ANNOTATION

dissertation work of Dinara Yelubaнevna Kaliyeva on the topic:
“Optimization of methodological approaches for studying the accessibility of medicines in the Republic of Kazakhstan”, for the degree of Doctor of Philosophy (PhD) Doctor in the specialty 8D10103 -” Public Health”.
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The relevance of the topic. At the international level, access to medicines is established as one of the core targets of United Nations Sustainable Development Goal 3 (SDG 3), which aims to ensure universal health coverage and access to safe, effective, and high-quality essential medicines (UNE & SC, 2019). Ensuring access to pharmacotherapy is an integral part of realizing the right to health, as enshrined in both international agreements and the national legislation—specifically, the Code of the Republic of Kazakhstan on the Health of the People and the Healthcare System.

In the Message of the President of the Republic of Kazakhstan (RK) Kassym-Zhomart Tokayev " A Fair State. A united nation. A prosperous society" (September 1, 2022) it is emphasized that the primary value of the state is its people, and creating conditions for improving the quality of life and health of citizens is a priority task for the country’s sustainable development (Message to the People of Kazakhstan, 2022). In this context, access to medicines (A2M) is considered a key component of an effective healthcare system, directly impacting public health and the social well-being of citizens.

Particular importance is given to generic medicines, which serve as cost-effective alternatives to originator drugs and help reduce the financial burden on healthcare systems (AAM Report, 2021). In Kazakhstan, generic medicines are registered only upon presentation of evidence of bioequivalence with the originator product (Order No. ҚР DSM-10/2021), while national pricing policy mandates setting their prices at 30% below the average price of the original over the past three years (Order No. ҚР DSM-247/2020). These measures aim to lower healthcare expenditures and improve the financial accessibility of treatment for the population.

However, a significant barrier to the widespread and rational use of generics remains the insufficient awareness among physicians and patients (Mostafa S et al., 2021). Previous studies conducted in Kazakhstan were fragmented, had limited scope, and utilized non-validated survey tools, hindering the formation of an objective picture and the development of effective management decisions. Therefore, assessing the level of awareness about generics among key stakeholders

in the healthcare system and identifying factors that influence their use represents an important direction for scientific inquiry.

In addition, access to medicines should be assessed not only in terms of awareness but also through the lens of physical and economic availability (Kettler H et al., 2021), especially in the case of high-cost treatments. According to 2023 data, over 30% of outpatient pharmaceutical expenditures in Kazakhstan were allocated to the treatment of orphan diseases, significantly exceeding spending on socially significant conditions such as diabetes (20%) and cancer (15%) (Report SK-Pharmacia, 2023; Report MoH RK, 2024).

The limited number of studies devoted to access to medicines in Kazakhstan, along with previously identified disparities between the public and private sectors (WHO/HAI Report, 2005), highlight the need for a systematic approach to monitoring and analyzing indicators of medicine availability.

Thus, in the context of healthcare system transformation and changes in the pharmaceutical market of the Republic of Kazakhstan, studying access to medicines is highly relevant. Special attention should be given to the analysis of awareness about generics and, given the high burden of rare diseases, to the assessment of the physical and economic accessibility of medicines—specifically using orphan drugs as a case study. The findings of this research allow for the identification of key barriers and the formulation of practical recommendations aimed at improving the pharmaceutical supply system in line with national priorities and the global goals of sustainable development.

The purpose of the study is the theoretical justification and implementation of methodological approaches to studying the accessibility of medicines, as well as the development of recommendations for improving medicine accessibility for the population of the Republic of Kazakhstan.

Research objectives

1. To study the current state of the issue of medicine availability at the global level and in the Republic of Kazakhstan.
2. To study and determine the level of awareness of generic medicines among physicians and patients.
3. To analyze the physical and economic availability of medicines using orphan drugs as an example.
4. To develop evidence-based recommendations for improving medicine availability for the population of the Republic of Kazakhstan.

Materials and methods of research

To address the research objectives, methodological approaches were optimized and validated to assess key aspects of medicine accessibility, including awareness of generic medicines as well as assortment (physical) and price (economic) availability, using orphan drugs as a case example.

The theoretical part of the study involved an analysis of contemporary scientific literature, identification of relevant issues, and determination of the key factors influencing medicine accessibility.

The empirical part of the study included a cross-sectional survey to assess the level of awareness of generic medicines among physicians and patients, a structural comparative analysis of orphan drug lists, and a price analysis of procurement costs. The empirical component was based on a developed set of tools providing optimized methodological approaches to assessing medicine accessibility according to established criteria.

