP, lower poverty, and lower unemployment, exhibit slightly elevated transmission coefficient. In contrast, the linear effect of PC 2 is markedly stronger and highly significant at 0.110. Higher scores on PC 2, reflecting greater CHE and considerable financial and social assistance for TB patients are robustly linked to substantially higher transmission coefficient.

The inclusion of quadratic terms reveals important non-linear patterns. The negative quadratic coefficient for PC 1 ($PC1^2$ = -0.029) indicates an inverted relationship between the transmission coefficient and economic and social stability. The transmission coefficient rises with initial improvements in social and economic condition but eventually declines at very high levels of PC 1.

A significant negative interaction term (PC 1*PC 2 = -0.014) further demonstrates that the influence of CHE and social support on the TB transmission coefficient is moderated by the level of economic development. In less prosperous settings, increases in PC 2 have a larger positive association with the transmission coefficient. In wealthier settings, however, additional CHE and social patient support produce a smaller effect on the transmission coefficient.

The positive quadratic term for PC 2 points to a convex relationship between CHE and the transmission coefficient. TB transmission tends to be higher at both very low and very high levels of PC 2, with potential minimum occurring at intermediate levels. Together, these non-linear and interactive effects highlight the complex, context-dependent ways in which socioeconomic factors shape TB transmission dynamics.

The apparent counterintuitive increase in the transmission rate parameter in TB model, despite improved control measures, is a well- recognized phenomenon in epidemiological modeling. When diagnostic and treatment improvements substantially shorten the average infectious period [157]. A parallel mechanism underlies the positive association between PC 2 and the transmission coefficient. As periods of heightened CHE typically coincide with stronger control measures and shorter infectious periods, thereby elevating the apparent transmission coefficient. Moreover, the nonlinear and interaction effects captured I the quadratic regression, evidenced by the negative $PC1^2$ and PC1*PC2 terms, point to a threshold dynamic. Once a high level of socioeconomic development is attained, the apparent transmission coefficient begins to decline, consistent with patterns observed in low-burden countries. Overall, the dynamics of the transmission coefficient in the model do not signal a deteriorating epidemiological situation but rather reflect the success of the national program in reducing the duration of infectiousness and improving case detection, while projections based on the quadratic dependence of the transmission coefficient on the socioeconomic factors indicate that continue progress in the economic and social stability will lead to stabilization or a decline in the transmission coefficient, ultimately accelerating the reduction in TB incidence.

Finally, the key performance metrics for the quadratic regression model predicting the TB transmission coefficient using PC 1 and PC 2 show that prediction errors are low, with the MAE of 0.043, RMSE of 0.052, and MAPE of 6.97%. This indicates that the model's predictions are both accurate and precise for this dataset (Table 11).

Table 11 – Quality metrics of the quadratic regression model

| Metric | Value |
|---|---|
| MAE | 0.043 |
| MAPE | 6.97% |
| RMSE | 0.052 |

### 3.5 Impact of the variation of socioeconomic parameters on TB incidence

Sensitivity analysis is a powerful and essential tool in epidemiological modeling. The primary aim is to systematically evaluate how variations in input parameters affect the model's output. By quantifying the contribution of each parameter to the overall variability in predictions, sensitivity analysis helps identify which factors matter most, reveals the model's robustness, and uncovers potential interactions. In practice, methods like Sobol's variance-based approach provide deeper insights because real socioeconomic determinants of TB rarely change in isolation. The analysis shows where standalone changes could have strong leverage and where synergies or trade-offs amplify impacts. For epidemiological models, this is especially helpful since small changes in key drivers can lead to disproportionately large epidemiolocal gains over a decade-long period.

Overall, sensitivity analysis transforms a model from a descriptive tool into a strategic one. It bridges the gap between theory and action by revealing not just «what happens if a parameter changes», but «which changes matter most, why, and how to prioritize them». It ultimately helping policymakers, health authorities, and researchers make informed decisions.

The Sobol's indices reveal that CHE is by far the most influential factor. It accounts for 38% of the variance in TB incidence through its direct effect and up to 52% when including all interactions. The unemployment rate also exerts a substantial influence, contributing 28% directly and 45% in total, highlighting strong interaction effects with the other variables. In contrast, the following socioeconomic variables, such as per-capita GDP, poverty rate, and especially the volume of social support to TB patients, show relatively low direct impacts, with their total contributions remaining modest. It suggests that these factors primarily influence TB incidence indirectly through interactions rather than independently.

Furthermore, for every single parameter in the analysis, the total-order index is noticeably higher than the first-order index. This consistent difference clearly demonstrates that interactions among the socioeconomic factors play an important role in the model. None of the factors acts completely independently. Instead, the combined influence of any one parameter becomes amplified when it interacts with changes in the others, through both pairwise and higher-order interactions. The largest gaps

between the two indices, therefore the strongest contributions from interactions, are observed for CHE and unemployment rate. These two factors not only exert high direct effect but also interact most strongly with the remaining variables. Even for parameters with relatively low overall indices, such as TB patients' social assistance or GDP per capita, interactions still contribute a measurable additional influence, even though their total contributions remain small. This pattern is typical of complex systems, where improvements in one area tend to become effective depending on the prevailing conditions in poverty and unemployment rates, economic growth, as well as targeted social assistance for TB patients.

Sobol's sensitivity indices of the socioeconomic predictors are presented in Figure 9.


Figure 9 – Sensitivity indices of the socioeconomic predictors on the projected TB incidence

Overall, the results emphasize that CHE and unemployment rate dominate the uncertainty in TB incidence predictions, while targeted social support provided to TB patients appear to play a comparatively minor role in explaining the variance of TB incidence.

### 3.6 Projection of TB incidence under the baseline scenario

The baseline parameters of the SIR model for forecasting TB incidence in Kazakhstan over the period 2025-2035 are defined under the baseline scenario that assumes the continuation of current transmission intensity and treatment effectiveness, with no additional improvements in control measures. This setup provides a realistic projection of the minimum expected effect on TB dynamics.

Initial conditions of the compartments at the beginning of 2025 are presented in Table 12. The initial number of susceptible populations is 20,149,630 individuals. The initial number of infectious individuals is 8,991, based on the estimated active TB prevalence at the end of 2024 from reported data. The recovered compartment is set to

0 by model design, assuming negligible long-term immunity, as well as no negligible recovered pool.

Table 12 – Initial number of the SIR model compartments for the projection in the period 2025-2035

| Initial state | Description | Value | Source |
|---|---|---|---|
| S (0) | Initial number of susceptible individuals | 20,149,630 | Calculated |
| I (0) | Initial number of infectious individuals | 8,991 | Data [5] |
| R (0) | Initial number of recovered individuals | 0 | Assumed |

Annual net population growth is approximated at 0.26 million people per year, with the total population at the start of 2025 estimated at approximately 20,158,621. This increment is added each year to the S compartment to maintain demographic balance in the total population and reflects Kazakhstan's observed and projected natural growth, including births, deaths, and net migration.

The recovery rate is set at 2.8 per year, corresponding to an average infectious period pf 4.3 months. This value is applied uniformly across all projections and reflects standard treatment regimens without acceleration of therapy.

The TB-specific mortality rate is assigned a value of 0.0228 per year, indicating the annual proportion of infectious individuals who due from the disease.

The annual probability of recurrence is fixed at 0.105, which represents the probability of recovered individuals to return to active TB disease each year. This figure was derived empirically through calibration of the model against historical data from 2006 to 2024.

In the baseline scenario, key socioeconomic predictors were held constant at their 2024 levels. This fixed approach assumes no additional socioeconomic improvements beyond the status quo, thereby establishing a conservative reference point that models minimum expected decline in the epidemic under unchanged conditions.

Therefore, the transmission coefficient is also held constant at 0.749 per year. This value was calculated empirically based on 2024 and remains unchanged under the baseline scenario to simulate the absence of further reductions in TB transmission.

The initial values of the socioeconomic factors serving as the baseline level for all the scenarios were set at their levels of 2024. GDP per capita stood at 14,155 USD. CHE amounted to 4.7% of GDP. Poverty and unemployment rates were 5.2% and 4.7%, respectively. Finally, social support to TB patients totaled 2.641 million KZT.

The projections of TB incidence under the baseline scenario shows a steady and consistent decline from 2025 through 2035 (Table 13). Beginning with 6,537 incident

cases in 2025, the projection shows the number of new cases falling each year by approximately 2.8% to 3.7%. The year-on-year percentage reductions start relatively stable at 3% in 2026, 2.8% in 2027, and 2.9%-3% in 2028and 2029, before accelerating to 3.6% annually from 2030 onward.

Table 13 – Projection of TB incidence under the baseline scenario

| Year | Projected number of incident cases | Lower 95% CI | Upper 95% CI |
|---|---|---|---|
| 2025 | 6,537 | 6,404 | 6,670 |
| 2026 | 6,341 | 6,093 | 6,589 |
| 2027 | 6,166 | 5,798 | 6,534 |
| 2028 | 5,990 | 5,501 | 6,479 |
| 2029 | 5,812 | 5,200 | 6,424 |
| 2030 | 5,613 | 4,865 | 6,361 |
| 2031 | 5,435 | 4,538 | 6,332 |
| 2032 | 5,263 | 4,219 | 6,307 |
| 2033 | 5,977 | 3,881 | 6,273 |
| 2034 | 4,892 | 3,545 | 6,239 |
| 2035 | 4,711 | 3,212 | 6,210 |

Over the first five year, from 2025-2030, the cumulative reduction reaches 14.1%. By the end of the period in 2035, when TB incident cases are projected to fall to 4,711, the total decrease from the 2025 baseline amounts to 27.9%.

