

ABSTRACT

of the dissertation by **Dana Burkitbekovna Dadanbekova**,
submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy (PhD)
in the Educational Program **8D10102 – Pharmacy**,
entitled:

«Pharmacotherapeutic and Pharmacoeconomic Studies in the Treatment of Patients with Post-COVID-19 Cardiomyopathy»

Relevance of the Research Topic.

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, claiming millions of lives each year. This problem affects countries with different levels of socioeconomic development, particularly low- and middle-income countries. According to the World Health Organization, by 2030 approximately 25 million people are expected to die annually from cardiovascular diseases, mainly ischemic heart disease and stroke, which will continue to rank among the leading causes of global mortality.

The rapid spread of the coronavirus causing severe acute respiratory syndrome (SARS-CoV-2) and coronavirus disease 2019 (COVID-19) has had a negative impact on healthcare systems and economies worldwide. According to the international statistical resource Worldometer, from December 2019 to May 2026, more than 704 million people worldwide were infected with SARS-CoV-2, and the associated disease (COVID-19) resulted in more than 7 million deaths. Furthermore, according to Worldometer, Kazakhstan ranks 54th among countries in terms of the prevalence of coronavirus infection, with approximately 1.5 million cases reported and more than 13,000 deaths.

A particular concern is the high prevalence of cardiovascular comorbidities among patients with COVID-19 and their significant impact on disease severity and prognosis. According to a systematic review of studies indexed in the PubMed and Embase databases, the most common comorbid conditions among patients with COVID-19 include arterial hypertension, diabetes mellitus, cardiovascular diseases, and chronic respiratory diseases. Overall, at least one of these comorbidities was present in 64% of patients with COVID-19. Furthermore, the presence of cardiovascular disease was associated with a significantly increased risk of severe, critical, and fatal outcomes of COVID-19 compared with patients without cardiovascular comorbidity.

In this regard, the investigation of the clinical characteristics of post-COVID-19 cardiomyopathy, the optimization of pharmacotherapy, and the pharmacoeconomic evaluation of modern treatment strategies represent an

important scientific and practical challenge aimed at improving the effectiveness of medical care, enhancing patients' quality of life, and ensuring the rational use of healthcare resources.

According to the statistics of the Ministry of Health of the Republic of Kazakhstan, diseases of the circulatory system rank first among the leading causes of mortality in the country, accounting for 22.3 cases per 100,000 population. The principal contributors to cardiovascular mortality include ischemic heart disease, chronic heart failure (CHF), and stroke. Consequently, patients with chronic heart failure and COVID-19-induced cardiomyopathy, who constitute the target population of the present study, represent a subject of considerable scientific and clinical importance.

The prevalence of chronic heart failure continues to increase worldwide. In European countries, the prevalence ranges from 0.4% to 2% of the population, corresponding to approximately 10 million affected individuals. In the United States, more than 5.8 million people are living with CHF, with over 550,000 new cases diagnosed annually. In the Russian Federation, epidemiological studies indicate that approximately 8.1 million individuals suffer from CHF, including 3.4 million patients with advanced stages of the disease.

In the Republic of Kazakhstan, chronic heart failure has also become a major public health concern. More than 1,800 patients with CHF receive inpatient treatment annually at the Almaty City Cardiology Center. Moreover, the number of patients with COVID-19-induced cardiomyopathy associated with chronic heart failure has been increasing since the emergence of the COVID-19 pandemic in 2019, reflecting the long-term cardiovascular consequences of SARS-CoV-2 infection and its growing burden on the healthcare system.

Current approaches to the management of patients with chronic heart failure (CHF) and COVID-19-induced cardiomyopathy require further optimization of pharmacotherapy in accordance with the current clinical guidelines of the Ministry of Health of the Republic of Kazakhstan and the Kazakhstan National Drug Formulary. In this context, pharmacoeconomic studies are of particular importance, as they provide an evidence-based assessment of the clinical effectiveness and economic feasibility of various pharmacotherapeutic strategies, facilitate the optimization of patient management across outpatient and inpatient healthcare settings, contribute to reducing hospitalization and mortality rates, and promote the rational allocation of healthcare resources.

Thus, the substantial medical and social burden of chronic heart failure and COVID-19-induced cardiomyopathy, the increasing prevalence of these conditions, the need for improved pharmacotherapeutic approaches, and the limited evidence regarding their pharmacoeconomic efficiency within the healthcare system of the

Republic of Kazakhstan underscore the relevance of the present study. These considerations formed the basis for selecting the topic of this dissertation, which focuses on pharmacotherapeutic and pharmacoeconomic studies of the treatment of patients with COVID-19-induced cardiomyopathy at both outpatient and inpatient levels of healthcare delivery.

