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ЯРОСЛАВСКОГО ГОСУДАРСТВЕННОГО МЕДИЦИНСКОГО УНИВЕРСИТЕТА
И РОССИЙСКОГО НАЦИОНАЛЬНОГО ИССЛЕДОВАТЕЛЬСКОГО МЕДИЦИНСКОГО
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DIGITALIZATION OF THE HEALTHCARE SYSTEM IN RUSSIA: UPCOMING TRENDS AND RISKS

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Digital technologies are currently entering a human life and changing it drastically. Education, economy and healthcare go hand in hand with digitalization. The author of the article stresses that digital technologies spawn fear and mistrust in many people. This applies especially to digitalization of the healthcare system. To overcome the mixed feelings arising in people, we need to understand what digitalization is and review its perspectives and threats. Thus, the purpose of this paper is to consider perspective trends of digitalization of the Russian healthcare system and reveal the existing risks. The author of the article analyzes the normative legal base devoted to the development of healthcare system in Russia, examines the available articles of scientists on the subject, and analyzes the interviews undertaken by IT company representatives, which assess the use of digital technologies in medicine. Based on the performed analysis, the author underlines the following upcoming trends in healthcare digitalization: rapid data generation and processing, remote medical aid, remote enrollment in a medical institution, and easy access to an electronic medical record. The author mentions the following risks: a set of personal data, which could be stolen from digital media, mistakes existing when telehealth technologies are used, and impossibility to get access to a high-speed Internet connection in some Russian regions. According to the author, coordinated work of all actors of healthcare digitalization will allow to keep to a minimum or completely avoid the mentioned risks.

Key words: digitalization, medicine, healthcare, digital medicine, risks, perspectives

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ЦИФРОВИЗАЦИЯ РОССИЙСКОЙ СИСТЕМЫ ЗДРАВООХРАНЕНИЯ: ПЕРСПЕКТИВНЫЕ НАПРАВЛЕНИЯ И РИСКИ

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В настоящее время цифровые технологии входят в жизнь человека и меняют ее кардинальным образом. Наверно, уже нельзя представить образование, экономику и сферу здравоохранения без использования цифры. Автор статьи обращает внимание на то, что цифровые технологии вызывают у многих людей страх и недоверие. Особенно это касается цифровизации системы здравоохранения. Чтобы побороть смешанные чувства у людей, необходимо разобраться в том, что из себя представляет цифровизация, какие перспективы несет и какие угрозы таит. В связи с этим цель данной работы — рассмотреть перспективные направления цифровизации российской системы здравоохранения и выявить существующие риски. Автор статьи анализирует нормативно-правовую базу, посвященную развитию системы здравоохранения в России, рассматривает уже существующие работы ученых по данной тематике, а также анализирует интервью представителей IT-компаний, посвященных оценке использования цифровых технологий в медицине. На основе проведенного анализа автор работы выделяет следующие перспективы цифровизации в сфере здравоохранения: быстрое получение и обработка данных о пациенте, дистанционное получение медицинской помощи, удаленная запись в медицинское учреждение, удобный доступ к электронной медицинской карте. Среди рисков автор отмечает: существование массива личных данных, который может быть похищен с цифровых носителей, ошибки, существующие при использовании телемедицинских технологий, невозможность доступа к высокоскоростному Интернету в некоторых регионах России. По мнению автора, при слаженной работе всех акторов процесса цифровизации здравоохранения можно минимизировать или полностью избежать указанные риски.

Ключевые слова: цифровизация, медицина, здравоохранение, цифровая медицина, риски, перспективы

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We are currently facing the fourth industrial revolution, which produces a fundamental impact on a human life by putting new technologies into practice. We are witnessing large-scale projects of innovative companies. They include 3D printing, robot-cars, artificial intelligence, automated cars, biotechnologies, etc., which became part of everyday life.

'The fourth industrial revolution is unique because of growing harmonization and integration of many various academic disciplines and discoveries, apart from rates of development and a wide coverage' [1]. Digital technologies are used in education, economy and healthcare. It should be noted that many cardiovascular and oncological diseases have a genetic component allowing doctors to decide on the methods of treatment. Use of information technologies to examine the genetic composition will make the healthcare system more personalized and effective. For instance, the IBM Watson system has been widely used at the present day. The system is capable of analyzing medical records, scanning and analyzing genetic data within several minutes and forming a customized program of treating oncological diseases [2]. When a person comes across something new and comprehended like digital technologies, he develops fear, mistrust and misunderstanding. To overcome the emotions arising during healthcare digitalization, we need to know what digitalization is, and what perspectives and threats it has. Thus, in this article, we aim to consider perspective trends of digitalization of the Russian healthcare system and detect the existing risks.

MATERIALS AND METHODS

Many modern researchers display their scientific interest to healthcare issues. The issues of health administration in the Russian Federation are considered in articles by K. A. Bogma, who mentions that 'in Russia, the effectiveness of healthcare system modernization control is based on the combination of assessments on the part of the society (social assessment) and on the part of healthcare system management entities (administrative self-assessment)' [3]. Some articles examine the quality of public health service. A. N. Zubets and A. V. Novikov mention that the quality of health service depends on the budgetary financing of the Russian healthcare system [4]. A. N. Zubets and A. V. Novikov state that the lack of unified approaches to the structure of medical aid quality currently influences the healthcare system marker [4]. When examining the Russian healthcare system, the researchers discuss the system development trends [5], one of which is represented by digitalization of this sphere [6]. In the researchers' articles devoted to medicine digitalization it is mentioned that the model of healthcare control is altered due to digital transformation [7]. Besides, certain digital technologies in medicine are analyzed. For instance, electronic medical records are viewed [8]. Scientists also examine the models of the unified medical information and analytical system [9]. Apart from the perspectives of healthcare digitalization, its issues are considered as well [10]. Though the examined issue is being actively discussed by scientists, we believe that the last events of coronavirus pandemics made implementation of digital technologies into healthcare more active. This enabled to look at the issue of perspectives and risks of healthcare digitalization.