The baseline scenario of the SIR model for projecting TB incidence trends over 2025-2035 fixes all the parameters as well as the socioeconomic predictors at their 2024 levels to simulate the minimum anticipated decline in the epidemic under the assumption that current transmission intensity, treatment conditions, and broader socioeconomic circumstances persist without any further enhancements. This no-improvement reference point reflects the absence of additional measures in areas such as improved treatment effectiveness, strengthened economic growth, increased healthcare funding, poverty alleviation, or expanded targeted social assistance for TB-affected individuals. By holding these factors constant, the model provides a clear benchmark for assessing the limitations of the status quo. It also highlights the potential for gradual reduction in TB burden, emphasizing the need for intensified, multi-domain interventions to accelerate meaningful progress.

### 3.7 Long-term effects of socioeconomic interventions on future TB incidence

Prognostic scenarios represent one of the core instruments of modern epidemiological modeling and strategic planning in public health. They enable a systematic assessment of possible trajectories of the epidemic process under various hypothetical conditions. The use of scenarios is not merely desirable but an obligatory condition for obtaining reliable and practically applicable forecasts. Without scenarios, a model can produce only. A single trajectory corresponding to current trends, which

substantially limits understanding of the full range of possible outcomes and associated risks. Such a single-pathway approach fails to address key «what-if» questions facing public health authorities. By considering multiple, explicitly defined scenarios, the analysis moves beyond descriptive historical fitting to proactive decision support [158].

The baseline scenario reflects the epidemic's inherent momentum in the absence of any deliberate additional actions, providing a neutral reference trajectory for comparing the outcomes of proposed interventions. In each alternative scenarios, only a single socioeconomic variable was altered, while all the other. Parameters were held constant at baseline levels. By adopting this univariate approach, we could isolate the specific contribution of each intervention and directly compare their individual effects on TB incidence rate. This separation of influences clarifies which measures deliver the greatest benefit and reveals their relative effectiveness.

### 3.7.1 Scenario1 – 3% annual growth in GDP per capita

The model projections present a consistent and gradually accelerating decline in the predicted TB incidence from 2025 through 2035. Starting from a baseline of 6,483 cases in 2025, the incidence decreases each year at an annual rate that begins 3.1% and steadily rises to 3.9% by 2035. This results in a compound average annual reduction of 3.4% over the full period.

Over the first five years from 2025 to 2030, the incidence rate is projected to fall from 6,483 to 5,472 cases. It corresponds to a cumulative reduction of 15.6%. By the end of the ten-year period from 2025 to 2035, the rate declines further to 4,577 cases. It yields a total cumulative reduction of 29.4% from the 2025 starting level. The pattern reflects steady compounding progress. The early years deliver relatively stable annual declines of 3.1%, while the second half of the period benefits from a modest acceleration to 3.9% per year, producing a noticeable larger overall drop by 2035 (Table 14).

Table 14 – Projected number of TB incidence cases under Scenario 1

| Year | Per-capita GDP, USD | CHE, % | Poverty rate, % | Unemployment rate, % | Financial support, million KZT | Incident cases [95%CI] |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 2025 | 14,580 | 4.7 | 4.9 | 5.2 | 2.641 | 6,483 [6,283-6,683] |
| 2026 | 15,017 | 4.7 | 4.9 | 5.2 | 2.641 | 6,281 [6,032-6,530] |
| 2027 | 15,468 | 4.7 | 4.9 | 5.2 | 2.641 | 6,079 [5,783-6,375] |
| 2028 | 15,932 | 4.7 | 4.9 | 5.2 | 2.641 | 5,877 [5,521-6,233] |
| 2029 | 16,410 | 4.7 | 4.9 | 5.2 | 2.641 | 5,675 [5,247-6,103] |
| 2030 | 16,902 | 4.7 | 4.9 | 5.2 | 2.641 | 5,472 [4,935-6,009] |

Continuation of Table 14

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| 2031 | 17,409 | 4.7 | 4.9 | 5.2 | 2.641 | 5,281 [4,610-5,952] |
| 2032 | 17,932 | 4.7 | 4.9 | 5.2 | 2.641 | 5,090 [4,238-5,942] |
| 2033 | 18,470 | 4.7 | 4.9 | 5.2 | 2.641 | 4,899 [3,886-5,912] |
| 2034 | 19,024 | 4.7 | 4.9 | 5.2 | 2.641 | 4,708 [3,470-5,946] |
| 2035 | 19,595 | 4.7 | 4.9 | 5.2 | 2.641 | 4,577 [3,112-6,042] |

3.7.2 Scenario 2 – annual reduction in the poverty rate by 0.1%

The projections of TB incidence under Scenario 2 illustrate a steady and gradually accelerating decline in the predicted TB incidence from 2025 to 2030. The number of TB incident cases starts at 6,515 cases in 2025 and falls each year at an annual percentage reduction, which begins around 3.1% and increases modestly to 5% by the final year. This produces an average annual reduction of 3.9% across the full study period.

Over the first five years from 2025 to 2030, the number of incident cases is projected to decrease from 6,515 to 5,382 cases. This resulted in a cumulative reduction of 17.4%. By the end of the ten-year period from 2025 to 2035, the rate falls further to 4,378 cases, which corresponds to a total cumulative reductio of 32.8% from the 2025 baseline year.

The trajectory demonstrates consistent progress. Early annual declines remain stable at 3.1%, while the second half of the period shows a modest acceleration to 5% per year, leading to a noticeably larger overall drop in the number of TB incident cases by 2035 (Table 15).

Table 15 – Projected number of TB incidence cases under Scenario 2

| **Year** | **Per-capita GDP, USD** | **CHE, %** | **Poverty rate, %** | **Unemployment rate, %** | **Financial support, million KZT** | **Incident cases [95%CI]** |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 2025 | 14,155 | 4.7 | 4.8 | 5.2 | 2.641 | 6,515 [6,315-6,715] |
| 2026 | 14,155 | 4.7 | 4.7 | 5.2 | 2.641 | 6,310 [6,067-6,553] |
| 2027 | 14,155 | 4.7 | 4.6 | 5.2 | 2.641 | 6,105 [5,800-6,410] |
| 2028 | 14,155 | 4.7 | 4.5 | 5.2 | 2.641 | 5,900 [5,535-6,265] |
| 2029 | 14,155 | 4.7 | 4.4 | 5.2 | 2.641 | 5,695 [5,265-6,125] |

Continuation of Table 15

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| 2030 | 14,155 | 4.7 | 4.3 | 5.2 | 2.641 | 5,382 [4,855-5,909] |
| 2031 | 14,155 | 4.7 | 4.2 | 5.2 | 2.641 | 5,189 [4,517-5,861] |
| 2032 | 14,155 | 4.7 | 4.1 | 5.2 | 2.641 | 4,996 [4,149-5,843] |
| 2033 | 14,155 | 4.7 | 4.0 | 5.2 | 2.641 | 4,803 [3,765-5,841] |
| 2034 | 14,155 | 4.7 | 3.9 | 5.2 | 2.641 | 4,610 [3,283-5,937] |
| 2035 | 14,155 | 4.7 | 3.8 | 5.2 | 2.641 | 4,378 [2,729-6,027] |

3.7.3 Scenario 3 – annual reduction in the unemployment rate by 0.1%

The projections depict a consistent and gradually accelerating decline in the predicted number of TB incident cases from 2025 to 2035. The figure starts at 6,523 cases in 2025 and decreases each year. The annual rate of decline begins at 3.2% in the early years and gradually increases, reaching 5.2% in the final year. The compound average annual reduction across the full period is 4%.

Regarding cumulative progress relative to the 2025 baseline of 6,523 cases, the incidence rate is projected to fall to 5,362 by 2030. This corresponds to a cumulative reduction of 17.8% over the first five years. By 2035 the number is expected to reach 4,338 cases, which results in a total cumulative reduction of 33.5% over the ten-year period.

The pattern reflects steady compounding progress. The early years deliver relatively stable annual declines of 3.2%, while the second half of the period benefits from a modest but noticeable acceleration of 5.2% per year. This resulted in a significantly larger overall reduction by 2035 (Table 16)

Table 16 – Projected number of TB incidence cases under Scenario 3

| **Year** | **Per-capita GDP, USD** | **CHE, %** | **Poverty rate, %** | **Unemployment rate, %** | **Financial support, million KZT** | **Incident cases [95%CI]** |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 2025 | 14,155 | 4.7 | 4.9 | 5.1 | 2.641 | 6,523 [6,323-6,723] |
| 2026 | 14,155 | 4.7 | 4.9 | 5.0 | 2.641 | 6,317 [6,073-6,561] |
| 2027 | 14,155 | 4.7 | 4.9 | 4.9 | 2.641 | 6,111 [5,806-6,416] |
| 2028 | 14,155 | 4.7 | 4.9 | 4.8 | 2.641 | 5,905 [5,543-6,267] |
| 2029 | 14,155 | 4.7 | 4.9 | 4.7 | 2.641 | 5,699 [5,250-6,148] |

Continuation of Table 16

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| 2030 | 14,155 | 4.7 | 4.9 | 4.6 | 2.641 | 5,362 [4,792-5,932] |
| 2031 | 14,155 | 4.7 | 4.9 | 4.5 | 2.641 | 5,166 [4,476-5,856] |
| 2032 | 14,155 | 4.7 | 4.9 | 4.4 | 2.641 | 4,970 [4,101-5,839] |
| 2033 | 14,155 | 4.7 | 4.9 | 4.3 | 2.641 | 4,774 [3,706-5,842] |
| 2034 | 14,155 | 4.7 | 4.9 | 4.2 | 2.641 | 4,578 [3,211-5,945] |
| 2035 | 14,155 | 4.7 | 4.9 | 4.1 | 2.641 | 4,338 [2,666-6,010] |

3.7.4 Scenario 4 – annual increase in CHE by 0.1%

The projections under Scenario 4 show a consistent downward trajectory in the predicted number of TB incident cases from 2025 to 2035. The TB incidence starts at 6,473 cases in 2025 and decreases each year. The annual rate of decline starts at 3.8% in the early years and gradually accelerates, reaching 4% per year in the second half of the period. The average annual reduction over the full study period is 3.6%.