1. A literature review was conducted with analysis of data from leading international bibliographic and full-text databases: MEDLINE (PubMed), ProQuest, Cochrane Library, ClinicalTrials.gov, Web of Science, EMBASE, Springer, and Elsevier.

2. The level of awareness of generic medicines among physicians was studied

The study included 450 physicians from 6 regions. The minimum sample size was calculated using the formula for cross-sectional studies (95% confidence interval, 5% margin of error). The questionnaires underwent a validation process. IBM SPSS Statistics 23 was used for data processing, descriptive, and inferential statistical analysis. Respondents' age and years of work experience were converted into categorical variables. Physicians' responses regarding their knowledge and attitudes toward generics were grouped into three categories: "agree," "neutral," and "disagree."

To assess the influence of demographic factors on the level of knowledge and attitudes toward generics, binary logistic regression analysis was applied. Dependent variables were dichotomized based on the median: "sufficient" (above the median) and "insufficient" (below the median). Factor assessment included p-values, odds ratios (OR), and 95% confidence intervals (CI). Statistical significance was set at $\alpha = 0.05$ ($p \leq 0.05$).

3. The level of awareness of generic medicines among patients was studied and determined

A total of 450 patients participated in a cross-sectional survey using an adapted but non-validated questionnaire. Statistical analysis was conducted using IBM SPSS Statistics 23. Categorical variables were presented as absolute (n) and relative (%) frequencies. To compare groups of patients who were aware and unaware of generics, as well as those who had used and not used them, a chi-square (χ^2) test with two-sided analysis was applied. A p-value of less than 0.05 was considered statistically significant.

4. Analysis of physical availability of orphan medicines

A structural comparative analysis was conducted on orphan drugs included in the lists of the Republic of Kazakhstan, the United States, and the European Union. The comparison was carried out based on the ATC classification, international nonproprietary name (INN), or active substance, using official registers of regulatory authorities. The availability of medicinal products was assessed in both absolute and relative terms, including the proportion of drugs from the U.S. FDA and the European Medicines Agency (EMA) registers that are represented in the orphan drug list of the Republic of Kazakhstan. Data processing was performed using Microsoft Excel 2022 MSO (version 2312, build 16.0.17126.20132).

5. A price analysis of the procurement costs of medicinal products was conducted in comparison with reference data (Pharmaceutical Schedule, New Zealand, 2023–2024). For each medicine, the trade name, international nonproprietary name (INN), type (original or generic), dosage form, strength, and manufacturer were identified. A descriptive analysis was performed, including the calculation of mean values and standard deviations. Data processing was carried out using Microsoft Excel 2022 MSO (version 2312, build 16.0.17126.20132).

6. The results of the study served as the basis for the development of recommendations aimed at improving the accessibility of medicines in the Republic of Kazakhstan. The proposed measures focus on optimizing resource allocation strategies and ensuring equitable access to essential medicines for all population groups.

Scientific novelty

1. The scientific novelty of the study lies in the optimization and validation of methodological approaches to assessing key aspects of medicine accessibility, including the level of awareness of generic medicines, as well as assortment (physical) and price (economic) availability, using orphan drugs as a case example. The proposed approaches are of a universal nature and can be adapted for conducting similar research in other countries facing comparable challenges in ensuring access to medicines for their populations.

2. The level of awareness of generic medicines among physicians and patients across six regions of the country was assessed. Key factors influencing the level of awareness were identified, including age, length of service, place of employment, and others. The main barriers hindering the widespread use of generics were also determined, along with differences in knowledge and perception of generic medicines depending on professional experience and access to information..

3. Physical and economic accessibility of medicines was assessed using orphan drugs as a case example. The study identified key patterns influencing medicine accessibility and developed approaches aimed at improving access for patients. The findings provide a basis for the implementation of effective strategies that can significantly enhance the availability of medicines for the country’s population.

4. Scientifically grounded recommendations have been proposed to improve the accessibility of medicines in the Republic of Kazakhstan. These recommendations are based on the results of the study and include measures to enhance physical, economic, and informational accessibility. The implementation of the proposed solutions will enable the optimization of resource allocation and improvement in the quality of healthcare, ensuring equitable access to medicines for all population groups.

