MEDICAL SCIENCES
PROCEEDINGS OF THE SHEVCHENKO SCIENTIFIC SOCIETY
Open Access. Peer Reviewed
ISSN 2708-8634
ISSN 2708-8642
Founded in 1898
#1
2024

Proceedings of the Shevchenko Scientific Society. Medical Sciences **2024**, *1 (73)*. https://doi.org/10.25040/ntsh www. mspsss.org.ua
DOI: 10.25040/ntsh2024.01.01

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Received: 30 Oct, 2023
Accepted: 30 Apr, 2024
Published: 19 June, 2024

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Disclosures: The authors declared no conflict of interest.

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Review & editing: Petro Oliinyk; Bohdan Hromovyk; Taras Gutor; Roman Lysiuk.

Ethical approval: This study did not require ethical approval.

Funding: The authors received no financial support for their study.

Original research: Clinical sciences

Possible solution for the global problem of the high cost of medicines

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A new range of threats arose at the beginning of the 21st century, and the current global and national security systems could not respond effectively. Climate change threatens human health and well-being. Extreme weather events, food and water shortages, and the growth of infectious diseases increase the burden on healthcare systems. Progress in international health partnerships in 2022 has stalled and, in some cases, is reversing. The constant increase in the cost of medical services and medicines has a negative impact on the effectiveness of the functioning of national healthcare systems. Out-of-pocket healthcare costs cause financial hardship for more than 930 million people and push about 90 million into extreme poverty each year. If current trends continue, the World Health Organization predicts that by 2030, up to 5 billion people will be unable to access or afford health services. For further advancement in global health security and to ensure better health for all in a changing world, reducing the cost and guaranteeing access for indigent patients to innovative medicines for treating a wide range of life-threatening diseases is essential. To minimize the cost and ensure access to medicines, it is proposed to create international research centers for developing innovative medicines without patent protection with centralized funding and appropriate planning for high-level interdisciplinary fundamental and applied research based on the needs of healthcare systems worldwide.

Keywords: Healthcare; cost of medicines; patent protection; research center.

Introduction

A new range of threats to which the current global and national security systems could not respond effectively emerged at the beginning of the 3rd millennium. There are discussions about the need to adapt the current international security structures to new challenges and threats of modernity [1].

National security is interpreted as a system where concerns of the individual, society, the state, and threats to these interests interact continuously. Its main elements include political, economic, social, informational, scientific and technological, environmental, humanitarian and, mainly, military security. Threats to national security are such actions that complicate or make the realization of national interests impossible and create danger for socio-economic and political systems, national values, and the livelihood of the country's population [2, 3].

The main components of ensuring national security, as a rule, comprise protecting the social and state order, ensuring sovereignty and territorial integrity, fighting crime and maintaining public order, ensuring economic and political independence, and protecting against natural and man-made disasters and threats to human health. The results of modern studies related to the analysis of conceptual and practical connections between healthcare systems and health security indicate that healthcare security is considered in terms of exclusivity, focusing on acute emergencies, as a component of state security, and not as safety for the health of each individual [4]. This is evidenced by the definition of the World Health Organization (WHO), which interprets global public health security as "the activities required, both proactive and reactive, to minimize the danger and impact of acute public health events that endanger people's health across geographical regions and international boundaries" [5].

Since the late 20th century, the world community has been concerned about the risk of new diseases and their threats to the economy and the general safety of the population [4, 6]. The need to strengthen or increase the health system resilience is assumed or roughly outlined in many healthcare systems around the world [5], including ones based on the International Health Regulations (IHR) [7], as well as discussions in key global structures such as the WHO, the governments of G7 and G20 countries, the World Bank and the United Nations Security Council. In addition, measures to strengthen health systems have begun to appear in several national strategic plans and global initiatives, such as the Global Health Security Agenda (GHSA) and the "One Health," which primarily aim at better promotion of IHR implementation [4, 8].

During discussions in key global structures, development of national strategic plans and global initiatives, various measures are envisaged to strengthen national healthcare systems: adequate leadership and management; effective healthcare workforce; a good healthcare financing system; efficiency of medical services; functioning of the health information system; access to basic medicines and health products [9, 10, 11]. However, the issue of the constant rise in the cost of medical services and, especially, medicines and their impact on global and national security systems and the effectiveness of the functioning of national health care systems are practically not considered.