Over the first five years from 2025 to 2030, the incidence rate falls from 6,473 to 5,417 cases, corresponding to a cumulative reduction of 16.3%. By the end of the ten-year horizon, the number declines further to 4,486. It results in a total cumulative reduction of 30.7% from the 2025 baseline (Table 17).

Table 17 – Projected number of TB incidence cases under Scenario 4

| **Year** | **Per-capita GDP, USD** | **CHE, %** | **Poverty rate, %** | **Unemployment rate, %** | **Financial support, million KZT** | **Incident cases [95%CI]** |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 2025 | 14,155 | 4.8 | 4.9 | 5.2 | 2.641 | 6,473 [6,273-6,673] |
| 2026 | 14,155 | 4.9 | 4.9 | 5.2 | 2.641 | 6,262 [6,018-6,506] |
| 2027 | 14,155 | 5.0 | 4.9 | 5.2 | 2.641 | 6,051 [5,746-6,356] |
| 2028 | 14,155 | 5.1 | 4.9 | 5.2 | 2.641 | 5,840 [5,478-6,202] |
| 2029 | 14,155 | 5.2 | 4.9 | 5.2 | 2.641 | 5,629 [5,180-6,078] |
| 2030 | 14,155 | 5.3 | 4.9 | 5.2 | 2.641 | 5,417 [4,847-5,987] |
| 2031 | 14,155 | 5.4 | 4.9 | 5.2 | 2.641 | 5,231 [4,541-5,921] |
| 2032 | 14,155 | 5.5 | 4.9 | 5.2 | 2.641 | 5,045 [4,176-5,914] |

Continuation of Table 17

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| 2033 | 14,155 | 5.6 | 4.9 | 5.2 | 2.641 | 4,859 [3,791-5,927] |
| 2034 | 14,155 | 5.7 | 4.9 | 5.2 | 2.641 | 4,673 [3,305-6,041] |
| 2035 | 14,155 | 5.8 | 4.9 | 5.2 | 2.641 | 4,486 [2,845-6,127] |

3.7.5 Scenario 5 – 5% annual increase in the volume of social support to TB patients

The projections of TB incident cases under Scenario 5 illustrate a clear and steadily accelerating decline from 2025 and 2035. The incidence rate starts at 6,463 in 2025 and falls each year. The annual rate of decline begins 3.7% and gradually increases, reaching 5.5% in the final year. The average annual reduction over the full study period is 4.7%.

Over the first years, the number of TB incident cases decreases from 6,463 to 5,196 cases, corresponding to a cumulative reduction of 19.6%. By the end of the ten-year period, the rate falls further to 3,975 cases, resulting in a total cumulative reduction of 38.5% from the 2025 baseline.

The early years deliver solid annual reductions of 3.7%, while the second half of the period benefits from noticeably faster declines of 5.5% per year, leading to a substantially larger overall drop by 2035 (Table 18).

Table 18 – Projected number of TB incidence cases under Scenario 5

| **Year** | **Per-capita GDP, USD** | **CHE, %** | **Poverty rate, %** | **Unemployment rate, %** | **Financial support, million KZT** | **Incident cases [95%CI]** |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| 2025 | 14,155 | 4.7 | 4.9 | 5.2 | 2.773 | 6,463 [6,263-6,663] |
| 2026 | 14,155 | 4.7 | 4.9 | 5.2 | 2.912 | 6,250 [6,006-6,494] |
| 2027 | 14,155 | 4.7 | 4.9 | 5.2 | 3.057 | 6,036 [5,731-6,341] |
| 2028 | 14,155 | 4.7 | 4.9 | 5.2 | 3.210 | 5,823 [5,461-6,185] |
| 2029 | 14,155 | 4.7 | 4.9 | 5.2 | 3.371 | 5,609 [5,160-6,058] |
| 2030 | 14,155 | 4.7 | 4.9 | 5.2 | 3.539 | 5,196 [4,647-5,745] |
| 2031 | 14,155 | 4.7 | 4.9 | 5.2 | 3.716 | 4,952 [4,342-5,562] |
| 2032 | 14,155 | 4.7 | 4.9 | 5.2 | 3.902 | 4,707 [4,038-5,376] |

Continuation of Table 18

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| 2033 | 14,155 | 4.7 | 4.9 | 5.2 | 4.097 | 4,463 [3,695-5,231] |
| 2034 | 14,155 | 4.7 | 4.9 | 5.2 | 4.302 | 4,219 [3,389-5,049] |
| 2035 | 14,155 | 4.7 | 4.9 | 5.2 | 4.517 | 3,975 [3,085-4,865] |

3.7.6 Relative effectiveness of socioeconomic interventions

The projected percentage decline if TB incidence under five alternative scenarios compared to the baseline scenario from 2025 to 2035 is presented in Figure 10.

During the initial period from 2025 through 2029, all the alternative scenarios demonstrate relatively modest and closely aligned reduction in TB incidence, ranging from 1% to 3%. This suggests that the early effects of socioeconomic interventions are gradual across modeled strategies.

A clear divergence between the scenarios begins to emerge from 2030 onward. Scenario 1 shows the weakest overall impact. The percentage decline remains limited throughout the period, peaking at 3.8% in 2034. It was followed by a slight decrease to 2.8% by 2035.

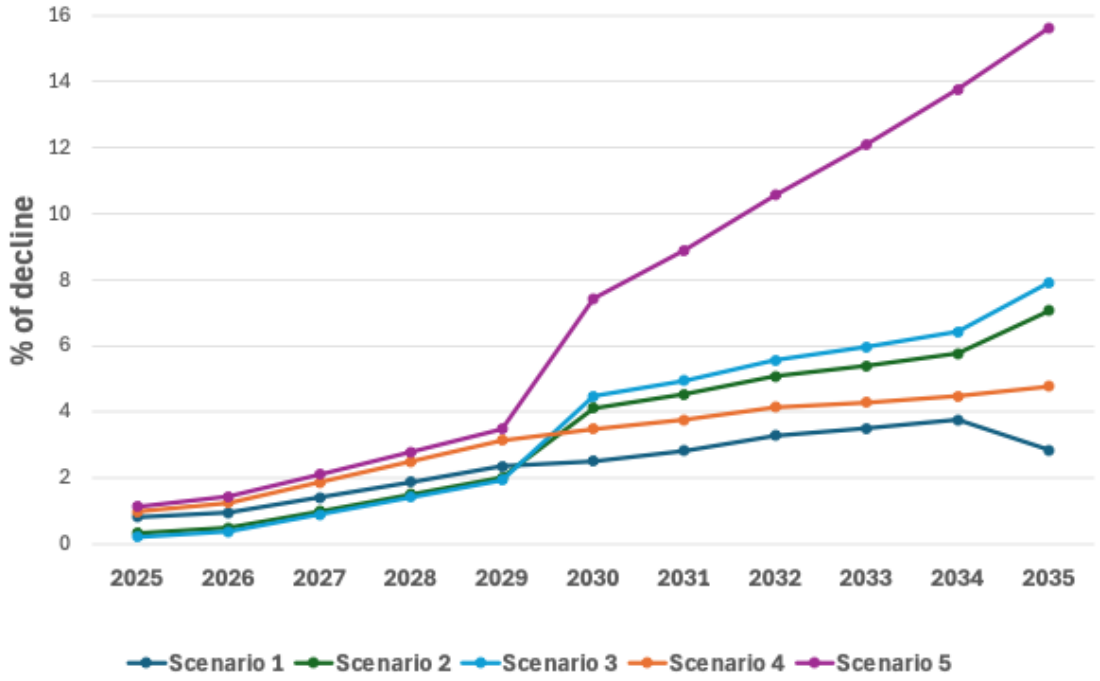


Figure 10 – Relative effectiveness of the five alternative scenarios in the decline of TB incidence

Scenario 4 exhibits moderate improvement, achieving a steady but limited reduction that reaches 4.7% by 2035. Scenarios 2 and 3 demonstrate more noticeable progress. Scenario 3 achieves a reduction of 7.0%, Scenario 3 performs slightly better,

reaching 7.9% decline in TB incidence by the end of the projection period. These two scenarios follow a similar upward trajectory, particularly after 2030.

The most significant and striking pattern is observed in Scenario 5. After a relatively modest start like the other scenario until 2029, this scenario shows a sharp and sustained acceleration in effectiveness beginning in 2030. The percentage decline increases rapidly and consistently, culminating in the highest reduction of 15.7% by 2035. This represents nearly three to five times greater impact compared to the baseline scenario.

The substantial gap between Scenario 5 and the other scenarios underscores that more ambitious, multi-component strategies can lead to markedly greater long-term reductions in TB burden. These findings suggest that the implementation of stronger measures, particularly those reflected in Scenario 5, has the potential to substantially accelerate progress toward national and global TB control targets.

### 3.8 Socioeconomic pathway to achieve the WHO's End TB strategy targets

In 2014, the WHO adopted the new global End TB strategy, which set a goal to eliminate TB by 2035. This strategy establishes clear quantitative targets, benchmarked against 2015 baseline levels. By 2030, the goal includes at least an 80% reduction in TB incidence. While by 2035, the target is at least a 90% reduction in TB incidence [3].

In the Republic of Kazakhstan, the 2015 baseline TB incidence level was 10,262 cases (58.6 per 100,000 population). Based on this value, the absolute target for Kazakhstan is defined as no more than 2,052 new cases by 2030 and 1,026 new cases by 2035.

The optimization results show target thresholds across socioeconomic factors, which should be attained to achieve the WHO' targets by 2030 and 2035 (Table 19).