In this article, perspectives and risks of healthcare system digitalization are found while analyzing the regulatory basis devoted to development of the Russian healthcare system, review of the current works on this topic, analysis of the interviews by company representatives aimed at assessment of digital technologies in medicine.

RESEARCH RESULTS

To understand the perspectives of Russian healthcare digitalization and the risks covered by it, we need to refer to such basic notions as 'digitalization' and 'healthcare'.

What is digitalization? It is defined in different ways. From a more general point of view, digitalization is a specified approach creating the digital environmental picture, though in the format suitable for computer treatment. Digitalization is a process of using the newest information technologies to improve or accelerate certain operations/actions [11]. If this or that activity wasn't possible, digitalization enables to perform any activity using innovative technologies. Digital technologies help exchange various data, in spite of temporal and spatial boundaries.

Based on the Decree signed by President of the Russian Federation in 2020 'On the National Purposes of Development of the Russian Federation up to 2030', we can see that one of national purposes of our country is digital transformation associated with achievement of 'digital maturity' of the key branches of economy and social sphere, including healthcare [12]. Healthcare is a state branch organizing and ensuring protection of public health. Healthcare is a set of political, economic, sanitary, ant epidemic and cultural measures aimed at the preservation and strengthening of physical and mental health of every human, support of healthy life and provision of medical aid in case of health worsening. The abovementioned Decree poses a goal to increase a share of electronically available essential services to 95%. The indices can be achieved through a high-speed Internet connection at medical institutions, and use of digital technologies during treatment and prevention of diseases in patients.

The Federal Project 'Creation of the Unified Digital Contour in Healthcare based on the Single State Health Information System' [13] is currently acting in the Russian Federation [13]. The project has come into effect in 2019. It is aimed to increase the effectiveness of health system functioning. Buildup of interaction mechanisms of medical organizations based on the unified state health system and implementation of digital technologies and platform decisions up to 2024 are allowed withing the project. They form a unified digital health contour. It is suggested that the system of electronic recipes and automatic management of preferential provision of medicines will be available in Russia by 2024. Medical appointment and periodic health examination booking, filing an application to the policy and medical documents can be done using My Health account at State Services Portal irrespective of the patient's region.

On the official website of the Ministry of Health of the Russian Federation we can see that the Order of the Ministry of Health of the Russian Federation 'On Approval of the Records System Arrangement Procedure in the Sphere of Health Concerning Maintenance of Medical Electronic Documentation' has come into action since January 2021 [14]. According to the Order, health workers will not make paper copies of source medical records any longer. Thus, they will pay more attention to patients. People will obtain data on the services provided in their electronic medical records at the State Services Portal.

Apart from making a unified digital contour in health, it is important to pay attention to the existing and currently used digital technologies to treat and prevent diseases. We won't use all the utilized technologies to treat diseases in this article, as it is impossible. We'll try to give examples of the technologies used during the pandemics. For instance, an electronic health care application Zdorovye.ru has been developed and remains in effect. The application is available on a mobile phone as well. The application can be used to make an appointment with the doctor, determine a number of a medical insurance policy, insurance company and medical institutions, have free tests for disease risk factors and get recommendations on doctor's appointment and delivery of medical tests.

The message stating that 'a human being is a coauthor of his/her medical experience' is relevant as never before. Medical companies must be partners of patients and use the experience of cooperation, whereas manufacturers of IT technologies need to find ways how to provide people with more freedom of cooperation and make everyone a coauthor of its digital experience.

The current unfavorable epidemiological situation in the world explores certain trends in the medical system market development. Maxim Kuznetsov, head of Philips in Russia, countries of the Central and Eastern Europe and CIS, said in his interview that the company was trying to respond to the situation and helped healthcare struggle with the disease. For instance, Philips equips CT scanners with software that makes the working process more effective (reducing the number of actions produced by the technician, decreasing the acquisition time, reducing the exposure dose). The company also makes ultrasound decisions with telehealth care functionality: Lumify, ultraportable ultrasound, enables to perform an ultrasound examination using compact sensors plugged into smartphones. The videos can be sent to ***colleagues*** in a real-time mode. The decision is useful when used in red zones of medical institutions.

Philips also creates decisions that improve the quality of medical aid provided to patients in hospitals: digital resuscitation is a system of taking clinical decisions (ICCA), which collects medical data of patients from bedside equipment of different manufacturers in a resuscitation ward and operation theater, and correlates them with prescriptions, laboratory findings, and keeps automatic recording.

In the interview by Oleg Abdiev, head of PM&HM, it is stated that many IT companies started to develop robot devices, which can perform certain work instead of people. For instance, Youibot robot can disinfect the surface with ultraviolet, measure temperature in those who visit hospitals and find out other primary signs of diseases. In the end of 2020, Sberbank launched a disinfection robot to struggle with viruses both in the air, and on the surfaces of the European Medical Center.

In the annual report of 2021 provided by the Government at the State Duma, Chairman of the Government of the Russian Federation Mikhail Mishustin stated that COVID-19 pandemics accelerated the launch of digital technologies in healthcare. For instance, remotely recorded electronic sick notes have been actively implemented, it became possible to register for vaccination through the Internet, and experience of using artificial technologies to get insights into medical scans was available.

DISCUSSION OF RESULTS

As it is seen from regulatory instruments and Internet sources analyzed by us, digitalization of health system in Russia has been on the rise (this was especially evident during the last year in the view of an unfavorable epidemiological situation in the world and in Russia). Digital technologies in health make medicine more affordable and qualitative for the Russian people. The technologies mentioned above enable fast information gaining and processing, saving doctor's time and giving more attention to patients.

Digital medical aid allows to provide 'medical aid to patients using digital medical services, including the ones at a distance, with application of telehealth technologies and distance exchange of clinical data between a patient and a medical specialist' [15].

IT technologies in the form of various applications make every person a coauthor of his/her digital medical experience. Everyone can use the devices for independent control of own health indicators. The device data can automatically transfer the results into users' accounts to ensure further working with data [15].