Practical significance of the study

The practical significance of this work lies in the applicability of the research findings and recommendations to improve the accessibility of medicines in the

Republic of Kazakhstan. The results of the study can be utilized by healthcare managers, government bodies, and pharmaceutical companies to develop and implement effective strategies for ensuring the population's access to medicines. These findings may serve as a foundation for the development of a national strategy aimed at improving medicine accessibility in Kazakhstan. The proposed recommendations are intended to ensure equitable access to medicines, reduce the financial burden on patients, and improve the quality of healthcare services.

The conducted research and its outcomes are presented in the following methodological guidelines: "The Role of Generic Medicines in Ensuring Equal Access to Medicines for All Patients" and "Monitoring of Drug Safety Information within the Framework of Pharmacovigilance in the Republic of Kazakhstan" (Protocol of the Academic Council of the Faculty of Medicine and Healthcare, Al-Farabi Kazakh National University, No. 10 dated June 28, 2024).

The theoretical significance of the work

The theoretical significance of this study lies in identifying the influence of social and economic factors on the accessibility of medicines in the Republic of Kazakhstan. The research contributes to the development of the conceptual framework for improving access to medicines, thereby supporting the formulation of effective strategies to ensure the population’s access to essential pharmaceutical products.

The findings of the study may facilitate the optimization of methodological approaches to evaluating medicine accessibility, including awareness of generics among physicians and patients, as well as assortment and price accessibility, using orphan drugs as an example. The obtained data open new perspectives for further research and practical implementation. The developed and validated methodological approaches can be employed in future studies aimed at enhancing the accessibility of medicines and in the development of new methodological frameworks in this field.

Moreover, the findings and conclusions may be applied in the educational process, including the preparation of lecture materials and practical assignments, contributing to the professional development of specialists in pharmacy and public health.

The main provisions submitted for Defense:

1. The accessibility of medicines remains a global challenge, particularly in countries with limited healthcare funding. In Kazakhstan, the main barriers are associated with a high dependence on imports, rising prices, an uneven pharmacy infrastructure, a significant share of expenditures on orphan drugs, a limited generic medicine policy, and a low level of public healthcare spending.

2. The level of awareness of generic medicines among physicians and patients depends on the availability of educational resources, regulatory support, and the quality of information regarding bioequivalence. Patients’ willingness to use generics largely depends on the information provided by their treating physicians.

3. The physical and economic accessibility of medicines for the treatment of orphan diseases remains limited due to the absence of state registration for a number of drugs, excessive price regulation, and an insufficient range of registered medicinal products.

4. Scientifically grounded practical recommendations include systematic monitoring of the pharmaceutical market with a focus on medicine accessibility; implementation of educational initiatives to increase trust in generic medicines; updating the lists of orphan drugs; improving mechanisms of price regulation; and encouraging further scientific research in the field of medicine accessibility.

Approbation of the dissertation:

The reliability of the results is confirmed by multiple repetitions of the experiments, sufficient sample size, comparison of the obtained data with previous studies, and the correct application of statistical and analytical methods.

The main provisions and research findings were presented at:

- 5th Global Public Health Conference – GLOBEHEAL 2022 «Future of Global Health in changing world» (Shri-Lanka, 2022 – February 24–25);
- III Online Conference. «Modern science. Management and standards of scientific research collection of articles and theses» (Prag, 2021 April 22-23);
- XV International Scientific and Practical Conference "ECOLOGY. RADIATION. HEALTH" dedicated to the 30th anniversary of the closure of the Semipalatinsk nuclear test site" (Semey, 2021- August 28);

Personal Contribution of the PhD Candidate

The PhD candidate conducted a comprehensive analysis of the literature, collected, processed, and statistically analyzed the obtained results. The author made a significant contribution to the development of methodological recommendations for improving medicine availability. The study results have been reflected in scientific publications and conference presentations, confirming their significance and relevance.

Implementation into practice

The results of the dissertation work have been implemented in practical healthcare:

1. City polyclinic No. 13 of Almaty city.

2. City Cancer Center of the Shymkent city Health Department.

3. Pharmidea Kazakhstan Limited Liability Partnership (LLP).

4. Individual entrepreneur "Support team" (Annex B).

Publications on the topic of the dissertation

A total of 10 scientific papers have been published on the topic of the dissertation, including:

– 1 article in journals indexed in the Web of Science and Scopus databases;

– 3 articles in journals recommended by the Committee for Quality Assurance in the Field of Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan;

– 4 theses at international scientific and practical conferences;

– 2 methodological recommendations (Protocol of the Academic Council of the Faculty of Medicine and Healthcare of Al-Farabi Kazakh National University No. 10 dated 28.06.2024);

– 3 certificates of state registration of ownership rights to the copyright object No. 3369 dated 13.11.2022, No. 50524 dated 17.10.2024, No. 50525 dated 17.10.2024.