Table 19 – Target levels of socioeconomic factors

| Predictor | Baseline | Target value for 2030 goal | Target value for 2035 goal |
|---|---|---|---|
| Per-capita GDP, USD | 14,155 | 14,900 | 15,900 |
| CHE, % | 4.7 | 5.2 | 5.5 |
| Poverty rate, % | 5.2 | 4.4 | 3.9 |
| Unemployment rate, % | 4.7 | 4.1 | 3.7 |
| The volume of social support, million KZT | 2.641 | 3.2 | 3.9 |

The foundation of these required improvements lies in the sustained economic growth, as measure by per-capita GDP. With the current baseline standing at 14,155

USD, per-capita GDP needs to rise to a minimum of 14,900 USD by 2030, which is equivalent to an increase of 5.3%. Looking further ahead to 2035, it needs to reach at least 15,900 USD, reflecting a cumulative rise of 2.3% from the baseline level.

Closely linked to the economic growth is the level of CHE as a share of GDP. Starting from the current baseline of 4.7%, CHE needs to increase to at least 5.2% by 2030. This represents a relative rise of 6.1%. By 2035, it needs to attain a minimum if 5.5% of GDP, which is equivalent to a cumulative relative increase of 12.2% from the level of 2024.

In parallel with these economic and healthcare financing advances, two major social risk factors need to be significantly reduced. First, poverty rate, currently standing at 5.2%, needs to be lowered to 4.4% or below by 2030. This equates to a relative reduction of 15.4% from the baseline. By 2035, it needs to fall further to 3.9% or lower, representing a cumulative relative decrease of 25%. Likewise, unemployment rate needs to be declined from its present level of 4.7% to 4.1% by 2030. This corresponds to a relative reduction of 12.8%. While, by 2035, the figure should decline further to 3.7%, which is a relative reduction of 21.3%.

Finally, among the socioeconomic factors, the most directly actionable and TB-specific intervention is the level of social assistance provided to individuals with TB. Currently averaging 2.641 million KZT, it needs to rise to a minimum of 3.2 million KZT by 2030, corresponding to a relative increase of 21.2% from the level of 2024. By 2035, it needs to reach 3.9 million KZT, reflecting a cumulative relative increase of 47.7% from the baseline level.

Meeting the 2030 target already demands concerted policy action, while the 2035 targets require even deeper structural reforms. Delaying progress on any single indicator risks undermining the other, as the relationship are synergistic. Therefore, national TB strategies should integrate these socioeconomic targets into their core planning. Only through the implementation of this multi-sectoral approach, the socioeconomic conditions for sustainable TB elimination can be fully realized by the WHO’s deadlines.

## CONCLUSION

This thesis presents a comprehensive study of TB dynamics in the Republic of Kazakhstan over the period 1997-2024, with forward projections extending through 2035 utilizing a deterministic SIR compartmental model enriched with key socioeconomic determinants. The developed model demonstrates high accuracy in reproducing the observed TB incidence trends. This confirms its adequacy and strong predictive capability.

An important contribution of the work is the integration of socioeconomic factors into the model through dimensionality reduction via PCA followed by quadratic regression. The identified non-linear and iterative effects reveal that, in the early stages of socioeconomic progress, the apparent transmission coefficient may temporarily increase due to improved case detection and shorter infectious periods, whereas sustained high levels of social and economic development eventually lead to stabilization and subsequent decline of the TB transmission coefficient.

Projections under the baseline scenario indicate a gradual decline in TB incidence. Simulation of individual interventions shows that the most substantial additional effect is achieved through sustained annual real increase in direct social support to TB patients. Furthermore, sensitivity analysis further highlights CHE and unemployment rate as the dominant drivers of forecast uncertainty, with significant portion of their influence realized through interactions with other factors.

Achieving the WHO's End TB strategy targets for 2030 and 2035 requires coordinated, multi-sectoral progress across all key socioeconomic predictors. This involves moderate but sustained improvements in per-capita GDP, increases in CHE, reductions in poverty and unemployment rates, and a substantial expansion of targeted social assistance to individuals with TB.

In summary, the thesis offers a scientifically robust, evidence-based decision support tool that not only reconstructs the historical trajectory of TB in Kazakhstan but also quantitatively assesses the contribution of key socioeconomic factors to future TB dynamics. The findings emphasize that, under current conditions, further progress toward TB elimination as a public health problem will critically depend on synergistic action across the health, social protection, and economic development sectors.

Based on the results of the study, the following conclusions are drawn:

1. The incidence rate of TB in the Republic of Kazakhstan decreased on average by 5.91 cases per year from 2000 to 2020 (b = -5.91, $p < 0.001$). However, between 2021 and 2024, the rate of decline slowed considerable (b = -0.85, $p = 0.312$). Socioeconomic factors characterizing social protection ($sr$ = 0.444) and financial protection of the population ($sr$ = -0.398) made the largest contribution to the dynamics of TB incidence.

2. The developed mathematical model serves as a reliable tool for forecasting TB incidence dynamics. It accurately reproduces current trends (MAPE = 7.6%) and demonstrates high predictive accuracy for future trends (MAPE = 2.3%).

3. Among the socioeconomic factors examined, the two indicators with the greatest influence on TB incidence in the republic of Kazakhstan are current health expenditure (38%) and the unemployment (28%).

4. The most effective long-term socioeconomic measure for reducing TB incidence is an annual 5% increase in the volume of social assistance to TB patients. This scenario is projected to reduce TB incidence by 19.6% by 2030 and by 38.5% by 2035 compared to 2024 levels.

5. Achieving the WHO's target indicators for reducing TB incidence by 2030 and 2035 is possible through the following integrated changes: increasing GDP per capita by 5.3% and 12.3%; raising CHE to 5.2% and 5.5% of GDP, reducing poverty rate to 4.4% and 4.9%; lowering unemployment rate to 4.1% and 3.7%; increasing the volume of social assistance by 21.2% and 47.7%, respectively.

Based on the findings of the present study, the following recommendations were formulated:

1. The developed model can be used by regulatory authorities for forecasting and assessing the epidemiological situation regarding TB, as well as for analyzing and studying the interrelationships between various factors and the health status of the population.

2. It is necessary to implement gradual and long-term strengthening of targeted social support for TB patients as one of the most effective measures to reduce the incidence rate of TB.

3. Particular attention should be paid to the monitoring and stabilization of healthcare financing and unemployment levels, as these two key socioeconomic indicators have the greatest influence on the level of TB incidence.

4. The results of the conducted study and the proposed approaches demonstrate the advisability of including thematic sections on mathematical modeling and forecasting of the epidemiological situation for infectious diseases in the educational programs of «Public Health».

## REFERENCES


1 Global Tuberculosis Report 2025. 1st ed. Geneva: World Health Organization, 2025. https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2025.

2 Sachs J., Lafortune G., Fuller G. Financing Sustainable Development to 2030 and Mid-Century. Dublin: Dublin University Press, 2025.

3 Global Tuberculosis Report 2024. 1st ed. Geneva: World Health Organization, 2024. https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2024

4 Global Tuberculosis Report 2023. 1st ed. Geneva: World Health Organization, 2023. https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2023

5 National scientific center of phthisiopulmonology. https://www.nncf.kz.

6 Ledesma J. R. et al. Global, regional, and national age-specific progress towards the 2020 milestones of the WHO End TB Strategy: a systematic analysis for the Global Burden of Disease Study 2021 // Lancet Infect. Dis. - 2024. - Vol. 24, № 7. - P. 698–725.

7 Kolahdooz F. et al. A Scoping Review of the Current Knowledge of the Social Determinants of Health and Infectious Diseases (Specifically COVID-19, Tuberculosis, and H1N1 Influenza) in Canadian Arctic Indigenous Communities // Int. J. Environ. Res. Public. Health. - 2024. - Vol. 22, № 1. - P. 1.

8 Social Determinants of Health. World Health Organization. https://www.who.int/health-topics/social-determinants-of-health#tab=tab_1

9 Idayat M. et al. Prevalence of Tuberculosis in Central Asia and Southern Caucasus: A Systematic Literature Review // Diagnostics. - 2025. - Vol.15, № 18. P. 2314.

10 Jiang H. et al. Changes in Incidence and Epidemiological Characteristics of Pulmonary Tuberculosis in Mainland China, 2005-2016 // JAMA Netw. Open. - 2021. - Vol. 4, № 4. - P. e215302.

11 Raviglione M., Sulis G. Tuberculosis 2015: Burden, Challenges and Strategy for Control and Elimination // Infect. Dis. Rep. - 2016. - Vol. 8, № 2. - P. 6570.

12 World Health Organization. Global tuberculosis report 2020. Geneva: World Health Organization, 2020. https://www.who.int/publications/i/item/9789240013131

13 Kant S., Tyagi R. The impact of COVID-19 on tuberculosis: challenges and opportunities // Ther. Adv. Infect. Dis. - 2021. - Vol. 8. - P. 20499361211016973.

14 McQuaid C. F. et al. The potential impact of COVID-19-related disruption on tuberculosis burden // Eur. Respir. J. - 2020. - Vol. 56, № 2. - P. 2001718.

15 Wingfield T. et al. Challenges and opportunities to end tuberculosis in the COVID-19 era // Lancet Respir. Med. - 2021. - Vol. 9, № 6. - P. 556–558.

16 Chen H., Zhang K. Insight into the impact of the COVID-19 epidemic on tuberculosis burden in China // Eur. Respir. J. - 2020. - Vol. 56, № 3. - P. 2002710.

17 Bekshin Z. et al. Tuberculosis and Impact of COVID-19 on Spread of Epidemics in Kazakhstan // Pathogens. - 2025. - Vol. 14, № 6. - P. 559.

18 Vega V. et al. Recurrent TB: a systematic review and meta-analysis of the incidence rates and the proportions of relapses and reinfections // Thorax. - 2021. - Vol. 76, № 5. - P. 494–502.

19 Li T. et al. Recurrent Pulmonary Tuberculosis in China, 2005 to 2021 // JAMA Netw. Open. - 2024. - Vol. 7, № 8. - P. e2427266.

