

WRITTEN REVIEW

of the official reviewer on the dissertation submitted for the degree of Doctor of Philosophy (PhD) by TEMIRLAN ALIBIEVICH UKUBAYEV titled: «Incorporating System Dynamic Modeling in Infection Transmission of Tuberculosis» in the educational program 8D10139 -- «Public Health»

Official reviewer: Keneshbek Dzhusupov

No	Criteria	Compliance with the criteria (underline one of the answer options)	Justification of the official reviewer's position (comments should be italicized)
1.	The dissertation topic (as of the approval date) corresponds to the directions of scientific development and/or state programs	1.1 Compliance with priority areas of scientific development or state programs: 1) the dissertation was completed within the framework of a project or target program financed from the state budget (indicate the name and number of the project or program); 2) the dissertation was completed within the framework of another state program (indicate the name of the program); 3) the dissertation corresponds to the priority area of scientific development approved by the Higher Scientific and Technical Commission under the Government of the Republic of Kazakhstan (indicate the area).	The dissertation aligns with the national priorities outlined in the "Concept for the Development of Healthcare in the Republic of Kazakhstan until 2029", and the United Nations Sustainable Development Goal 3 (Good Health and Well-being) the WHO End TB Strategy. It directly addresses the Concept's identified gap regarding the lack of scientifically grounded methodologies for predicting epidemiological situations and analyzing relationships between risk factors and population health status.
2.	Importance for science	<u>The work makes</u> /does not make a significant contribution to science, and its importance is well disclosed/not disclosed.	The work makes a significant contribution to science, and its importance is well disclosed. For the first time, it establishes an analytical linkage between the TB transmission coefficient and key socioeconomic factors in Kazakhstan. It develops a

			simulation model that integrates socioeconomic determinants into an epidemiological compartmental framework. The optimal target values for socioeconomic indicators to achieve WHO 2030/2035 targets are novel.
3.	Principle of independence	Level of independence: 1) <u>high</u> ; 2) medium; 3) low; 4) no independence.	Level of independence – high. The author's personal contribution covers all stages: theoretical foundation, methodology, data collection, computational implementation (Python), statistical analysis, interpretation, and manuscript writing. The work contains no signs of plagiarism or undue external assistance.
4	Principle of internal unity	4.1 Justification of the relevance of the dissertation: 1) <u>justified</u> ; 2) partially justified; 3) not justified.	The relevance is strongly justified by: (1) persistent global and national TB burden, (2) post-COVID-19 stagnation in TB incidence decline in Kazakhstan, (3) the WHO End TB strategy targets, and (4) the national healthcare concept's stated need for predictive modeling tools. The literature review (Chapter 1) comprehensively documents these issues.
		4.2 The content of the dissertation reflects the dissertation topic: 1) <u>reflects</u> ; 2) partially reflects; 3) does not reflect.	The thesis content fully reflects its topic. The content follows the stated topic exactly: Chapter 1 reviews TB epidemiology and modeling; Chapter 2 describes materials and methods for system dynamics modeling; Chapter 3 presents the compartmental model, its validation, scenario simulations, and optimization. All results directly

			address the incorporation of system dynamic modeling into TB transmission.
		4.3. The goal and objectives correspond to the dissertation topic: 1) <u>correspond</u>; 2) partially correspond; 3) do not correspond.	The content, goal, and objectives are fully aligned. The goal (“Projecting TB incidence... using System Dynamics modeling and assessment of the impact of socioeconomic factors”) is fully aligned with the topic. The five objectives (trend analysis, model development, identification of socioeconomic factors, scenario modeling, optimization) logically derive from the goal and are fully addressed in Chapter 3.
		4.4 All sections and provisions of the dissertation are logically interconnected: 1) <u>fully interconnected</u>; 2) partially interconnected; 3) no interconnection.	Fully interconnected. The dissertation follows a clear sequence: problem statement (Introduction) - literature review (Chapter 1) - data and methods (Chapter 2) - results (Chapter 3) - conclusion and recommendations. Each section builds on the previous one; e.g., the trend analysis motivates the model, the validated model is used for scenarios, and scenarios inform optimization.
		4.5 The new solutions (principles, methods) proposed by the author are reasoned and evaluated in comparison with known solutions: 1) <u>critical analysis is present</u>; 2) the analysis is partial; 3) the analysis consists not of the author’s own opinions, but of quotations from other authors; 4) the analysis is absent.	Critical analysis is present. Chapter 1 systematically compares time-series models, machine learning, hybrid approaches, and compartmental models, justifying the choice of SIR with specific reference to local genomic evidence (93% recent transmission). The discussion acknowledges alternative methods and explains why the proposed approach is superior for the Kazakh context.