Conclusions

Based on the conducted research, the following conclusions were drawn:

1. The accessibility of medicines remains a global issue: over 30% of the population experience difficulties in accessing essential medicines. In developing countries, 20–60% of healthcare expenditures are allocated to medicines, up to 90% of which are paid out-of-pocket by the population.
In Kazakhstan, imported medicines account for 82% of the market, which is accompanied by rising prices. Accessibility is higher in urban areas, where 73% of pharmaceutical sales are controlled by pharmacy chains, and 25% of pharmacies are concentrated in Almaty and Astana. Expenditures on orphan drugs reached 94 billion KZT (21% of the total procurement of medicines and medical products), which places a significant burden on the healthcare budget given the low level of public health expenditure (3.1% of GDP). The absence of a systematic policy to promote the se of generics also presents a serious barrier to expanding access to therapy.

2. Despite a relatively high level of awareness of generic medicines among physicians in Kazakhstan (57.8%), distrust in their effectiveness and safety remains considerable: 44.9% express doubts about their effectiveness, and 32% about their safety. The only statistically significant factor influencing knowledge about generics was gender ($p = 0.014$), with female physicians demonstrating higher awareness. Patient awareness is low (41.1%); 43.2% of patients refuse to use generics due to distrust, and 25% due to a lack of information. The primary source of information for patients is healthcare professionals (58.4%).

3. The physical (assortment-based) accessibility of orphan medicines in Kazakhstan remains limited: out of 152 international nonproprietary names (INNs),

93 (61.1%) are registered, while 59 (38.8%) are not. Among the registered medicines, original products dominate (67.7%), whereas the share of generics and biosimilars is 36.8%. Only 14.8% of orphan medicines from the U.S. FDA list and 11.6% from the EU list are registered in Kazakhstan, indicating a restricted market.

In the analysis of economic accessibility, it was found that procurement prices are on average 28.26% lower than reference prices, though they exhibit high variability.

4. The recommendations developed in the course of this study are aimed at establishing systematic monitoring of the pharmaceutical market with a focus on medicine accessibility, implementing educational initiatives to increase trust in generic medicines, updating the lists of orphan drugs, and improving pricing and regulatory mechanisms. The optimized and implemented methodological approaches introduced in this study may serve as a foundation for further research aimed at evaluating and improving access to medicines. These tools can also be adapted and applied in other countries facing similar challenges in ensuring equitable access to medicines..

PRACTICAL RECOMMENDATIONS

1. Continuous and systematic monitoring of the pharmaceutical market in the Republic of Kazakhstan, in the context of medicine accessibility, is a crucial tool for the timely identification of problems and the adoption of effective solutions. Such monitoring enables prompt responses to price fluctuations, medicine shortages, and key factors affecting accessibility.

2. Educational campaigns serve as an effective tool for increasing trust in generic medicines among physicians and patients. The implementation of educational initiatives for healthcare professionals and patients, the standardization of procedures for transitioning to generics, and the active involvement of physicians and pharmacists in informing the public will help build confidence in the use of generics. This, in turn, will contribute to improving the accessibility of medicines in Kazakhstan.

3. An essential step in improving the pharmaceutical supply system in Kazakhstan is the revision of the national list of orphan drugs, taking into account international experience, and its expansion through the inclusion of essential medicines. Despite the overall reduction in procurement prices for orphan drugs compared to reference values, there remains a high degree of price variability. This indicates the need for further improvement of pricing policies to ensure the economic accessibility of these medicines for the population.

4. The proposed methodological approaches are of a universal nature and can be adapted for conducting similar studies in other countries facing comparable challenges in ensuring access to medicines for their populations. Continued research in this area is essential for developing effective strategies aimed at improving medicine accessibility, optimizing distribution, and enhancing the quality of healthcare services. A thorough analysis of the factors influencing medicine

accessibility will allow for the formulation of evidence-based solutions to improve the efficiency of the pharmaceutical supply system.

The volume and structure of the dissertation. The dissertation comprises 174 pages and includes the following sections: introduction, literature review, materials and methods, theoretical and practical sections (5 chapters), conclusion, and practical recommendations. The manuscript contains 18 tables, 6 figures, and 7 appendices. The reference list includes 155 sources, 105 (68%) of which are in English.