20 Vega V. et al. Risk factors for pulmonary tuberculosis recurrence, relapse and reinfection: a systematic review and meta-analysis // BMJ Open Respir. Res. - 2024. - Vol. 11, № 1. - P. e002281.

21 Dilmagambetov D. S. et al. Clinical course of respiratory tuberculosis relapses in the Kazakh population depending on HLA-DRB1 gene alleles // VirusDisease. - 2024. - Vol. 35, № 2. - P. 281–292.

22 Takenov N. et al. Genetic diversity, drug resistance, and transmission patterns of tuberculosis based on whole-genome sequencing in Almaty, Kazakhstan // Front. Microbiol. - 2025. - Vol. 16. - P. 1649137.

23 Houben R. M. G. J. et al. Tuberculosis prevalence: beyond the tip of the iceberg // Lancet Respir. Med. - 2022. - Vol. 10, № 6. - P. 537–539.

24 Chen C. et al. Global, regional, and national characteristics of the main causes of increased disease burden due to the covid-19 pandemic: time-series modelling analysis of global burden of disease study 2021 // BMJ. - 2025. - Vol. 390. - P. e083868.

25 Chipinduro M. et al. TB prevalence in Zimbabwe: a national cross-sectional survey, 2014 // Int. J. Tuberc. Lung Dis. - 2022. - Vol. 26, № 1. - P. 57–64.

26 Senkoro M. et al. Prevalence of pulmonary tuberculosis in adult population of Tanzania: a national survey, 2012 // Int. J. Tuberc. Lung Dis. - 2016. - Vol. 20, № 8. - P. 1014–1021.

27 Tale S., Meitei Soibam P. Care of tuberculosis patients in the times of COVID-19 // Indian J. Tuberc. - 2021. - Vol. 68, № 2. - P. 285–286.

28 De Almeida C. P. B. et al. Predictors of In-Hospital Mortality among Patients with Pulmonary Tuberculosis: A Systematic Review and Meta-analysis // Sci. Rep. - 2018. - Vol. 8, № 1. - P. 7230.

29 Ryskulov G. et al. Trends in Tuberculosis Incidence and Treatment Outcomes in Kazakhstan: A Decade of Observational Data // Trop. Med. Infect. Dis. - 2026. - Vol. 11, № 3. - P. 75.

30 Hannah H. A., Miramontes R., Gandhi N. R. Sociodemographic and Clinical Risk Factors Associated With Tuberculosis Mortality in the United States, 2009-2013 // Public Health Reports®. - 2017. - Vol. 132, № 3. - P. 366–375.

31 Girum T. et al. Epidemiology of multidrug-resistant tuberculosis (MDR-TB) in Ethiopia: a systematic review and meta-analysis of the prevalence, determinants and treatment outcome // Trop. Dis. Travel Med. Vaccines. - 2018. - Vol. 4, № 1. - P. 5.

32 Chawla G. K. et al. Pattern of drug resistance among patients of pulmonary tuberculosis // Indian J. Tuberc. - 2022. - Vol. 69, № 4. - P. 669–674.

33 van den Hof S. et al. The socioeconomic impact of multidrug resistant tuberculosis on patients: results from Ethiopia, Indonesia and Kazakhstan // BMC Infect. Dis. - 2016. - Vol. 16, № 1. - P. 470.

34 Martini M., Barberis I., Icardi G. The fight to end tuberculosis: a global challenge in strong partnership // J. Prev. Med. Hyg. Journal of Preventive Medicine and Hygiene, - 2020. - Vol. 61, №.1. - P. 1.

35 Vasiliu A. et al. Tuberculosis prevention: current strategies and future directions // Clin. Microbiol. Infect. - 2024. - Vol. 30, № 9. - P. 1123–1130.

36 Qu M., Zhou X., Li H. BCG vaccination strategies against tuberculosis: updates and perspectives // Hum. Vaccines Immunother. - 2021. - Vol. 17, № 12. - P. 5284–5295.

37 World Health Organization. BCG vaccine: WHO position paper, February 2018 – Recommendations // Vaccine. - 2018. - Vol. 36, № 24. - P. 3408–3410.

38 Looney M. M. et al. Conference report: WHO meeting summary on mRNA-based tuberculosis vaccine development // Vaccine. - 2023. - Vol. 41, № 48. - P. 7060–7066.

39 Swinkels H. M., Jilani T. N., Tobin E. H. Tuberculosis Prevention, Control, and Elimination // StatPearls. Treasure Island (FL): StatPearls Publishing, 2026.

40 Cole B. et al. Essential Components of a Public Health Tuberculosis Prevention, Control, and Elimination Program: Recommendations of the Advisory Council for the Elimination of Tuberculosis and the National Tuberculosis Controllers Association // MMWR Recomm. Rep. - 2020. - Vol. 69, № 7. - P. 1–27.

41 Yayan J. et al. Early detection of tuberculosis: a systematic review // Pneumonia. - 2024. - Vol. 16, № 1. - P. 11.

42 Bartolomeu-Gonçalves G. et al. Tuberculosis Diagnosis: Current, Ongoing, and Future Approaches // Diseases. - 2024. - Vol. 12, № 9. - P. 202.

43 Chaturvedi M. et al. An insight to the recent advancements in detection of Mycobacterium tuberculosis using biosensors: A systematic review // Prog. Biophys. Mol. Biol. - 2024. - Vol. 186. - P. 14–27.

44 Holtgrewe L. M. L. et al. Innovative COVID-19 Point-of-Care Diagnostics Suitable for Tuberculosis Diagnosis: A Scoping Review // J. Clin. Med. - 2024. - Vol. 13, № 19. - P. 5894.

45 Chen Y. et al. Sensitive diagnosis of paucibacillary tuberculosis with targeted next-generation sequencing: a molecular diagnostic study // BMC Med. - 2025. - Vol. 23, № 1. - P. 178.

46 Prikhodchenko O. et al. Epidemiology, detection, diagnosis and treatment of TB in children in Kazakhstan // Int. J. Tuberc. Lung Dis. - 2025. - Vol. 29, № 3. - P. 135–140.

47 Eralieva L. T. et al. Improvement of Organizational Measures for Detection and Diagnosing of Tuberculous Infection and Tuberculosis in Adolescents in the Republic of Kazakhstan // Tuberc. Lung Dis. - 2024. - Vol. 102, № 1. - P. 46–51.

48 Daniyarov A. et al. Whole-Genome Sequence-Based Characterization of Pre-XDR M. tuberculosis Clinical Isolates Collected in Kazakhstan // Diagnostics. - 2023. - Vol. 13, № 12. - P. 2005.

49 Lopes S. R. et al. Update in tuberculosis treatment: a scoping review of current practices // Breathe. - 2025. - Vol. 21, № 1. - P. 240232.

50 Dorman S. E. et al. Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis // N. Engl. J. Med. - 2021. - Vol. 384, № 18. - P. 1705–1718.

51 Conradie F. et al. Treatment of Highly Drug-Resistant Pulmonary Tuberculosis // N. Engl. J. Med. - 2020. - Vol. 382, № 10. - P. 893–902.

52 Rossato Silva1 D. et al. Bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) for multidrug- or rifampin-resistant tuberculosis: a systematic review // J. Bras. Pneumol. - 2024. - P. e20240295.

53 Nunn A. J. et al. A Trial of a Shorter Regimen for Rifampin-Resistant Tuberculosis // N. Engl. J. Med. - 2019. - Vol. 380, № 13. - P. 1201–1213.

54 Felker I., Trajman A. Shorter regimens for multidrug-/rifampicin-resistant TB // Int. J. Tuberc. Lung Dis. - 2023. - Vol. 27, № 1. - P. 3–4.

55 Kozhamkulov U. et al. Multidrug-Resistant Tuberculosis in Central Asia and Predominant Beijing Lineage, Challenges in Diagnosis, Treatment Barriers, and Infection Control Strategies: An Integrative Review // Antibiotics. - 2025. - Vol. 14, № 7. - P. 673.

56 Akhmedullin R. et al. Treatment outcomes for drug-resistant tuberculosis: a retrospective longitudinal study // BMC Infect. Dis. - 2025. - Vol. 25, № 1. - P. 1125.

57 Sorokina M., Ukubayev T., Koichubekov B. Tuberculosis incidence and its socioeconomic determi-nants: developing a parsimonious model // Ann. Ig. Med. Prev. E Comunita. - 2023. - Vol. 35, № 4. - P. 468–479.

58 Kussainova A. et al. Impact of Social Determinants of Health on the Incidence of Tuberculosis in Central Asia // Int. J. Environ. Res. Public. Health. - 2026. - Vol. 23, № 1. - P. 68.

59 Todd H. et al. Social Protection Interventions for TB-Affected Households: A Scoping Review // Am. J. Trop. Med. Hyg. - 2023. - Vol. 108, № 4. - P. 650–659.

60 Jesus G. S. et al. Effects of conditional cash transfers on tuberculosis incidence and mortality according to race, ethnicity and socioeconomic factors in the 100 Million Brazilian Cohort // Nat. Med. - 2025. - Vol. 31, № 2. - P. 653–662.

61 J Carter D. et al. The impact of a cash transfer programme on tuberculosis treatment success rate: a quasi-experimental study in Brazil // BMJ Glob. Health. - 2019. - Vol. 4, № 1. - P. e001029.

62 Richterman A. et al. Cash interventions to improve clinical outcomes for pulmonary tuberculosis: systematic review and meta-analysis // Bull. World Health Organ. - 2018. - Vol. 96, № 7. - P. 471–483.

63 Menon S., Koura K. G. Artificial intelligence for tuberculosis control: a scoping review of applications in public health // J. Glob. Health. - 2025. - Vol. 15. - P. 04192.

64 Galea S., Keyes K. M. Epidemiology at the Heart of Population Health Science // Am. J. Epidemiol. - 2019. - Vol. 188, № 5. - P. 883–885.