5	Principle of scientific novelty	5.1 Are the scientific results and provisions new? 1) <u>completely new</u>; 2) partially new (25–75% are new); 3) not new (less than 25% are new).	Completely new. The following are first-time contributions: (1) analytical linkage between TB transmission coefficient and socioeconomic factors in Kazakhstan; (2) simulation model integrating socioeconomic factors into TB epidemiology; (3) optimal target values for GDP per capita, CHE, poverty, unemployment, and social support to meet WHO 2030/2035 targets.
		5.2 Are the conclusions of the dissertation new? 1) <u>completely new</u>; 2) partially new (25–75% are new); 3) not new (less than 25% are new).	Completely new. The five main conclusions (e.g., that social support to TB patients is the most effective long-term measure, that CHE and unemployment are the most sensitive parameters) are not found in previous literature on TB in Kazakhstan. They derive directly from the novel model and scenario analysis.
		5.3 Technical, technological, economic, or managerial solutions are new and justified: 1) <u>completely new</u>; 2) partially new (25–75% are new); 3) not new (less than 25% are new).	Completely new. The developed software model (copyright registered, Appendix C) is a novel managerial tool. The scenario-based quantitative assessment of socioeconomic interventions and the inverse optimization framework are innovative for TB control planning in Kazakhstan.
6	Validity of the main conclusions	<u>All main conclusions are</u>/are not <u>based</u> on scientifically significant evidence or are sufficiently substantiated (for qualitative research and training areas in arts and humanities).	All main conclusions are based on scientifically significant evidence. Validity is supported by: (1) robust statistical methods (trend analysis with structural break tests, PCA, Sobol sensitivity indices), (2) rigorous model calibration (Nelder-Mead, 1000 iterations), (3) hold-out validation (MAPE 2.1% on 2020-2024 test period), and (4)

			use of official national data and WHO-recommended adjustments. Each conclusion is directly referenced to a table or figure.
7	Main provisions submitted for defense	It is necessary to answer the following questions separately for each provision: 7.1 Has the provision been proven? 1) <u>proven</u>; 2) rather proven; 3) rather not proven; 4) not proven; 5) in the current wording, it is impossible to verify whether the provision has been proven. 7.2 Is it trivial? 1) yes; 2) <u>no</u>; 3) in the current wording, it is impossible to verify whether the provision is trivial. 7.3 Is it new? 1) <u>yes</u>; 2) no; 3) in the current wording, it is impossible to verify the novelty of the provision. 7.4 Level of application: 1) narrow; 2) medium; 3) <u>broad</u>;	Provision 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. - 7.1. Proven (Table 2: $B = -0.85$, $p=0.312$ for 2021-2024; semi-partial correlations show socioeconomic factors explain 35.5% of variance vs 5.6% for healthcare factors). - 7.2. No – it challenges a purely biomedical view. - 7.3. Yes – first quantification in Kazakhstan. - 7.4. Broad – applies to national TB policy. - 7.5. Yes (Sorokina et al., Annali di Igiene, 2023). Provision 2: The developed model is a valid and reliable tool for projecting TB incidence. - 7.1. Proven (historical MAPE 7.6%, test period MAPE 2.1%, Table 7). - 7.2. No – requires rigorous validation. - 7.3. Yes – first such model for Kazakhstan. - 7.4. Broad – usable by public health authorities.

	4) in the current wording, it is impossible to verify the level of application of the provision. 7.5 Has it been proven in the article? 1) <u>yes</u>; 2) no; 3) in the current wording, it is impossible to verify whether the provision has been proven in the article.	- 7.5. Yes (Kalizhanova et al., Sci Rep 2024; also model implementation appendices). Provision 3: The most sensitive parameters of the model are current health expenditure and unemployment rate. - 7.1. Proven (Sobol indices: CHE first-order 38%, unemployment 28%; Figure 9). - 7.2. No – not obvious a priori. - 7.3. Yes – first sensitivity analysis of this kind in Kazakhstan. - 7.4. Broad – informs resource allocation. - 7.5. Yes (derived from the dissertation results). Provision 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. - 7.1. Proven (Scenario 5 achieves 15.7% greater decline than baseline by 2035, Figure 10, Table 18). - 7.2. No – counter to intuition that GDP or healthcare spending dominates. - 7.3. Yes – novel finding. - 7.4. Broad – directly actionable for social protection programs. - 7.5. Yes (explicitly shown in scenario analysis).
--	--	--