Digital technologies in health enable provision of distant medical aid and registration for a medical institution not waiting in line. Health digitalization is a convenient access to an electronic medical record, which can be shown to a necessary specialist for the purpose of consultation.

Apart from the denoted positive perspectives for health system digitalization in Russia, certain risks are available. The risks include slow Internet speed or its lack in the remote areas of the Russian Federation. Thus, digital health services can't be provided to the fullest extent to those living in the remote regions of the Russian Federation. Another problem is that a village lacks the necessary infrastructure to provide digital medical aid and competent personnel to deal with digital technologies. The digital health network has a large amount of patient's personal data, which can be stolen by malicious users. That's why cybersecurity must be strengthened. Moreover, a number of errors associated with the use of telehealth technologies while rendering medical aid can be increased. Telehealth development includes new requirements to provision of medical aid quality assessment by patients and even insurers.

CONCLUSIONS

The analyzed material has shown that use of digital technologies in the health system is the most important element for future successful development of the Russian healthcare. The use of digital technologies when struggling with a new coronavirus infection is currently confirmed. Digital instruments make medicine more comfortable, affordable and qualitative. When diagnosing diseases, digital technologies promote fast gaining and processing of patient data. The applied technologies make it possible to improve the procedures of monitoring and control of activity of medical organizations, expand the possibilities of remote patient management, and help create new support services of taking medical decisions.

Apart from positive effects of digitalization, the health system has certain threats. According to them, the existing body of digital data about patients can be stolen by malicious users. Errors associated with the use of telehealth technologies while rendering medical aid cannot be excluded. Those living in the remote regions of the Russian Federation can't be provided with digital health services to the full extent due to the lack of high-speed Internet. This violates rights of the citizens based on the principles of guaranteed health protection of all service recipients.

Thus, digitalization of health system in Russia is a huge step forward. However, actors implementing digitalization (state, medical institutions, IT companies and patients) must act as partners. This is how wise solutions will be found to avoid the risk for digitalization of the health system.

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DIGITAL HEALTH: CHALLENGES FACING MEDICAL ETHICS

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This article addresses problems stemming from the implementation and development of digital health in general and telehealth in particular. It focuses on ethical and legal issues associated with the progress of new information technologies and other technologies used in health care. The aim of the article was to define the role of ethical and legal norms in the implementation and development of telehealth. The analysis of the currently effective legislation, its application and lacunae in the regulation of new forms of social relations suggests the need to expedite development of legal and ethical guidelines for the implementation of new technologies in health care. Higher standards of data security for vulnerable groups of patients should be established in the legislation and ethical guidelines.

Keywords: telehealth, information technologies, technologies in health care, digital health, ethics, law, legislation

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ЦИФРОВИЗАЦИЯ МЕДИЦИНСКИХ УСЛУГ: ВЫЗОВЫ ДЛЯ МЕДИЦИНСКОЙ ЭТИКИ

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В статье рассматриваются проблемы, возникающие в связи с попытками внедрения и развития телемедицинских технологий, шире — цифровизации процесса оказания медицинских услуг. Основное внимание уделяется этическим и этико-правовым проблемам развития новых информационных и иных технологий в отрасли здравоохранения. Цель: определение роли этических и правовых норм на этапе внедрения и развития телемедицинских технологий в отрасли. По результатам анализа действующего законодательства и практики его применения, лакун в регулировании новых групп общественных отношений, формулируется вывод о необходимости ускоренного развития правового регулирования и этического обеспечения технологического развития здравоохранения. В силу дифференциации правового статуса отдельных групп пациентов (в первую очередь, исходя из их потенциальной уязвимости), специфики оказания медицинской помощи (по различным критериям) необходимо вырабатывать и предлагать более высокие стандарты защиты информации на законодательном и этическом уровнях.

Ключевые слова: телемедицина, информационные и иные технологии в здравоохранении, цифровизация медицинских услуг, этика, право, законодательство

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Information technologies are a group of technologies harnessed to solve a broad range of therapeutic, diagnostic, rehabilitation and management challenges in public health, both locally and nationwide. To patients, information technologies that are directly incorporated into the therapeutic, diagnostic, rehabilitation or other processes forming the substance of medical care or those bearing a close relation to medical services (electronic workflow, including electronic health records and electronic prescribing, medical devices or other health care products) matter the most.

Information technologies were introduced into clinical practice in the second half of the 20th century. At that time, their use was limited to space medicine, air ambulance, medical consultations for patients and advisory services for health care practitioners residing or working in remote regions. Although the experience was overall positive, the spread of information technologies in the medical field was obstructed by the underdeveloped and expensive telecommunication infrastructure and equipment, inadequate quality of information services and medical care (signal quality was low, affected by distortion, etc.), organizational, financial, administrative, legal and other barriers.

Over time, the majority of constraints holding back the implementation of digital health were overcome through the advancements of information- and telecommunication-enabled services and active digitalization of socioeconomic activities. Those that remain until today are mostly organizational. Besides, there are some legal, ethical, moral and other issues associated with the current social reality, familial, cultural, and religious traditions.

The Federal Law No.242 (dated July 29, 2017) on the Amendments to Some Legislative Acts of the Russian Federation Regulating the Use of Information Technologies in Health Care made some amendments to the Federal Law No.323 (dated November 21, 2011) on the Fundamental Principles of Public Health Protection in the Russian Federation in the attempt to address statutory obstacles to the development of new technologies in health care. For example, the term *telehealth* was introduced and some algorithms of delivering medical care by means of telehealth technologies were legally established. However, this was not enough to solve even the basic legal issues related to the use of information technologies in health care. Besides, some collateral ethical and ethico-legal issues associated with the emergence of new and supplantation of old forms of relationships were overlooked.