65 Skrip L. A., Townsend J. P. Modeling Approaches Toward Understanding Infectious Disease Transmission // Immunoepidemiology. - 2019. - P. 227–243.

66 Den Boon S. et al. Guidelines for multi-model comparisons of the impact of infectious disease interventions // BMC Med. - 2019. - Vol. 17, № 1. - P. 163.

67 Knight G. M. et al. Bridging the gap between evidence and policy for infectious diseases: How models can aid public health decision-making // Int. J. Infect. Dis. - 2016. - Vol. 42. - P. 17–23.

68 Yang W., Zhang J., Ma R. The Prediction of Infectious Diseases: A Bibliometric Analysis // Int. J. Environ. Res. Public. Health. - 2020. - Vol. 17, № 17. - P. 6218.

69 Phoobane P., Masinde M., Mabhaudhi T. Predicting Infectious Diseases: A Bibliometric Review on Africa // Int. J. Environ. Res. Public. Health. - 2022. - Vol. 19, № 3. - P. 1893.

70 Lewnard J. A., Reingold A. L. Emerging Challenges and Opportunities in Infectious Disease Epidemiology // Am. J. Epidemiol. - 2019. - Vol. 188, № 5. - P. 873–882.

71 Olesen S. W., Trabert E. Infectious Disease Modeling: Recommendations for Public Health Decision-Makers // Disaster Med. Public Health Prep. - 2022. - Vol. 16, № 6. - P. 2686–2688.

72 Johnson K. et al. Use of Modeling to Inform Decision Making in North Carolina during the COVID-19 Pandemic: A Qualitative Study // MDM Policy Pract. - 2022. - Vol. 7, № 2. - P. 23814683221116362.

73 James L. P. et al. The Use and Misuse of Mathematical Modeling for Infectious Disease Policymaking: Lessons for the COVID-19 Pandemic // Med. Decis. Making. - 2021. - Vol. 41, № 4. - P. 379–385.

74 Van Kleef E. et al. Modelling practices, data provisioning, sharing and dissemination needs for pandemic decision-making: a European survey-based modellers' perspective, 2020 to 2022 // Eurosurveillance. - 2025. - Vol. 30, № 42.

75 Rao D. et al. The utility of infectious disease modelling in informing decisions for outbreak response: A scoping review // PLOS Glob. Public Health. - 2025. - Vol. 5, № 9. - P. e0005120.

76 Kosova A. A., Chalapa V. I., Kovtun O. P. Methods for modellind and forecasting dynamics of infectious diseases // Ural Med. J. - 2023. - Vol. 22, № 4. - P. 102–112.

77 Yadav S. K., Akhter Y. Statistical Modeling for the Prediction of Infectious Disease Dissemination With Special Reference to COVID-19 Spread // Front. Public Health. - 2021. - Vol. 9. - P. 645405.

78 Barnett A. G. et al. Time series models of environmental exposures: Good predictions or good understanding // Environ. Res. - 2017. - Vol. 154. - P. 222–225.

79 Zheng Y. Predictive Study of Tuberculosis Incidence by ARMA Model Combined with Air Pollution Variables // Complexity. - 2020. - Vol. 2020. - P. 1–11.

80 Liu Q. et al. Forecasting the seasonality and trend of pulmonary tuberculosis in Jiangsu Province of China using advanced statistical time-series analyses // Infect. Drug Resist. - 2019. - Vol. 12. - P. 2311–2322.

81 Ribeiro R. C. M. et al. Forecasting incidence of tuberculosis cases in Brazil based on various univariate time-series models // Int. J. Innov. Educ. Res. - 2019. - Vol. 7, № 10. - P. 894–909.

82 Kaur J., Parmar K. S., Singh S. Autoregressive models in environmental forecasting time series: a theoretical and application review // Environ. Sci. Pollut. Res. - 2023. - Vol. 30, № 8. - P. 19617–19641.

83 Ab Rashid M. A. et al. Forecasting New Tuberculosis Cases in Malaysia: A Time-Series Study Using the Autoregressive Integrated Moving Average (ARIMA) Model // Cureus. - 2023.

84 Yang C. et al. Analysis and Prediction of Pulmonary Tuberculosis Using an ARIMA Model in Shaanxi Province, China // J. Phys. Conf. Ser. - 2020. - Vol. 1624, № 2. - P. 022013.

85 Chen S. et al. Application of the ARIMA Model in Forecasting the Incidence of Tuberculosis in Anhui During COVID-19 Pandemic from 2021 to 2022 // Infect. Drug Resist. - 2022. - Vol. 15. - P. 3503–3512.

86 Zheng Y. et al. Statistical methods for predicting tuberculosis incidence based on data from Guangxi, China // BMC Infect. Dis. - 2020. - Vol. 20, № 1. - P. 300.

87 Cong J. et al. Predicting Seasonal Influenza Based on SARIMA Model, in Mainland China from 2005 to 2018 // Int. J. Environ. Res. Public. Health. - 2019. - Vol. 16, № 23. - P. 4760.

88 Zhao D. et al. Spatial and temporal analysis and forecasting of TB reported incidence in western China // BMC Public Health. - 2024. - Vol. 24, № 1. - P. 2504.

89 Kalizhanova A. et al. Modeling tuberculosis transmission dynamics in Kazakhstan using SARIMA and SIR models // Sci. Rep. - 2024. - Vol. 14, № 1. - P. 24824.

90 Cicchelero L. M. et al. From Patterns to Projections: A Spatiotemporal Distribution of Drug-Resistant Tuberculosis in Paraná, Brazil (2012–2023) // Pathogens. - 2025. - Vol. 14, № 10. - P. 1046.

91 Abegaz E. A., Mesfin M. A., Bazie G. W. Time trend prediction of multidrug-resistant/rifampicin-resistant tuberculosis in treatment initiation centers of North East Ethiopia (2015–2023) // BMC Infect. Dis. - 2025. - Vol. 25, № 1. - P. 1374.

92 Yun W. et al. Time trend prediction and spatial–temporal analysis of multidrug-resistant tuberculosis in Guizhou Province, China, during 2014–2020 // BMC Infect. Dis. - 2022. - Vol. 22, № 1. - P. 525.

93 Fatima S. S. W., Rahimi A. A Review of Time-Series Forecasting Algorithms for Industrial Manufacturing Systems // Machines. - 2024. - Vol. 12, № 6. - P. 380.

94 Mao Q. et al. Forecasting the incidence of tuberculosis in China using the seasonal auto-regressive integrated moving average (SARIMA) model // J. Infect. Public Health. - 2018. - Vol. 11, № 5. - P. 707–712.

95 Chen B. et al. Time Series Data for Equipment Reliability Analysis With Deep Learning // IEEE Access. - 2020. - Vol. 8. - P. 105484–105493.

96 K.B. H. M. et al. A comprehensive study on tuberculosis prediction models: Integrating machine learning into epidemiological analysis // J. Theor. Biol. - 2025. - Vol. 597. - P. 111988.

97 Santangelo O. E. et al. Machine Learning and Prediction of Infectious Diseases: A Systematic Review // Mach. Learn. Knowl. Extr. - 2023. - Vol. 5, № 1. - P. 175–198.

98 Chiu H.-Y. R. et al. Machine learning for emerging infectious disease field responses // Sci. Rep. - 2022. - Vol. 12, № 1. - P. 328.

99 Abade A. et al. A comparative analysis of classical and machine learning methods for forecasting TB/HIV co-infection // Sci. Rep. - 2024. - Vol. 14, № 1. - P. 18991.

100 Azeez A. et al. Machine-learning forecasting model of tuberculosis cases among children in South Africa // South Afr. J. Sci. - 2025. - Vol. 121, № 11. - P.12.

101 Jue W. Prediction model of pulmonary tuberculosis based on gray kernel AR-SVM model // Clust. Comput. - 2019. - Vol. 22, № 2. - P. 4383–4387.

102 Wang H. et al. Time-series analysis of tuberculosis from 2005 to 2017 in China // Epidemiol. Infect. - 2018. - Vol. 146, № 8. - P. 935–939.

103 Harlianto D., Mardiyati S., Lestari D. The comparison between recurrent neural network and grey model to predict Indonesia tuberculosis morbidity rate // J. Phys. Conf. Ser. - 2021. - Vol. 1722, № 1. - P. 012093.

104 Tang N. et al. Machine Learning Prediction Model of Tuberculosis Incidence Based on Meteorological Factors and Air Pollutants // Int. J. Environ. Res. Public. Health. - 2023. - Vol. 20, № 5. - P. 3910.

105 Sina L. B. et al. Hybrid Forecasting Methods—A Systematic Review // Electronics. - 2023. - Vol. 12, № 9. - P. 2019.

106 Li Z. et al. Application of a hybrid model in predicting the incidence of tuberculosis in a Chinese population // Infect. Drug Resist. - 2019. - Vol. 12. - P. 1011–1020.

107 Wang Y. et al. An Advanced Data-Driven Hybrid Model of SARIMA-NNNAR for Tuberculosis Incidence Time Series Forecasting in Qinghai Province, China // Infect. Drug Resist. - 2020. - Vol. 13. - P. 867–880.

108 Li J. et al. Forecasting the Tuberculosis Incidence Using a Novel Ensemble Empirical Mode Decomposition-Based Data-Driven Hybrid Model in Tibet, China // Infect. Drug Resist. - 2021. - Vol. 14. - P. 1941–1955.

109 Zhao R. et al. A hybrid model for tuberculosis forecasting based on empirical mode decomposition in China // BMC Infect. Dis. - 2023. - Vol. 23, № 1. - P. 665.

110 Wang Y. et al. Temporal trends analysis of tuberculosis morbidity in mainland China from 1997 to 2025 using a new SARIMA-NARNNX hybrid model // BMJ Open. - 2019. - Vol. 9, № 7. - P. e024409.

111 Zhang Y. et al. A hybrid machine learning model for pulmonary tuberculosis forecasting of Chongqing with adjacent-region data // PLOS One. - 2025. - Vol. 20, № 12. - P. e0339453.