The aim: This study aims to develop recommendations for increasing the sustainability of the functioning of national healthcare systems and prioritizing safety for the health of each individual by optimizing the cost of medicines. For further study and analysis of the impact of the increase in the price of medical services and medication on global and national security systems, a review of peer-reviewed scientific publications and current WHO initiatives and regulatory acts has been conducted.

General scientific methods of cognition are used: analysis and synthesis, abstraction, deduction, modeling, generalization. The materials were publications from the Google Scholar and PubMed electronic search systems, the Crossref bibliographic database.

Healthcare as an element of the system of global and national security

The spread of the coronavirus disease (COVID-19) in the world revealed critical problems in the healthcare and social protection systems, causing a threat to global and national security due to increased unemployment and the destruction of the established way of life [12]. Despite the facts that the healthcare system contributes to the well-being of every person and society as a whole, and the state of the economy depends on the health of the population, the idea of connecting healthcare with national security has not always been recognized by statesmen, politicians and scientists [13].

However, in recent decades, the situation has begun to change, and the concept of health security has gained recognition. Nevertheless, there is great debate about the true meaning of this concept and the way it is understood by

specialists from various fields related to the healthcare system [13,14]. However, the coronavirus disease spread in the world, and its consequences force both politicians and scientists to recognize that the state of health of the country's population, which depends on the effectiveness of the functioning of the national healthcare system, is one of the most important elements of social and economic security, which in turn, are elements of the country's national security system.

There is growing recognition worldwide that health issues are an element of national and global security and must be addressed at the international level. Despite ongoing debate about its exact meaning, the concept of "global health" has been widely adopted at the institutional level. Health is increasingly becoming an issue of diplomacy, foreign policy, and international politics [15, 16].

Climate change threatens human health and well-being. Extreme weather events, food and water shortages, and the growth of infectious diseases increase the burden on healthcare and social systems, disproportionately affect the most disadvantaged groups of society, and widen injustice in access to medicines and medical services. This is evidenced by the availability of a vaccine against COVID-19 in 2021. In high-income countries, more than 60% of the population received at least one dose of the COVID-19 vaccine, compared to only 3.5% in low-income countries. The extraordinary demand for healthcare caused disruptions in the provision of basic health services in 94 of 105 countries surveyed. Due to multiple concurrent and interacting health risks, climate change threatens to reverse decades of progress in health and sustainable development [17].

In turn, wars, primarily the ongoing Russo-Ukrainian war, cause harmful consequences for global health:

- first, the threat to security and democracy in Europe and the international order as a result of this war forced countries of the world community to spend more and more political, economic, diplomatic and military resources on this crisis, which makes it difficult to solve global health problems, including recovery after COVID-19, increasing pandemic preparedness and climate change adaptation [18];

- second, the ongoing war in Ukraine caused the largest migration crisis that Europe faced in the 21st century – more than 8.2 million Ukrainians became refugees throughout Europe [19]. The vast majority of refugees are women, children, and the elderly, so their medical needs are different, which causes an increase in the state burden on healthcare systems due to in-donor refugee costs [20];

- third, concern about the Russo-Ukrainian war affects the mental health of the population at the global level, even if it does not take a direct part in the conflict [19, 21].

Therefore, it is necessary to begin a rethinking and strategic transition to the structure of global healthcare, considering that the expansion of healthcare coverage is slowing down around the world, as public spending does not meet the demands of society [22, 23]. Out-of-pocket healthcare costs have been found to cause financial hardship for more than 930 million people and push nearly 90 million into extreme poverty each year, with the worsening of impoverishment rate. If current trends continue, WHO predicts that by 2030, up to 5 billion people will be unable to access or afford healthcare [23, 24]. A human rights-based global approach to health governance would enable low- and middle-income countries to have equitable access to essential resources such as medicines and personal protective equipment regardless of ability to pay, while at the same time obliging high-income countries, the private sector and major donors to contribute a greater share in the financing of health care systems [25, 26].

Transforming global health governance

The organization and provision of affordable medical and pharmaceutical services to the population is an important element of global security and national security of each state. The lessons of Ebola, COVID-19, and the Russo-Ukrainian war indicate the need to transform the existing global architecture of the healthcare system into a purposeful and effective system with strong national healthcare systems under the supervision of the WHO [27].

The transformation of the existing global architecture of the healthcare system should provide for the general coverage of the population of all countries of the world with medical services. This means that all groups of the population in all countries should have free access to high-quality medical services and medicines that they need. People need to be protected from the financial consequences of paying exorbitantly for medical services and medicines out of their own pockets, as an unexpected illness forces them to spend their savings and fall into poverty. Universal health coverage (UHC) is one of the goals that the countries of the world set during the adoption in 2015 of the Sustainable Development Goals (SDGs) until 2030 [28].