The Federal Law No.323 requires health care providers to comply with the norms of ethics while delivering any type of medical care (medical service) to the patient, including care that involves the use of new technologies. Apart from delivering an effective, safe and adequate treatment, it is important to

safeguard a patient's physical and mental health [1] without violating their legally protected interests. Otherwise, despite the seemingly good quality of medical care, an ethical dilemma or an ethico-legal conflict may arise that will almost inevitably have ramifications for the involved health care provider [2]. The risks increase if a combination of technologies is used. For example, genetic testing generates important data, which, apart from its clinical significance for the case, has prognostic significance for the patient, indicating health risks, predisposition to certain diseases, etc. This data can be digitized, stored and used not only for medical purposes, including implementation of a personalized preventive health care strategy, a personalized screening program or a checkup schedule, but also for non-medical purposes by other parties (law enforcement agencies, banks, insurance companies, employers). In other words, ethical risks associated with the use of new technologies in health care are increasing, raising the need to identify ethical challenges associated with digital health and find adequate solutions.

The comprehensive analysis of such risks, the associated problems and misconceptions are beyond the scope of this publication. This article seeks to outline the key problematic areas in health care digitalization, looking through the lens of the existing paradigm of bioethics and the principles of law, which are becoming increasingly important not only for the theoretical framework but also for medical practice and the application of law in a rule-of-law-based state.

The principle of non-maleficence is pivotal to bioethics and law. For years, it has been the basis of doctor-patient relationships. Today, there is a possibility of its exclusion from the normative principles and other legal norms established by the Federal Law No.323, such as the primacy of the patient's interests, respect for personal freedoms and medical liability.

The principle of personal data and privacy protection in information systems established by the Federal Law No.149 on Information, Information Technologies and Protection of Information (dated July 27, 2006) is especially interesting for our analysis.

The general rule is that the use of information technologies should not threaten a person's life or health. However, due to poor organization of medical care, wrong diagnostic or therapeutic decisions and the breach of medical ethics, the patient may sustain physical, emotional or pecuniary damage. Besides, negligence or noncompliance with the guidelines for handling privileged and confidential data may also result in, most commonly, emotional damage to the patient. In some cases, information about the patient's personality and other characteristics can be used for nonmedical purposes or without authorization. The threats of biohacking and biocrime, which were impossible to imagine just a few decades ago, are now a subject of active discussion [3]. Consequently, patients may lose their trust in doctors, medical organizations, public healthcare systems and the state in general.

Sometimes, the patient is not ready to comprehend information about their condition, does not know what to do with it or worries about its disclosure to third parties or potential leaks from the databases (registries, medical records, etc.) where such data is submitted as required by law or in accordance with the rules of the medical organization the patient has signed an agreement with. In light of this, the usual doctor-patient communication practices and the use of information resources should be rethought to reduce the risk of conflict. It is important that the patient clearly understand the significance of information about their health for themselves and for the entire medical community today and in the future (if such information is subject to long-term storage). Besides, the patient must be informed in plain words about the data security measures, tools, mechanisms and warranties. The healthcare provider may find this procedure time-consuming; however, it is a necessary and even mandatory component of digital health. Today, informed consent forms that inform the patient about the procedures of collecting, storing, using, or sharing patient data by medical personnel as part of their work are gaining importance.

Ethics is becoming a ubiquitous trend in digitalized sectors, and the dynamically developing medical service market abounding with new technologies is not an exception. Currently, the Russian information legislation does not contain requirements for ethical collection and processing of patient data, including health-related information; however, increasing attention is being paid to this problem in the information law doctrine [4].

Certainly, it is impossible to build and maintain trust with patients without adhering to the ethico-legal medical privacy principle. In the era of personalized preventive medicine and the expanding diversity of biomedical trials (clinical trials of drugs, medical products, clinical testing, etc.), the role of ethical and legal principles cannot be underestimated. Legal practitioners are witnessing a rise in litigations stemming from patient data breaches. Despite 25 years of history of medical privacy in contemporary Russia, amendments are still being made to health legislation, expanding the range of legal grounds for disclosing confidential information and the scope of persons and entities this information can be disclosed to (family members, in-laws, heirs, law enforcement agencies, etc).

As the legislation on information, personal data, medical and other privacy is transforming at a fast pace, it is becoming increasingly important to inform the patient about the future of their personal health-related data in an ethical way.

The beneficence principle (do no harm, do good) is very difficult to translate into practice. The evaluation of new biological, medical, information and other technologies is now almost exclusively performed by scientists and experts, as opposed to clinical practitioners. Chapter 37 of the Federal Law No.323 maintains that medical care must be delivered in accordance with the established procedures, clinical recommendations and standards of medical care. Not much is left at the clinician's discretion. The choice of medications approved for use in a given therapeutic situation is limited, which may result in a so-called iatrogenic injury. The clinician should have more freedom in decision making, finding guidance in the beneficence principle and the knowledge of the patient's age, sex, genetic, psychophysiological or other characteristics.

For instance, drugs, medical devices, other medical products or treatments prescribed to a professional athlete should not contain ingredients and/or be based on the methods included in the list of substances and methods prohibited in sport. Russian athletes must abide by the Russian Antidoping Rules[1], otherwise they will be sanctioned, possibly with disqualification. The Order No. 927 of the Russian Ministry of Sport dated December 16, 2020 on the Approval of the List of Substances and/or Methods Prohibited in Sport contains an extensive list of substances and methods that cannot be used by athletes during and/or between competitions. A lot of medications routinely used in clinical practice cannot be prescribed to athletes or the athlete should apply for a therapeutic use exemption prior to taking such medications. In some cases, it may be reasonable to prescribe a medication that can produce the desired effect but is not on the prohibited list. So, treating a professional athlete poses a certain challenge to the clinician. Ignoring the legal status of the athlete may result in disqualification, pecuniary or moral damage.

Therefore, development and implementation of clinical guidelines should account for both typical and atypical yet not extremely rare clinical cases and the legal status of different patient categories (groups of populations).

[1] Approved by the Russian Ministry of Sport (December 11, 2020)

Genetic research generates new robust data that will significantly affect clinical decision making. Patient data accumulated in special databases (electronic health records, etc.) provides the clinician with a wealth of information about the patient, facilitating a personalized approach to therapy and prophylaxis and allowing the patient to be in control of their life trajectory. However, the benefits of health care technologies should indeed outweigh the potential risks. In our opinion, risk reduction is one of the primary goals of modern medical ethics that extends beyond the rigid organizational and legal framework of contemporary medicine.