112 Yadav B. K. et al. Time Series Modeling of Tuberculosis Cases in India from 2017 to 2022 Based on the SARIMA-NNAR Hybrid Model // Can. J. Infect. Dis. Med. Microbiol. - 2023. - Vol. 2023, № 1. - P. 5934552.

113 Azeez A. et al. Seasonality and Trend Forecasting of Tuberculosis Prevalence Data in Eastern Cape, South Africa, Using a Hybrid Model // Int. J. Environ. Res. Public. Health. - 2016. - Vol. 13, № 8. - P. 757.

114 Diez Roux A. V. The Unique Space of Epidemiology: Drawing on the Past to Project Into the Future // Am. J. Epidemiol. - 2019. - Vol. 188, № 5. - P. 886–889.

115 Cassidy R. et al. Mathematical modelling for health systems research: a systematic review of system dynamics and agent-based models // BMC Health Serv. Res. - 2019. - Vol. 19, № 1. - P. 845.

116 Ayinla A. Y., Othman W. A. M., Rabiu M. A Mathematical Model of the Tuberculosis Epidemic // Acta Biotheor. - 2021. - Vol. 69, № 3. - P. 225–255.

117 Liu S. et al. Mixed vaccination strategy for the control of tuberculosis: A case study in China // Math. Biosci. Eng. - 2017. - Vol. 14, № 3. - P. 695–708.

118 Nkamba L. N. et al. Mathematical model to assess vaccination and effective contact rate impact in the spread of tuberculosis // J. Biol. Dyn. - 2019. - Vol. 13, № 1. - P. 26–42.

119 Harris R. C. et al. Age-targeted tuberculosis vaccination in China and implications for vaccine development: a modelling study // Lancet Glob. Health. - 2019. - Vol. 7, № 2. - P. e209–e218.

120 Zhao Y., Li M., Yuan S. Analysis of Transmission and Control of Tuberculosis in Mainland China, 2005–2016, Based on the Age-Structure Mathematical Model // Int. J. Environ. Res. Public. Health. - 2017. - Vol. 14, № 10. - P. 1192.

121 Xue L., Jing S., Wang H. Evaluating Strategies For Tuberculosis to Achieve the Goals of WHO in China: A Seasonal Age-Structured Model Study // Bull. Math. Biol. - 2022. - Vol. 84, № 6. - P. 61.

122 Shrestha S. et al. Achieving a “step change” in the tuberculosis epidemic through comprehensive community-wide intervention: a model-based analysis // BMC Med. - 2021. - Vol. 19, № 1. - P. 244.

123 Mugwagwa T. et al. Comparing different technologies for active TB case-finding among the homeless: a transmission-dynamic modelling study // Sci. Rep. - 2018. - Vol. 8, № 1. - P. 1433.

124 Malek A., Hoque A. Mathematical model of tuberculosis with seasonality, detection, and treatment // Inform. Med. Unlocked. - 2024. - Vol. 49. - P. 101536.

125 Schwalb A. et al. Potential impact, costs, and benefits of population-wide screening interventions for tuberculosis in Viet Nam: A mathematical modelling study // PLOS Glob. Public Health. - 2025. - Vol. 5, № 9. - P. e0005050.

126 Xu A. et al. Prediction of different interventions on the burden of drug-resistant tuberculosis in China: a dynamic modelling study // J. Glob. Antimicrob. Resist. - 2022. - Vol. 29. - P. 323–330.

127 Lalli M. et al. Investigating the impact of TB case-detection strategies and the consequences of false positive diagnosis through mathematical modelling // BMC Infect. Dis. - 2018. - Vol. 18, № 1. - P. 340.

128 Cho H. et al. Predicting the impact of control strategies on the tuberculosis burden in South and North Korea using a mathematical model // BMJ Glob. Health. - 2021. - Vol. 6, № 10. - P. e005953.

129 Arinaminpathy N. et al. Modelling the impact of effective private provider engagement on tuberculosis control in urban India // Sci. Rep. - 2019. - Vol. 9, № 1. - P. 3810.

130 Kendall E. A. et al. MDR-TB treatment as prevention: The projected population-level impact of expanded treatment for multidrug-resistant tuberculosis // PLOS ONE. - 2017. - Vol. 12, № 3. - P. e0172748.

131 Yu Y., Shi Y., Yao W. Dynamic model of tuberculosis considering multi-drug resistance and their applications // Infect. Dis. Model. - 2018. - Vol. 3. - P. 362–372.

132 Kim S., de Los Reyes V A. A., Jung E. Country-specific intervention strategies for top three TB burden countries using mathematical model // PloS One. - 2020. - Vol. 15, № 4. - P. e0230964.

133 Li T. et al. A Modeling Study Recurrent Tuberculosis Towards End TB Strategy - China, 2025-2035 // China CDC Wkly. - 2024. - Vol. 6, № 35. - P. 885–890.

134 Agbata B. C. et al. A comprehensive analysis of fractional-order model of tuberculosis with treatment intervention // BMC Infect. Dis. - 2025. - Vol. 25, № 1. - P. 1070.

135 McQuaid C. F. et al. Estimating the epidemiological and economic impact of providing nutritional care for tuberculosis-affected households across India: a modelling study // Lancet Glob. Health. - 2025. - Vol. 13, № 3. - P. e488–e496.

136 Mandal S. et al. The potential impact on tuberculosis of interventions to reduce undernutrition in the WHO South-East Asian Region: a modelling analysis // Lancet Reg. Health - Southeast Asia. - 2024. - Vol. 31. - P. 100423.

137 Yadav P. K., Goel P. Mathematical model for analysing the interplay between income, nutrition, and tuberculosis dynamics // Comput. Biol. Med. - 2025. - Vol. 196. - P. 110858.

138 Rubio F. A. et al. Evaluating social protection mitigation effects on HIV/AIDS and Tuberculosis through a mathematical modelling study // Sci. Rep. - 2024. - Vol. 14, № 1. - P. 11739.

139 Pedrazzoli D. et al. Modelling the social and structural determinants of tuberculosis: opportunities and challenges // Int. J. Tuberc. Lung Dis. - 2017. - Vol. 21, № 9. - P. 957–964.

140 Boccia D. et al. Modelling the impact of social protection on tuberculosis: the S-PROTECT project // BMC Public Health. - 2018. - Vol. 18, № 1. - P. 786.

141 Blackwood J., Childs L. An Introduction to Compartmental Modeling for the Budding Infectious Disease Modeler // Lett. Biomath. - 2018. - Vol. 5, № 1. - P. 1.

142 Ackley S. F., Lessler J., Glymour M. M. Dynamical Modeling as a Tool for Inferring Causation // Am. J. Epidemiol. - 2022. - Vol. 191, № 1. - P. 1–6.

143 Worden L., Porco T. C. Products of Compartmental Models in Epidemiology // Comput. Math. Methods Med. - 2017. - Vol. 2017. - P. 1–16.

144 Huang J., Morris J. S. Infectious Disease Modeling // Annu. Rev. Stat. Its Appl. - 2025. - Vol. 12, № 1. - P. 19–44.

145 Alamo T. et al. Data-driven methods for present and future pandemics: Monitoring, modelling and managing // Annu. Rev. Control. - 2021. - Vol. 52. - P. 448–464.

146 Siegenfeld A. F., Kollepara P. K., Bar-Yam Y. Modeling Complex Systems: A Case Study of Compartmental Models in Epidemiology // Complexity. - 2022. - Vol. 2022, № 1. - P. 3007864.

147 Dankwa E. A., Brouwer A. F., Donnelly C. A. Structural identifiability of compartmental models for infectious disease transmission is influenced by data type // Epidemics. - 2022. - Vol. 41. - P. 100643.

148 Tang L. et al. A Review of Multi-Compartment Infectious Disease Models // Int. Stat. Rev. - 2020. - Vol. 88, № 2. - P. 462–513.

149 Tolles J., Luong T. Modeling Epidemics With Compartmental Models // JAMA. - 2020. - Vol. 323, № 24. - P. 2515.

150 Heitkamp P., Chijioke-Akaniro O., Pai M. From dependence to self-reliance: The future of the global tuberculosis response // PLOS Med. - 2025. - Vol. 22, № 11. - P. e1004824.

151 Bureau of national statistics agency for strategic planning and reforms of the Republic of Kazakhstan. https://stat.gov.kz/en/

152 World Health Organization. Global tuberculosis report 2021. Geneva: World Health Organization, 2021. https://www.who.int/publications/i/item/9789240037021

153 Bala B. K., Arshad F. M., Noh K. M. System Dynamics: Modelling and Simulation. 1st ed. 2017. Singapore: Springer Singapore: Imprint: Springer, - 2017. - P. 278.

154 United Nations Department of Economic and Social Affairs. World Population Prospects 2024: Summary of Results. Erscheinungsort nicht ermittelbar: United Nations, 2024.

155 Ministry of National Economy of the Republic of Kazakhstan. https://www.gov.kz/memleket/entities/economy?lang=en

156 Strategic Development Plan for 2025–2029 and the Socio-Economic Development Forecast. https://www.gov.kz/memleket/entities/economy?lang=en

157 Berra T. Z. et al. Effectiveness and trend forecasting of tuberculosis diagnosis after the introduction of GeneXpert in a city in south-eastern Brazil // PLOS ONE. - 2021. - Vol. 16, № 5. - P. e0252375.

158 Beishuizen B. H. H. et al. A systematic literature review on public health and healthcare resources for pandemic preparedness planning // BMC Public Health. - 2024. - Vol. 24, № 1. - P. 3114.