Aim of the Study.

The aim of this study was to conduct pharmacotherapeutic and pharmacoeconomic investigations of the treatment of patients with chronic heart failure and COVID-19-induced cardiomyopathy at both outpatient and inpatient levels of healthcare delivery.

Objectives of the Study:

1. To conduct a comparative analysis of the current prevalence of chronic heart failure in the Republic of Kazakhstan and other countries.
2. To conduct a pharmacotherapeutic study of the treatment of patients with chronic heart failure and COVID-19-induced cardiomyopathy.
3. To perform a pharmacoeconomic evaluation of sacubitril/valsartan therapy in patients with chronic heart failure at outpatient and inpatient levels of healthcare delivery.
4. To develop methodological recommendations for optimizing the pharmaceutical care and medication supply of patients with chronic heart failure at outpatient and inpatient levels of healthcare delivery.

Research Methods.

The study employed a combination of systematic, comparative, retrospective, and prospective research methods, as well as social research methods, including questionnaires and interviews. Pharmacoeconomic evaluation was performed using cost-effectiveness analysis (CEA), cost-utility analysis (CUA), quality-adjusted life years (QALY) assessment, and ABC/VEN analysis. Clinical and economic outcomes were predicted using a Markov model, Monte Carlo simulation, and economic modeling techniques.

Subject of the Study. Pharmacotherapy of patients with chronic heart failure and COVID-19-induced cardiomyopathy.

Object of the Study. The healthcare delivery system for patients with chronic heart failure and COVID-19-induced cardiomyopathy, including pharmacotherapy and pharmaceutical care at both outpatient and inpatient levels of healthcare delivery.

Main Provisions Submitted for Defense:

1. The clinical and social characteristics of patients with chronic heart failure and COVID-19-induced cardiomyopathy.

2. The clinical effectiveness of sacubitril/valsartan-based therapy in combination with guideline-directed standard therapy for chronic heart failure.

3. The scientifically substantiated pharmacoeconomic feasibility of sacubitril/valsartan-based therapy in patients with chronic heart failure and COVID-19-induced cardiomyopathy.

4. A Markov model for assessing the long-term clinical and economic effectiveness of treatment in patients with chronic heart failure and COVID-19-induced cardiomyopathy.

5. A scientifically substantiated model for optimizing pharmaceutical care and medication supply for patients with chronic heart failure and COVID-19-induced cardiomyopathy at both outpatient and inpatient levels of healthcare delivery.

Description of the Main Research Results.

During the dissertation research, a comprehensive analysis of contemporary scientific evidence regarding the prevalence of chronic heart failure (CHF) and COVID-19-induced cardiomyopathy, their risk factors, pathogenetic mechanisms, clinical manifestations, and current treatment approaches in the Republic of Kazakhstan and internationally was carried out. A review of both national and international literature demonstrated that COVID-19 infection exerts long-term adverse effects on the cardiovascular system by promoting structural and functional myocardial alterations and increasing the risk of the development and progression of chronic heart failure. Furthermore, patients with COVID-19-induced cardiomyopathy were found to have a more severe disease course, a higher rate of recurrent hospitalizations, and a substantial deterioration in quality of life.

At the clinical and social stage of the study, a comprehensive assessment of 237 patients with chronic heart failure and COVID-19-induced cardiomyopathy was conducted at the Almaty City Cardiology Center. The findings made it possible to characterize the socio-demographic profile of the study population. Among the participants, 67% were men and 33% were women. The majority of patients were over 41 years of age, indicating the high prevalence of this pathology among middle-aged and older adults.

To assess patients' quality of life and functional status, a sociological survey was conducted using the **Kansas City Cardiomyopathy Questionnaire (KCCQ)**. The findings demonstrated a marked reduction in physical activity among the majority of patients. In particular, a substantial proportion of respondents experienced varying degrees of functional limitation when walking distances of 800–1,000 meters. These results indicate that COVID-19-induced cardiomyopathy

aggravates the course of chronic heart failure, exerting a significant negative impact on patients' daily activities and overall quality of life.

In addition, the study revealed a high prevalence of the major clinical manifestations of the disease, including dyspnea, increased fatigue, orthopnea, reduced exercise tolerance, and limitations in social functioning. The findings highlight the considerable clinical and socio-medical burden of chronic heart failure in patients with COVID-19-induced cardiomyopathy and provide a strong rationale for further optimization of pharmacotherapeutic strategies and pharmaceutical care for this patient population.