Private autonomy is one of the fundamental ethical and legal principles actively developing in the Western world. In Russia, it is articulated in the Basic Principles of Legislation on Health Protection (Order 5487-I dated July 22, 1993). Today, it is derived from Chapters 5, 6 and some other chapters of the Federal Law No. 323. At the same time, advances in health care, the growing controlling potential of medicine, and the expansion of boundaries of the pursued biopolicy (new technologies open up new possibilities and help in solving large-scale tasks) have exacerbated a problem of balance between private, public and the state's interests.

Chapter 27 of the Federal Law No.323 specifies the duties of Russian citizens with regard to health care. At first, such duties were perceived as non-specific, not associated with any legal sanctions. However, the COVID-19 pandemic has sparked heated debate about the responsibilities of patients (citizens) to self-isolate and get vaccinated. Apart from the ethical and legal issues associated with the doctor-patient relationship, a number of problems surrounding the relationship between the doctor and the medical community have come to light. Owing to digitalization, we now have access to a tremendous variety of information sources encouraging us to make "the right choice" or "the right decision" and engage in "the best possible practice". Patients are becoming more aware but there are risks: loss of trust in doctors, refusal from therapy or engagement in self-treatment. The patient can share information about their health, results of laboratory and instrumental tests in real time with other specialists not involved in the patient's case, which may negatively affect the diagnostic and therapeutic processes because it is the treating physician who knows their patients best. There is a reason why Chapter 70 of the Federal Law No.323 has a provision that it is the treating physician who timely orders all necessary diagnostic procedures, prescribes therapy for the patient and provides comprehensive information about their health. Consultations with other specialists should be implemented after a discussion with the treating physician. Otherwise, the patient may follow different recommendations obtained from different sources (consultations with other trustworthy specialists, chats, web-sites containing information on medical products provided by their manufacturers). As a result, the patient may ignore recommendations of the treating physician and the desired outcome may not be achieved.

It has always been an ethical requirement that the doctor should perceive health care as a duty, not a business, refrain from advertising themselves, be accountable for their medical advice to patients and colleagues. The doctor should refrain from activities that can disrupt the authority of and respect for the medical profession.

Any deviation from the ethical norms should be decisively dealt with by the medical community and its institutions of self-regulation. In Russia, medical ethics, bioethics and professional ethics have not been fully institutionalized yet. There are no well-established mechanisms for managing ethical conflicts and holding medical professionals accountable for a breach of ethics. It might be necessary to establish sanctions in federal laws to prevent ethical breaches associated with health care digitalization.

The relatively recent ethico-legal vulnerability principle became widely recognized due to the popularity of some types of medical services (medical care) for certain groups of patients. Digitalization of health care and advances in information and other technologies used in medicine increase vulnerability risks for some groups of patients.

Access to personal data or information about the psychophysiological and genetic characteristics of the patient by the medical community or other parties may result in the discrimination of the patient (in health care, education, employment, sports and other fields). Some data can be "dormant" for decades but comes to light when a person enters into a certain relationship (seeks employment or is employed by the government, undergoes medical assessment, crosses the state border, applies for a resident permit, etc). Currently, biological samples, materials, information about individuals are being actively collected. There is no ironclad guarantee that such data will be used strictly for the purposes specified by law or the corresponding agreement. Improving such guarantees is a crucial challenge facing society and the state. Its resolution largely depends on the development of health and information legislation and ethics.

Higher standards of data security for vulnerable groups of patients should be established in federal laws and ethical guidelines.

Technological progress is accompanied by the transformation of medical ethics. The long-standing ethical principles used as a guidance by the medical community are subjected to the pressure of the new technological reality and legislation, which drives their development and the development of their regulatory potential.

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POTENTIAL OF DIGITAL TECHNOLOGIES SUPPORTING THE PRINCIPLE OF PERSONALIZED MEDICAL AID IN CARDIOVASCULAR DISEASES

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A study was undertaken to estimate the potential of digital technologies to support the principle of personalized medical aid in cardiovascular diseases. The study was done on the basis of the Kostroma region healthcare system. Information and methodological basis of the study comprised the polled data of 1400 patients aged 18–80 years old. A mixture of study methods was used: literature analysis, systemic and logical analysis, sociological (monitoring, expert assessment, content analysis, questioning, comparative analysis), statistical (grouping, ranking, correlation), pharmacoeconomic (cost-effectiveness, ABC/VEN-DDD-analysis, cost minimization) analysis, and organizational and functional modeling.

Key words: digital technologies, personalized aid, aid organization

Author contributions: Gruzdeva AA, Khokhlov AL, Ilyin MV — trial concept and design; Gruzdeva AA, Ilyin MV, Mushnikov DL– data capture and processing, Gruzdeva AA, Ilyin MV, Mushnikov DL — analysis and interpretation of results; Gruzdeva AA, Mushnikov DL — writing an article; Khokhlov AL, Ilyin MV — preparation and approval of a manuscript for publication.

Compliance with ethical standards: the study was approved by the Ethical Committee of the Yaroslavl State Medical University of the Ministry of Health of the Russian Federation (protocol No. 21 as of February 08, 2018). The informed voluntary consent was obtained for every participant. Adults were interviewed on a voluntary basis using questionnaires. The conducted trial doesn't expose participants to danger and corresponds to the requirements of biomedical ethics.

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ВОЗМОЖНОСТИ ЦИФРОВЫХ ТЕХНОЛОГИЙ В ОБЕСПЕЧЕНИИ ПРИНЦИПА ПЕРСОНАЛИЗАЦИИ МЕДИЦИНСКОЙ ПОМОЩИ КАРДИОЛОГИЧЕСКОГО ПРОФИЛЯ

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Проведено исследование с целью оценки возможностей использования цифровых технологий в обеспечении принципа персонализации медицинской помощи кардиологического профиля. Исследование проведено на базе системы здравоохранения Костромской области. Информационно-методическую основу исследования составили данные опроса 1400 пациентов в возрасте от 18 до 80 лет. Использовалась совокупность методов исследования: метод анализа литературы, системного и логического анализа, социологические (мониторинговый, экспертных оценок, контент-анализа, анкетирование, сравнительного анализа), статистические (группировка, ранжирование, корреляционный), фармакоэкономические («затраты — эффективность», ABC/VEN-DDD-анализа, минимизации затрат), организационно-функционального моделирования.