## APPENDIX A

## The results of correlation analysis and principal component analysis

Table A.1 – Correlation matrix

| Variable | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|
| 1.TB incidence | 1 | | | | | | | |
| 2.Vaccination coverage | -0.422* | 1 | | | | | | |
| 3.TB case detection | 0.435* | 0.072 | 1 | | | | | |
| 4.GDP per capita | -0.858* | 0.093 | -0.181 | 1 | | | | |
| 5.Current health expenditure | -0.615* | -0.220 | -0.305 | 0.758* | 1 | | | |
| 6.Poverty rate | 0.825* | 0.003 | 0.244 | -0.895* | 0.495* | 1 | | |
| 7.Unemployment rate | 0.712* | 0.186 | 0.269 | -0.876* | 0.434* | 0.866* | 1 | |
| 8.Social assistance | -0.891* | -0.722* | -0.408 | 0.502* | 0.763* | -0.459* | -0.736* | 1 |
| Note - *p < 0.05 | | | | | | | | |

Table A.2 – Principal components loadings

| Variable | Principal component 1 | Principal component 2 |
|---|---|---|
| Unemployment rate | 0.977 | -0.048 |
| Poverty rate | 0.969 | 0.135 |
| GDP per capita | -0.950 | -0.026 |
| Social assistance | -0.492 | 0.842 |
| Current health expenditure | 0.326 | 1.006 |

Table A.3 – Eigenvalue and proportion of variance

| Principal component | Eigenvalue | Variance proportion | Cumulative proportion |
|---|---|---|---|
| Principal component 1 | 3.198 | 0.640 | 0.640 |
| Principal component 2 | 1.680 | 0.336 | 0.976 |

## APPENDIX B

### The results of bivariate correlation analysis and multivariate linear regression

Table B.1 – Bivariate correlations between the transmission coefficient and socioeconomic factors

| Variable | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 1.The transmission coefficient | 1 | -0.838* | -0.955* | -0.929* | -0.970* | -0.991* |
| 2.Per-capita GDP | | 1 | 0.991* | -0.935* | -0.957* | 0.960* |
| 3.CHE | | | 1 | -0.912* | -0.934* | 0.945* |
| 4.Poverty rate | | | | 1 | 0.978* | -0.813* |
| 5.Unemployment rate | | | | | 1 | -0.855* |
| 6.The volume of social support | | | | | | 1 |
| Note – * $p < 0.001$ | | | | | | |

Table B.2 – Multivariate linear regression predicting the transmission coefficient

| Variable | B | Standard error | 95% CI | p-value |
|---|---|---|---|---|
| Intercept | 0.216 | 0.182 | -0.162; 0.594 | 0.248 |
| B1. Per-capita GDP | 6.01e-07 | 8.766e-07 | -1.22e-06; -2.42e-06 | 0.501 |
| B2. CHE | 0.053 | 0.035 | -0.021; 0.126 | 0.151 |
| B3. Poverty rate | -0.002 | 0.002 | -0.006; 0.002 | 0.283 |
| B4. Unemployment rate | 0.001 | 0.004 | -0.008; 0.007 | 0.841 |
| B5. Social support | 0.001 | 2.435e-06 | -9.51e-05; -1.05e-04 | < 0.001 |
| Note – $F(5,21) = 2680.64$, $p < 0.001$ | | | | |

# APPENDIX C

## A state certificate of copyright registration

ҚАЗАҚСТАН РЕСПУБЛИКАСЫ

РЕСПУБЛИКА КАЗАХСТАН

АВТОРЛЫҚ ҚҰҚЫҚПЕН ҚОРҒАЛАТЫН ОБЪЕКТІЛЕРГЕ ҚҰҚЫҚТАРДЫҢ МЕМЛЕКЕТТІК ТІЗІЛІМГЕ МӘЛІМЕТТЕРДІ ЕНГІЗУ ТУРАЛЫ

КУӘЛІК

2026 жылғы «20» ақпан № 67801

Автордың (лардың) жөні, аты, әкесінің аты (егер ол жеке басын куәландыратын құжатта көрсетілсе):
**УКУБАЕВ ТЕМИРЛАН АЛИБИЕВИЧ, СОРОКИНА МАРИНА АНАТОЛЬЕВНА, КОЙЧУБЕКОВ БЕРИК КЕНЖИБАЕВИЧ**

Авторлық құқық объектісі: **ғылыми туынды**

Объектінің атауы: **МОДЕЛЬ ПРОГНОЗИРОВАНИЯ ЗАБОЛЕВАЕМОСТИ ТУБЕРКУЛЕЗОМ**

Объектіні жасаған күні: **28.01.2026**

ҚР «ҰЛТТЫҚ ЗИЯТКЕРЛІК МЕНШІК ИНСТИТУТЫ» РМК
РГП «НАЦИОНАЛЬНЫЙ ИНСТИТУТ ИНТЕЛЛЕКТУАЛЬНОЙ СОБСТВЕННОСТИ» НИО РК

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РЕСПУБЛИКА КАЗАХСТАН

# СВИДЕТЕЛЬСТВО

## О ВНЕСЕНИИ СВЕДЕНИЙ В ГОСУДАРСТВЕННЫЙ РЕЕСТР ПРАВ НА ОБЪЕКТЫ, ОХРАНЯЕМЫЕ АВТОРСКИМ ПРАВОМ

**№ 67801 от «20» февраля 2026 года**

Фамилия, имя, отчество, (если оно указано в документе, удостоверяющем личность) автора (ов):
**УКУБАЕВ ТЕМИРЛАН АЛИБИЕВИЧ, СОРОКИНА МАРИНА АНАТОЛЬЕВНА, КОЙЧУБЕКОВ БЕРИК КЕНЖИБАЕВИЧ**

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С. Ахметов

# APPENDIX D

## Certificate of implementation

Ф КМУ 6-03/01

**УТВЕРЖДАЮ**
Директор
*должность руководителя организации*
КГП «Областной центр фтизиопульмонологии»
*наименование организации (куда внедряются результаты)*
_____ Исмаилов К.О.
*подпись руководителя организации*
«12» мая 2026 г.

**Акт внедрения**
**результатов научно-исследовательских, научно-технических работ (или) результатов научной и (или) научно-технической деятельности**

1. Наименование научно-исследовательских, научно-технических работ и (или) результатов научной и (или) научно-технической деятельности:
Модель анализа и прогнозирования тенденций эпидемической ситуации по туберкулезу

2. Краткая аннотация:
Модель инфекционного процесса туберкулёза с интеграцией социально-экономических предикторов обладает высокой практической ценностью для системы здравоохранения Казахстана. Она позволяет надёжно прогнозировать динамику эпидемиологических показателей при различных сценариях развития социально-экономической ситуации, что делает её эффективным инструментом стратегического планирования региональных и национальных противотуберкулёзных программ. Внедрение модели в управленческую практику даёт руководителям здравоохранения возможность обоснованно распределять ресурсы и целенаправленно планировать меры по контролю эпидемиологической ситуации по туберкулёзу.

3. Эффект от внедрения (экономический, социальный, экологический), подчеркнуть область эффекта:
Социальный

4. Место и дата внедрения:
КГП «Областной центр фтизиопульмонологии»

5. Форма внедрения:
Модель как инструмент оценки и прогнозирования эпидемиологической ситуации по туберкулезу

Представители заявителя, внедрившие результаты научно-исследовательских, научно-технических работ

Докторант _____ Укубаев Т.А.
(подпись)
Ассоциированный профессор _____ Сорокина М.А.
(подпись)

Представитель/представители организации, в которую внедряются результаты научно-исследовательских, научно-технических работ

Профессор _____ Тэбріз Н.С.
(подпись)

# APPENDIX E

## Certificate of implementation

Ф КМУ 6-03/01

**УТВЕРЖДАЮ**
**Председатель Правления - Ректор**
*должность руководителя организации*
НАО «Карагандинский Медицинский Университет»
*наименование организации (куда внедряются результаты)*
_____ Кошерова Б.Н.
*подпись руководителя организации*
«17» марта 2026 г.

**Акт внедрения**
**результатов научно-исследовательских, научно-технических работ (или) результатов научной и (или) научно-технической деятельности**

1. Наименование научно-исследовательских, научно-технических работ и (или) результатов научной и (или) научно-технической деятельности:
Оценка и прогнозирование эпидемиологической ситуации по туберкулезу на основе системно-динамического моделирования.

2. Краткая аннотация:
Модель инфекционного процесса туберкулёза с интеграцией социально-экономических предикторов внедряется в образовательный процесс кафедры инфекционных болезней как инновационный учебный инструмент. Данная модель позволяет обучающимся освоить современные методы прогнозирования, мониторинга и анализа эпидемиологической ситуации по туберкулезу, количественно оценивать влияние социальных факторов на динамику эпидемиологических показателей туберкулёза. Внедрение модели способствует формированию компетенций в области эпидемиологического анализа эпидемического процесса туберкулеза, а также оценки и прогнозирования тенденций эпидемической ситуации по туберкулезу.

3. Эффект от внедрения (экономический, социальный, экологический), подчеркнуть область эффекта:
Социальный

4. Место и дата внедрения:
Кафедра инфекционных болезней и фтизиатрии

5. Форма внедрения:
Изучение конкретного случая по анализу и прогнозированию эпидемиологической ситуации по туберкулезу в рамках лекционных и практических занятий.

Представители заявителя, внедрившие результаты научно-исследовательских, научно-технических работ

Докторант _____ (подпись) Укубаев Т.А.

Ассоциированный профессор _____ (подпись) Сорокина М.А.

Представитель/представители организации в которую внедряются результаты научно-исследовательских, научно-технических работ

Профессор _____ (подпись) Тәбріз Н.С.

«ҚАРАҒАНДЫ МЕДИЦИНА УНИВЕРСИТЕТІ» КОММЕРЦИЯЛЫҚ ЕМЕС АКЦИОНЕРЛІК ҚОҒАМЫ
Қолтаңбаның түпнұсқасын растаймын
АДАМИ РЕСУРСТАРЫ БАСҚАРУ ДЕПАРТАМЕНТІ
АРБД директоры