At the first UN high-level meeting, held in September 2019, world leaders accepted the comprehensive political declaration on health. However, according to the latest Global Monitoring Report on Universal Health Coverage, progress on UHC is not going as planned, and the COVID-19 pandemic and the Russo-Ukrainian war have pushed the world further away from the goals set by the political declaration. The main findings of the latest analysis of UHC 2030 commitments show that in 2022 UHC progress has stalled and in some cases reversed [29].

Factors affecting the cost of medicines

Creating a new drug is quite a complex process, which involves the selection of a disease and the identification of a biological target that will be affected by the newly created drug. The successive stages include synthesizing a new chemical compound or searching for a biologically active substance of natural origin; optimizing the pharmacological properties of the selected compound through biological studies; conducting preclinical and clinical research; and patenting and developing industrial production technology. Almost 15 years of work by hundreds of high-class scientists and 1.5 to 2.5 billion dollars are spent from synthesizing a molecule to introducing a new drug into the market. The costliness of measures to create new medicines has become the reason that a single, even the most talented scientist or a small scientific team cannot introduce a new drug [30, 31].

An important factor affecting the cost of medicines is the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). This agreement was adopted during the Uruguay Round of the General Agreement on Tariffs and Trade (GATT) in 1994 under the auspices of the World Trade Organization. TRIPS establishes standards for recognizing and protecting the main objects of intellectual property. The most controversial provision of the TRIPS agreement is its basic principle – to use the results of intellectual activity in a way that does not lead to excessive material damage to the legitimate interests of its owner. The TRIPS Agreement establishes a term of at least 20 years for the protection of property rights granted by a patent. Article 28 of TRIPS grants patent holders the exclusive right to manufacture patent-protected medicines [32]. Pharmaceutical companies try to keep patents in force as long as possible to prevent prices from falling after the patent expires. To provide it, pharmaceutical companies can manipulate their products, according to the applicable laws, to extend exclusivity, negotiate the schemes with generic companies, or obtain a new patent for an "improved" version of the branded product [33].

Intellectual property on innovative pharmaceuticals allows pharmaceutical companies to monopolize their pricing grades and set extremely high prices, putting public health at risk. Intellectual property rights are opposed to people's rights to health [34]. Therefore, policies that expand intellectual property rights and limit price controls work against public health and access to needed medicines [35].

According to the WHO estimates, one-third of the world's population cannot access essential medicines. It is obvious that the main purpose of the TRIPS agreement should be the protection of public interests, not the private interests of patent owners. Undoubtedly, soon, as a result of the further development of pharmaceutical research, new effective drugs will be created that are subject to strict rules regarding intellectual property rights: it is easy to predict that their high cost for patent protection will reduce their availability where they are most needed [36].

The profits received from the production of drugs by pharmaceutical companies are increasing significantly due to a permanent price increase. Pricing by drug companies is relatively unregulated, and they can often raise drug prices above the inflation rate. It allows pharmaceutical companies to increase their profits continuously, even if the demand for one or several drugs is low. Pharmaceutical companies set high prices for innovative medicines and argue the need to finance further research. If the pharmaceutical company does not get the maximum profit, it cannot fund new research. Accordingly, patients who need new drugs will suffer. This argument is based on the belief that it is unjustifiable to save the lives of the poor by providing them with life-saving medicines while at the same time denying new medicines to those who can afford to pay for them [37].

Pharmaceutical companies incorporate research and development (R&D), marketing fees, and post-approval clinical trials and transfer these costs to consumers in the price, justifying the extremely high initial investment in drug R&D [38, 39, 40].

However, today, there is no universally correct answer regarding the average cost of launching a new active pharmaceutical ingredient to the market [41]. Drug developers have long substantiated rising prices for new drugs as elevating R&D costs. However, the results of a study by British researchers argue that drug prices cannot be justified due to increasing R&D costs. Data from the world's 15 largest biopharmaceutical giants from open documents

between 1999 and 2018 reveal that the companies spent $2.2 trillion on sales, general and administrative (SG&A) expenses, compared to 1, 4 trillion dollars on R&D [42].

The manufacturer's selling price (MSP) is the initial price of the entire supply chain. MSP includes transport costs, local authorities' rates and taxes, overheads and other expenses. These processing fees are substantial; in some cases, they can exceed 100% of the drug's price based on production costs [40, 43, 44, 45, 46].