Ключевые слова: цифровые технологии, персонализированная помощь, организация помощи

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According to Presidential Decree of the Russian Federation as of December 1, 2016 No. 642 'On the Strategy of Science and Technology Development of the Russian Federation', 'implementation of personalized medicine and high-technology healthcare' refers to the priority areas of science and technology development of the country for the next 10–15 years. In the light of global trends, the Russian healthcare has entered the path of digitalization [1, 2, 3]. Being an important factor of successful development, digital medicine enables continuous control and monitoring of medical aid quality [4, 5], improves organizational processes based on the principles of lean management [6, 7], upgrades statistical data processing and exchange [8, 9], expands the processes of innovation implementation [10], and makes business activity of medical organizations more effective [11].

The role of information technology implementation in clinical practice quality improvement based on the 'smart hospital model' is significant [12]. Digitalization is especially important for implementation of the principle of personalized medicine,

as accounting of many factors that can influence a treatment outcome for a certain patient is rather a complex task. It can't be solved without digital support [13, 14]. This is about genetic, medical and social factors, factors of rational pharmacotherapy individual selection considering the drug effectiveness level of evidence [15, 16]. The issues are especially relevant as far as the cardiological aid goes, as it is required mainly by those of advanced and old age with a large factor loading of medical and social and medical and biological risk of cardiovascular complications [17]. Thus, digitalization of the cardiological aid system would allow to increase its productivity correcting the controlled factors. Analysis of these data has shown that in scientific publications, no attention was given to the issues of cardiological aid digitalization from the perspective of the personalized approach, making it relevant and necessary to study these aspects from a scientific point view.

Purpose of the study: to determine the potential of using digital technologies to support the principle of cardiological medical aid personalization.

METHODOLOGY

The study was carried out on the healthcare basis of the Kostroma region.

The information and methodological basis of the study comprised the interviews of 1,400 patients aged 18–80 years with the established diagnoses of arterial hypertension, coronary heart disease (exertional angina, acute coronary syndrome (acute myocardial infarction, instable angina) (based on the classification of WHO/Medical Society for Arterial Hypertension, 2004), who requested medical assistance in medical organizations of Kostroma and Kostroma region. The study included those patients who signed an informed consent form. The retrospective group (cases of aid provision) had 1,400 patients, the prospective group included 200 patients and 21 experts. The decisions made by the Expert Committee concerning 386 lethal cases and 71 complaints were analyzed as well. A set of research methods was used. They included methods of literature analysis, systemic and logical analysis, monitoring, expert assessment, content analysis, questioning, comparative analysis, statistical (grouping, ranking, correlation), pharmacoeconomic (cost effectiveness, ABC/VEN-DDD-analysis, cost minimization), organizational and functional modeling. The results of the Cardiological Medical Aid Effectiveness Factor Control automated monitoring were also used.

The study was conducted within the program of scientific research of the Yaroslavl State Medical University of the Ministry of Health of the Russian Federation, whereas the study protocol and design were approved by the Ethics Committee (protocol No. 21 as of February 08, 2018).

The data were processed using Statistica 11.0 software (StatSoft, Inc.). Qualitative attributes were tested to check whether they were normally distributed according to such known criteria as the Kolmogorov-Smirnov test, Shapiro-Wilk test, grouping of databases, and calculation of extensive values. Statistical significance of values in the trial arms was determined using the Student's t-test ($p < 0.05$ significance). Spearman's correlation analysis was used to study the interrelation between two attributes. The critical value for statistical significance is 5%.

RESULTS

The Cardiological Medical Aid Effectiveness Factor Control automated platform is a part of the organizational and functional cardiovascular aid digitalization in the Kostroma region (A. A. Gruzdeva et al. Management of cardiological medical aid effectiveness factors. Application software. Patent of Russia No. 2018612060, 2018. Bulletin No. 2). The method of automated monitoring is 1C: Accounting platform-based (i. e. can be accessed by any medical organization (MO)). An automated database is built based on the interviews of patients, registration of data associated with material-and-technical and carrier-oriented readiness of a medical organization for provision of aid and expert assessment of the aid provision technology. The base is the foundation for building predictive graphic models and finding the factors that need to be corrected. The base is built by medical workers in technical support of automated control system specialists (patient's data are entered by a doctor and a nurse, material and technical base data are entered by the chief nurse of the department/hospital, expert assessment results are introduced by a MO expert (head of the department)).

The medical and organizational structure of management of effectiveness limiting risks and quality of medical aid includes as follows: f) an automated platform necessary to build a database about factor dependence of aid effectiveness according to three blocks (medical and social, technological and infrastructure); b) algorithms and check lists correcting unfavorable factors; c) a model of expert activity concerning the cases of cardiological aid provision. It includes 10 options of building expert conclusions and determining pharmaco-economical therapy effectiveness.

The clinical and organizational approach of personalized continuous management of risks decreasing the effectiveness of pharmacotherapy and quality of aid for people with cardiovascular diseases is as follows: the leading factors determining the effectiveness of pharmacotherapy, quality and effectiveness of medical aid are provided; parameters and criteria of their estimation, automated monitoring technology are developed; an automated platform is created to build models of aid provision considering institutional, technological, medical and biological conditions and limitations at the individual, medical and organizational levels (at the level of a medical organization); algorithms and recommendations associated with correction and modification of quality reducing risks and cardiological aid effectiveness are established; the criteria assessing the effectiveness of risk management are suggested. The use of the automated monitoring method ensures continuous management; potential of building automated models of possible risk factorial dependence for every patient allows to implement not only a population, but also a personalized approach (for every case of patient management and aid provision). This is important when tasks of expert activity are implemented and reasons for unfavorable outcomes are found out.