During the pharmacotherapeutic phase of the study, the structure of drug therapy used in patients with chronic heart failure (CHF) and COVID-19-induced cardiomyopathy was analyzed. It was established that standard treatment regimens for chronic heart failure, including angiotensin-converting enzyme inhibitors (ACE inhibitors), β -blockers, mineralocorticoid receptor antagonists, diuretics, and cardiac glycosides, are widely used in routine clinical practice. In addition, in accordance with the principles of evidence-based medicine, the clinical effectiveness of sacubitril/valsartan-based therapy was evaluated. The results demonstrated that the use of sacubitril/valsartan in combination with carvedilol, bisoprolol, spironolactone, digoxin, and furosemide contributed to improvements in patients' clinical status, reduced the severity of disease symptoms, and enhanced quality of life.

At the outpatient stage of the study, a pharmacoeconomic analysis was performed to compare the economic efficiency of standard therapy with that of sacubitril/valsartan-based treatment. Contemporary pharmacoeconomic methods were employed, including cost-effectiveness analysis (CEA), cost-utility analysis (CUA), quality-adjusted life years (QALY) assessment, calculation of the incremental cost-effectiveness ratio (ICER), and decision-analytic modeling using a Markov model and Monte Carlo simulation.

The results of the pharmacoeconomic evaluation demonstrated that, despite the higher initial costs of drug therapy, the use of sacubitril/valsartan provides more favorable clinical outcomes and represents a cost-effective treatment strategy in the long term. The findings showed that this therapeutic approach contributes to a reduction in recurrent hospitalizations and episodes of chronic heart failure decompensation, improves patients' quality of life, and enhances the efficiency of healthcare resource utilization.

Pharmacoeconomic studies conducted at the inpatient level further confirmed the clinical and economic advantages of sacubitril/valsartan-based therapy in patients with chronic heart failure and COVID-19-induced cardiomyopathy. Decision-analytic modeling using a Markov model and

probabilistic sensitivity analysis demonstrated the long-term effectiveness of this therapeutic strategy. The calculated incremental cost-effectiveness ratio (ICER) indicated that the intervention is economically justified from the perspective of the healthcare system. Furthermore, long-term modeling showed improvements in quality-adjusted life years (QALYs), confirming the beneficial effects of the therapy on both patients' survival and health-related quality of life.

Based on the findings of the present study, a scientifically substantiated model for optimizing pharmaceutical care for patients with chronic heart failure and COVID-19-induced cardiomyopathy at both outpatient and inpatient levels of healthcare delivery was developed for the first time in the Republic of Kazakhstan. The proposed model is founded on the principles of clinical effectiveness, pharmacoeconomic efficiency, continuity of healthcare, a patient-centered approach, and the rational use of healthcare resources. The model incorporates patient risk stratification, the broad implementation of contemporary pharmacotherapeutic strategies, strengthened continuity between outpatient and inpatient care, an enhanced role for the clinical pharmacist in patient management, and the introduction of a pharmacoeconomic monitoring system to evaluate the effectiveness of pharmaceutical care.

Based on the results of the study, scientific and methodological recommendations aimed at improving pharmaceutical care for patients with chronic heart failure and COVID-19-induced cardiomyopathy were developed. The implementation of these recommendations into routine healthcare practice is expected to improve the quality and accessibility of medical care, enhance patients' quality of life, reduce hospitalization rates and the risk of disease progression, and increase both the clinical and economic efficiency of the healthcare system of the Republic of Kazakhstan.

Scientific Novelty of the Study.

For the first time in the Republic of Kazakhstan, a comprehensive pharmacotherapeutic and pharmacoeconomic evaluation of the treatment of patients with chronic heart failure and COVID-19-induced cardiomyopathy was conducted at both outpatient and inpatient levels of healthcare delivery. The study provides the first integrated assessment of the clinical and economic effectiveness of contemporary pharmacotherapeutic strategies for this patient population using advanced pharmacoeconomic modeling techniques.

For the first time, various combinations of sacubitril/valsartan-based therapy, including its use in combination with ivabradine, carvedilol, and digoxin, were scientifically substantiated and systematically investigated. In addition, the clinical effectiveness and pharmacoeconomic feasibility of these therapeutic

combinations were evaluated in patients with chronic heart failure and COVID-19-induced cardiomyopathy.

Practical Significance of the Research Findings.

The practical significance of the study lies in the pharmacoeconomic evaluation and the development of pharmacotherapeutic approaches for the use of sacubitril/valsartan-based therapy in patients with chronic heart failure at both outpatient and inpatient levels of healthcare delivery.