It is noted that prices of new drugs are often unfair because they exceed the affordability thresholds and price-quality ratio and are not justified by R&D costs. Such pricing is not necessary to bring desirable innovations to market. It simply reflects manufacturers' use of their market power to maximize profits. At the same time, their market power can cause an increase in prices for unpatented drugs [35].

It is possible that high prices for each new drug slow down the pace of innovation. It is less risky to make minor modifications to existing drugs ("me-too" drugs) and demonstrate incremental improvements in efficacy or safety than to invest in truly innovative drugs, where there is a greater chance of failure [47].

Creation of international research centers for the development of innovative medicines

A sharp deterioration of the man-made and ecological situation in the world, climate change, lack of food and water, and the growth of infectious diseases have a negative impact on the health of the population of all countries of the world. There can be no doubt about the need to increase the stability and efficiency of healthcare systems at the global level. One of the main directions of strengthening or improving the sustainability of healthcare systems is to reduce costs and ensure access to innovative medicines for insolvent patients with a wide range of life-threatening diseases.

Our analysis of the scientific literature concerning the pricing of innovative pharmaceuticals shows that a certain list of factors can impact it, but the differentiated pricing of the drug is mainly controlled by pharmaceutical companies and the supply chain.

The policy of compromise between socially acceptable reimbursement of R&D costs and simultaneous provision of access to a new drug for all patients should be based on:

- reducing R&D costs through digitization and application of artificial intelligence [48];

- patient orientation and concentration on healthcare systems in the field of R&D to generate more socially valuable innovations [49];

- value-based pricing (VBP) or pricing based on the assessment of the additional therapeutic value of a new drug, i.e., the price of a new drug should, on the one hand, reflect its benefits for patients, healthcare systems and, in some cases, society as a whole, and on the other hand, to reward successful innovations and create incentives for further R&D [49]. The added therapeutic value of a new drug should be a key factor in pricing and reimbursement decisions. No public resources should be wasted on drugs ("me-too" drugs) that offer little or no added value compared to already available treatments [50, 51]. New drugs with adequate additional therapeutic value provide a triple result: innovative treatment methods are available to patients, manufacturers enter the markets, and the state provides health care within limited budgets [52].

In our opinion, the main factor affecting the cost of medicines is the lack of WHO international research centers for developing new drugs with centralized funding and appropriate planning for high-level interdisciplinary fundamental and applied research based on the needs of the global healthcare system.

Taking into consideration the above-listed issues, an alternative to the current state of development of innovative medicines by individual, even if sufficiently numerous, pharmaceutical companies is to unite the efforts of scientists from all over the world through the creation of international scientific research centers for the development of innovative medicines (ISRCDIM) under the auspices of the WHO.

An example of such pooling of efforts by scientists from around the world is the international open-science project COVID Moonshot, launched in March 2020 by a group of scientists, pharmaceutical research groups and students to develop an oral antiviral drug without patent protection for the treatment of SARS-CoV-2. This drug will be able to be produced and sold by any drug manufacturer worldwide without the need for licensing and other legal barriers, thus reducing the cost of the drug [53].

The Innovative Medicines Initiative (IMI), a public-private partnership in life sciences, is another example of the joint efforts of scientists, pharmaceutical companies, and government regulators. It is a partnership between the European Union (represented by the European Commission) and the European pharmaceutical industry (represented by EFPIA, the European Federation of Pharmaceutical Industries and Associations). Public-private partnerships enable joint development and implementation of collaborative research initiatives by accelerating the development of patient access to innovative medicines, especially in regions with unmet medical or social needs. IMI's budget for the period 2014–2020 was EUR 3.3 billion. However, IMI practically does not provide for the development of drugs without patent protection and reducing their cost [54].

WHO is a specialized agency of the UN that deals with health issues on a global scale. The WHO includes 194 countries. All member countries of the organization pay annual contributions to the WHO, due to which it conducts its activities. Therefore, we propose to consider at the WHO level a proposal for creating International scientific research centers for the development of innovative medicines (ISRCDIM) under the auspices of the WHO with centralized funding and appropriate planning for conducting high-level interdisciplinary fundamental and applied research based on the needs of the global healthcare system.