Let's consider a digital approach to the management of cardiological aid effectiveness factor control based on situational factors. The situational factors include unfavorable time (night) and day of week (weekends, holidays) to provide aid; high workload of doctors, including serious patients; not typical pathology in a patient; health of the doctor who provides aid; intervention of third parties while rendering aid. The information platform enables analysis of factorial data, determines their frequency and specter of required administrative effects. Basic measures of management include organization of control checks and video-control; photography and work schedule recording; assignment of competent persons at departments during holidays; development of personnel duty cards during a shift; sorting patients by the aid provision priority; teaching medical personnel about the rules of interaction with patients' relatives; creating an individual surveillance plan for patients with unique and not typical signs of diseases, etc.

In our article, we didn't aim at introducing changes into the available structure of medical aid quality control and criteria

of its estimation. It is known that they are determined by the orders of the Ministry of Health of the Russian Federation and Federal Compulsory Medical Insurance Fund. Our work is based on the preventive strategy of aid quality support and effectiveness. We tried to determine which factors create conditions for aid unfavorable outcomes and prevent from complete implementation of medical aid quality potential (optimal level). It is important because not everything depends on medical workers; much is dependent on those factors that can't be changed or can be changed in the short-term (that takes time). This is important for timely determination and correction of deviations. We have found out that technically, it can be perfect as far as compliance with maintenance of orders, clinical protocols, standards go, though the outcome can be unfavorable. Working with digitalization of cardiological aid, we suggest a universal methodology instrument. The instrument can be used by doctors who could be aware of the factors influencing the outcome of their activity; by heads of medical organizations who could collect data about the factors, which have to be affected; by experts of medical aid quality who could obtain data about the reasons influencing the decrease in quality and unfavorable outcome.

The frequency of factors in two comparison groups was analyzed using the Cardiological Medical Aid Effectiveness Factor Control automated platform (A. A. Gruzdeva et al. Management of cardiological medical aid effectiveness factors. Application software. Patent of Russia No. 2018612060, 2018. Bulletin No. 2): in the group of patients with a positive (optimal) outcome (convalescence, condition improvement, reduced number of exacerbations) ('a group with a positive outcome') (GPO) (304 cases) and in the group of treatment with a non-optimal outcome (deterioration in condition, frequent cases of exacerbation, readmission, disability, death) ('a group with a negative outcome') (GNO) (96 cases). The data form the basis for building a model of factorial dependence of quality reduction risk implementation and effectiveness of cardiological aid in regions.

CONCLUSION

The data obtained during a trial allowed to offer the concept of the personalized strategy of risk management in cardiological patients. It is novel because of the individual approach assessing the influence of different factors on every patient and solving the set tasks considering distance barriers. Increased quality of cardiological aid in a region and improvement of demographic characteristics are achieved by improvement of health in every patient. Approval of this model using mathematical and statistical methods not considered in clinical recommendations enabled to decrease a number of unfavorable outcomes by a factor of 1.7 while rendering aid to cardiological patients.

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DIGITALIZATION OF HEALTHCARE AND ETHICAL CHALLENGES OF COVID-19 PANDEMIC

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By the end of the 20th century, medicine was the first to fly into the digital world. New practices of medical data collection and storage appeared, the interrelation between a patient and all subjects of medical activity altered, automatization and robotization transformed many medical technologies, and legislation underwent significant changes. It resulted in new possibilities of rendering medical aid and occurring risks. The article deals with principal notions associated with digital medicine and determines its pressing issues. The basic reasons for updating digital transformation of medicine and its leading trends are reviewed including for the purpose of emergency situations such as COVID-19 pandemics. Closer attention is paid to the ethical issues that arise when digital technologies have been implemented and applied in the healthcare system. They include voluntary informed consent, confidentiality, ethics of digital control, safety, equality, data accessibility and protection. An important role of legal regulation and observance of bioethical principles is stressed.

Keywords: digital economy, digital transformation of medicine, digital healthcare, COVID-19 pandemic, risks, ethical issues, bioethics, law

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ЦИФРОВИЗАЦИЯ МЕДИЦИНЫ И ЭТИЧЕСКИЕ ПРОБЛЕМЫ В УСЛОВИЯХ ПАНДЕМИИ COVID-19

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Медицина одной из первых с конца 20 века стремительно вошла в цифровой мир. Появились новые практики сбора и хранения медицинской информации, изменились взаимоотношения пациента и всех субъектов медицинской деятельности, автоматизация и роботизация трансформировали многие медицинские технологии, серьёзно менялось законодательство. Как следствие, появились новые возможности, как оказания медицинской помощи, так и возникающие риски. В статье рассматриваются основные понятия, связанные с цифровой медициной и определяются её актуальные проблемы. Анализируются основные причины актуализации цифровой трансформации медицины и её основные направления, в том числе в контексте чрезвычайных ситуаций на примере пандемии COVID-19. Особое внимание уделяется этическим вопросам, возникающим в ходе внедрения и практики применения цифровых технологий в системе здравоохранения, таким как добровольное информированное согласие, конфиденциальность, этичность цифрового контроля, безопасность, равенство, доступность и защита данных, подчеркивается важная роль правового регулирования и соблюдения биоэтических принципов.

Ключевые слова: цифровая экономика, цифровая трансформация медицины, цифровое здравоохранение, пандемия COVID-19, риски, этические проблемы, биоэтика, право

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Russia is exposed to the challenges of accelerating globalization and the technoeconomic paradigm shift. The 21st century is emerging as an age of high technology and high standards of living. At the same time, public health protection and measures required for its implementation are now high on the agenda because of the global threat posed by the COVID-19 pandemic.