Based on the study findings, scientific and methodological recommendations were developed to optimize pharmacotherapy and pharmaceutical care for patients with chronic heart failure and COVID-19-induced cardiomyopathy in both outpatient and inpatient settings. The proposed recommendations can be implemented in the routine practice of healthcare organizations in the Republic of Kazakhstan to improve treatment effectiveness, enhance patients' quality of life, reduce hospitalization rates, and promote the rational use of healthcare resources.

Personal Contribution of the Doctoral Candidate.

All stages of the dissertation research were carried out with the direct participation of the doctoral candidate. The author independently defined the aim and objectives of the study, conducted a comprehensive review and analysis of the scientific literature, and performed the clinical, sociological, pharmacotherapeutic, and pharmacoeconomic investigations. The doctoral candidate was also responsible for the statistical analysis and interpretation of the research findings.

Furthermore, the doctoral candidate independently carried out the economic modeling, analyzed and summarized the study results, prepared and published scientific papers, developed scientific and methodological recommendations, and compiled the dissertation manuscript.

Conclusion.

The present study provides a comprehensive evaluation of the clinical, pharmacotherapeutic, and pharmacoeconomic aspects of the management of patients with chronic heart failure (CHF) and COVID-19-induced cardiomyopathy. The study was conducted at the Almaty City Cardiology Center and included 237 patients, of whom 67% were men and 33% were women, while 88.6% of the participants were older than 41 years of age. The review of the scientific literature confirmed that previous COVID-19 infection has long-term adverse effects on the cardiovascular system and contributes to the progression of chronic heart failure.

The pharmacotherapeutic evaluation demonstrated that sacubitril/valsartan-based therapy is clinically more effective than standard treatment. The average number of hospitalizations per patient per year was 3.25 in the standard therapy group, whereas this figure decreased to 3.10 hospitalizations per patient in the group receiving sacubitril/valsartan-based therapy.

The pharmacoeconomic analysis demonstrated that the average annual cost of standard therapy per patient was KZT 74,872.91, whereas the corresponding cost of sacubitril/valsartan-based therapy was KZT 283,895.30. The incremental cost amounted to KZT 209,022.39, and the incremental cost-effectiveness ratio (ICER) was calculated at KZT 1,393,482.6 per hospitalization avoided. These findings indicate that, despite higher initial treatment costs, the sacubitril/valsartan-based strategy is economically justified in view of its superior clinical benefits.

The results of the five-year Markov model simulation confirmed that sacubitril/valsartan-based therapy contributes to a reduction in recurrent hospitalizations, improvements in both the quality and length of patients' lives, and more efficient utilization of healthcare resources. The modeling outcomes demonstrated the long-term clinical and economic effectiveness of this treatment strategy.

Based on the findings of the present study, a scientifically substantiated model for optimizing pharmaceutical care and scientific and methodological recommendations for the management of patients with chronic heart failure and COVID-19-induced cardiomyopathy at both outpatient and inpatient levels of healthcare delivery were developed for the first time in the Republic of Kazakhstan. The proposed model is designed to ensure continuity of care, improve patients' adherence to treatment, reduce the frequency of disease decompensation and recurrent hospitalizations, optimize pharmacotherapeutic management, and promote the rational use of healthcare resources. Ultimately, the implementation of this model is expected to enhance both the clinical and economic effectiveness of healthcare services provided to this patient population.

Approbation of the Research.

The main findings and results of the dissertation research were presented and discussed at scientific meetings and sessions of specialized academic units, including the Department of Organization, Management and Economics of Pharmacy and Clinical Pharmacy of the NJSC Asfendiyarov Kazakh National Medical University (Almaty, 2026), as well as at a meeting of the Scientific Committee of the School of Pharmacy of the NJSC Asfendiyarov Kazakh National Medical University (Protocol No. 15 dated June 30, 2026 Almaty).

Publications:

Based on the results of the dissertation research, ____ scientific publications have been published, including:

- 2 articles in international peer-reviewed scientific journals indexed in the **Scopus** and **Web of Science Core Collection** databases;

- 2 articles published in scientific journals recommended by the Committee for Quality Assurance in Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan;
- 2 publications (articles and conference abstracts) in the proceedings of international scientific and practical conferences held in the Republic of Kazakhstan;
- 1 certificate of registration in the State Register of Rights to Copyright-Protected Objects.

Dissertation Structure and Scope.

The dissertation comprises 220 pages of typed text and includes 25 tables, 50 figures, and a bibliography containing 120 references. The dissertation consists of an introduction, a literature review, a chapter describing the materials and methods of the study, three chapters presenting the author's original research findings, a conclusion, final conclusions, and a list of references.