In our opinion, the scope of the ISRCDIM should cover the entire list of diseases that require the development of innovative medicines. The WHO Coordination Centre should plan interdisciplinary fundamental and applied research on the development of innovative medicines based on the needs of the global healthcare system. Innovative medicines developed by the ISRCDIM will be available to any drug manufacturer worldwide without the need for licensing and other legal barriers, thus reducing the cost of the pharmaceutical without patent protection. The structure of the ISRCDIM we proposed is shown in Fig. 1.

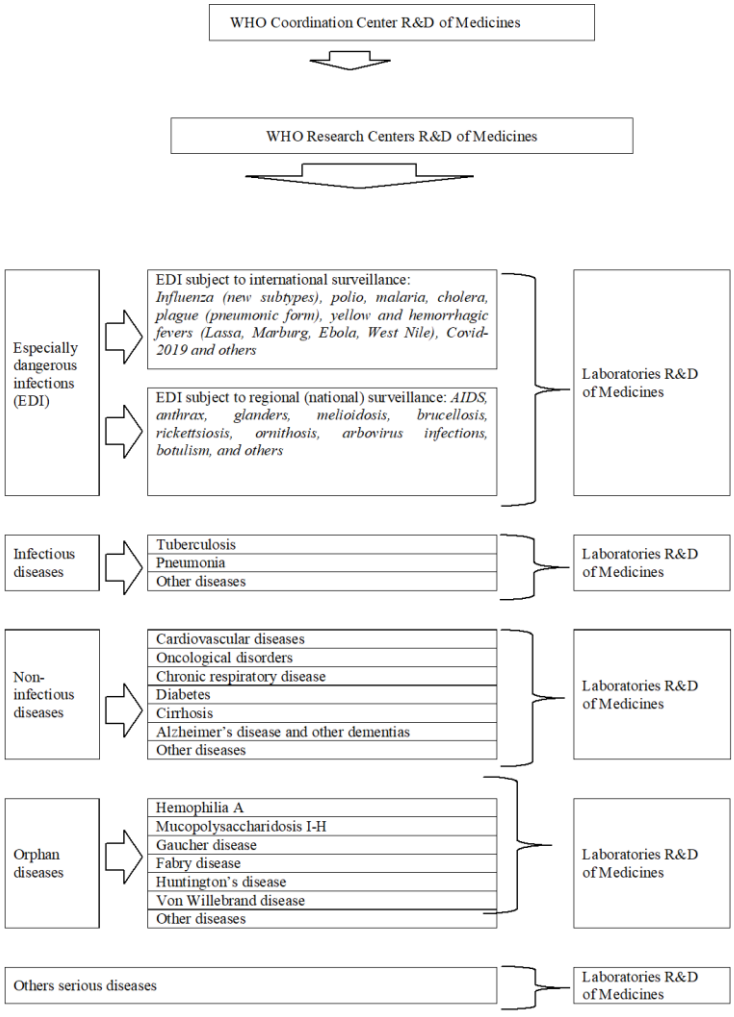

Figure 1. Structure of the International scientific research centers for the development of innovative medicines (ISRCDIM)

Chemical compounds synthesized in university laboratories can be used by ISRCDIM to develop innovative medicinal products. Worldwide, more than 15,000 chemical compounds are created daily, and they already have some degree of safety and activity data to rapidly screen them, mostly in university laboratories, for potential uses [55]. The Joint European Compound Library (JECL) is a screening collection that has been created from more than 321,000 compounds with a wide range of predicted biological activity and will be expanded to approximately 500,000 substances. JECL is available for free screening by European academic laboratories through the IMI European Lead Factory (ELF), which provides researchers with free access to a compound library and screening service to identify and evaluate chemical compounds to develop innovative medicines [56, 57]. In addition, the Molecular Libraries Probe Centers Network (MLPCN) unites critical aspects of the drug discovery process for the public, providing open access to comprehensive compound screening and advancing research through public data sharing through PubChem [58].

The creation of the WHO-led ISRCDIM is a further development of the strategy to improve global health security and ensure better health for all in a changing world. Reducing the cost of medicines will contribute to solving key challenges in the field of global health care and combating health threats in the era of pandemics.

In conclusions**:**To further develop the strategy to improve global health security and ensure better health for all in a changing world, reducing costs and guaranteeing access to innovative medicines for indigent patients with a wide range of life-threatening diseases is important.

As one of the main directions of strengthening and increasing the sustainability of the functioning of health care systems, it is proposed to create, under the auspices of the WHO, International scientific research centers for the development of innovative medicines without patent protection with centralized funding and appropriate planning for high-level interdisciplinary fundamental and applied research, based on the needs of the global health care system.

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