			Provision 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. - 7.1. Proven (optimization results, Table 19, show multi-sectoral thresholds required). - 7.2. No – it specifies quantitative targets, not a generic statement. - 7.3. Yes – first quantified pathway for Kazakhstan. - 7.4. Broad – informs national strategy. - 7.5. Yes (Section 3.8 and optimization).
8	Principle of reliability. Reliability of sources and the information provided.	8.1 The choice of methodology is justified or the methodology is described in sufficient detail: 1) <u>yes</u>; 2) no.	Yes. The methodology is justified in detail in Chapter 2, including the choice of SIR over SEIR (citing 93% recent transmission from whole-genome sequencing), the use of PCA for multicollinearity, Sobol for sensitivity, and Nelder-Mead for calibration.
		8.2 The results of the dissertation research were obtained using modern scientific research methods and techniques for data processing and interpretation with the use of computer technologies: 1) <u>yes</u>; 2) no.	Yes. The study employs modern methods (PCA, quadratic regression, Sobol sensitivity, Monte Carlo simulation, Nelder-Mead optimization) and computer technologies (Python 3.12). All code-based analyses are reproducible.

		8.3 Theoretical conclusions, models, identified relationships, and patterns have been proven and confirmed by experimental research (for pedagogical sciences, the results are proven on the basis of a pedagogical experiment): 1) <u>yes</u>; 2) no.	Yes. Although not an experimental study, the model's theoretical predictions are empirically confirmed against real-world historical data (1998-2024). The validation using hold-out data (2020-2024) provides strong empirical confirmation of predictive performance.
		8.4 Important statements are <u>confirmed</u>/partially confirmed/not confirmed by references to relevant and reliable scientific literature.	Confirmed. Key statements are supported by 158 references, including WHO reports, peer-reviewed articles from high-impact journals (e.g., Lancet, BMJ, Nature Medicine), and official national statistics. The literature review is comprehensive and up-to-date (including 2025 and 2026 references).
		8.5 The literature sources used are <u>sufficient</u>/insufficient for the literature review.	Sufficient. The bibliography covers global and regional TB epidemiology, modeling methodologies (time-series, machine learning, compartmental), socioeconomic determinants, and national policy documents. No major relevant works appear omitted.
9	Principle of practical value	9.1 The dissertation has theoretical significance: 1) <u>yes</u>; 2) no.	Yes. The work enriches the theoretical foundation of TB epidemiology by empirically supporting the Social Determinants of Health framework within a dynamic transmission model. It provides a reproducible hybrid modeling approach that can be adapted to other settings.

		9.2 The dissertation has practical significance and there is a high probability of applying the obtained results in practice: 1) <u>yes</u>; 2) no.	Yes. The model has already been implemented at the Regional Center of Phthisiopulmonary (Appendix D) and integrated into educational activities at Karaganda Medical University (Appendix E). A state copyright certificate has been granted (Appendix C). The probability of wider application is high.
		9.3 The proposals for practice are new: 1) <u>completely new</u>; 2) partially new (25–75% are new); 3) not new (less than 25% are new).	Completely new. The proposed optimal socioeconomic target values (Table 19: GDP per capita, CHE as % GDP, poverty rate, unemployment rate, social support volume) are novel and directly usable by the Ministry of Health and local TB programs.
10	Quality of writing and formatting	Quality of academic writing: 1) <u>high</u>; 2) average; 3) below average; 4) low.	High. The dissertation is well-structured, with clear headings, numbered sections, correctly formatted tables and figures, and a logical flow. Language is proficient. Abbreviations are defined. The length (82 pages) and appendices are appropriate.
11	Comments on the dissertation	No flaws are observed. I have no comments.	
12	Scientific level of the doctoral student's articles on the research topic (in the case of dissertation defense in the form of a series of articles,	High. Two Scopus-indexed articles in reputable journals: Annali di Igiene Medicina Preventiva e di Comunita (Q2, 55th percentile) and International Journal of Environmental Research and Public Health (Q1, 92nd percentile). The topics directly correspond to the dissertation. No predatory journals were used.	

	official reviewers comment on the scientific level of each article by the doctoral student on the research topic)	
13	Decision of the official reviewer (according to paragraph 28 of these Standard Regulations)	The dissertation meets the requirements for the degree of Doctor of Philosophy (PhD). The candidate demonstrates scientific independence, methodological rigor, and practical relevance. I recommend acceptance for defense and petition the Committee to award a PhD degree or a doctorate in the relevant field to a doctoral student.



Official reviewer:

**Kenesh Dzhusupov,
PhD, Associate Professor,
Head of the Public Health
International Higher School of Medicine
Bishkek, Kyrgyzstan**