A global economic, legal and information system is being built strategically. Global competition is increasing not only in the traditional markets of goods, capital, technologies and labor but also between the systems of public administration, innovation support and development of human potential. Among the major global challenges of today are:

- a global shift to the new technoeconomic paradigm (Industry 4.0) and digital economy.
- accelerating technological transformation of the global economy. Russia is facing competition not only from the world leaders in innovation but also from developing countries and post-Soviet states.
- global intensification of competition for factors that determine the competitive ability of innovative systems, including highly skilled workforce, “smart” money (investments that bring innovative expertise, technologies and competencies into a project), education, and the sharp rise in their mobility.
- global challenges facing mankind: climate change, population ageing, public health issues, food safety.

All of these problems raise the need for new public health concepts.

In order to be prepared for digital economy and Industry 4.0 and to update a healthcare system accordingly, one needs to analyze these terms in form and substance.

In 1951, the British food manufacturing and catering company J. Lyons & Co spearheaded the use of computers in business [1]. The Lyons Electronic Office (LEO) occupied a large room but was relatively primitive: today, a small hearing aid has more processing power and memory than LEO. However, LEO was able to

calculate the output of the company's bakeries and the cost of the sold products faster than any human. Later, modernized versions of LEO were commissioned and used by Ford Motor Co, Kodak and other industrial giants. This was the first wave of the digital revolution that replaced human teams with systems capable of first simple and later more complex computations.

The second stage of the digital revolution is associated with the development of the new Industry 4.0 paradigm. This was clearly articulated at the 2016 World Economic Forum in Davos by its Executive Chairman Klaus Schwab in his report on the new industrial revolution [2]. Schwab described the Fourth Industrial Revolution as a synergy of technologies that blur the lines between physical, digital and biological dimensions. Advances in digital technologies, genetics, artificial intelligence, robotics, nanotechnologies, 3D printing, and biotechnologies are mutually amplifying. Special attention is being paid to «end-to-end» digital technologies that serve as a basis for technological convergence. According to Schwab, digitalization of all sectors of life and the advent of the second digital revolution have paved the way for a revolution of unprecedented scope. Smart systems (homes, factories, farms, networks, cities) will change the way we can tackle a wide range of problems, from managing a chain of supplies to dealing with climate change. The more profound is the change, the greatest opportunities it opens; the main challenges that require preventive adaptation measures from corporations, governments and individuals are associated with consumption, production and employment. Parallel to the technological revolution are other mutually reinforcing, multidirectional, interacting socioeconomic, geopolitical and demographic drivers of change.

In July 2017, the Committee for Strategic Development and Priority Projects approved the *Digital Economy of the Russian Federation* state program. President of Russia, Vladimir Putin, emphasized that digital economy would create novel models of business, trade, logistics and production, change the formats of education, public healthcare, management, and communication between people and thus set a new paradigm of development for the state, economy and society. Seeking to speed up the introduction of digital technologies into economy and social sectors and guided by the Executive Order 204 on the *National Development Goals and Strategic Objectives of the Russian Federation through 2024*, dated May 7, 2018, and Order 474 on the *National Development Goals of the Russian Federation through 2030*, dated July 21, 2020, the Russian Government formulated a national program *Digital Economy of the Russian Federation*, which was approved by the Presidential Council for Strategic Development and National Projects on June 4, 2019 (Protocol No.7) [3].

What is digital economy?

In 1995, the American computer scientist Nicholas Negroponte (Massachusetts Institute of Technology) coined the term "digital economy" to describe a shift from atoms to bits, opposing virtual reality (weightless bits) to actual raw materials that have weight and need to be transported [4]. Today, digital economy is understood as an element of economic relations mediated by the Internet, mobile networks and information and communication technologies (ICT). Its development is essential for the establishment of the cluster of basic technologies that form the emerging sixth technological paradigm. This cluster will transform almost every sphere of human activity, be it economic, social, politic, cultural, etc. The new technological paradigm is associated with the Fourth industrial revolution. In the first decade of its existence, which began in 1994, digital economy was largely based on e-commerce; now it spans the IT and financial sectors, education, public healthcare, state services, and so on.

The 2016 *Digital dividends* report issued by the World Bank described the global state of digital economy. Since then, the term "digital economy" has been eagerly used by politicians, entrepreneurs and journalists all over the world. However, it has not been clearly defined yet, even by the World Bank [5].

According to the broad definition proposed by Ivanov V, Doctor of Economic Sciences and the corresponding member of the Russian Academy of Sciences, digital economy is a virtual environment supplementing reality. Prof. Meshcheryakov R (RAS) suggests there are two approaches to defining digital economy. According to the first (classical) approach, digital economy is an economy based on digital technologies and should be viewed as comprising exclusively the field of electronic products and services, such as telemedicine, distance learning and selling media content (films, TV programs, books, etc.) In the second approach, the definition is broadened to include production aided by digital technologies. Some experts think that this definition should also span the supply chains of products and services associated with the use of digital technologies, such as the Internet of things, Industry 4.0, smart factories, G5 mobile networks, engineering services, prototyping, etc. Professor Engovatova A. defines digital economy as an economy based on the novel methods of data generation, processing, storage and transmission, as well as on digital computer technologies [6].

The *Digital economy in the Russian Federation* state program defines digital economy as a management model involving the maximum use of computer technologies that can take the life of a person, relations of production, the structure of economy, and education to a totally new level [7].

In the modern world, where information is a fundamental resource, the amount of data generated every day is increasing at an exponential rate. This information revolution is being driven by the strategy of development centered around the individual and their changing needs.

Indeed, the strategy of digital economy in Russia is applied to public healthcare, too. New terms are emerging in the literature, including *digital healthcare, a digital platform, digital medical care, digital medical services, a digital medicine ecosystem,* and *digital medical services infrastructure* [8].

According to the experts of the Medtech portal [9], digital medicine contains the following elements:

- electronic document flow between the doctor, patient and medical organization;
- integration of digital diagnostic tools;
- a patient flow management system;
- an emergency care management system;
- use of telemedicine technologies;
- digital platforms for virtual health consultations between the doctor and the patient;
- remote patient monitoring using personal medical devices;
- use of mathematical methods for data processing, including AI and methods for processing large data arrays;
- development of information systems for medical diagnostics based on AI and large data arrays;
- development of decision support systems as auxiliary modules of medical information systems in the Internet of things, etc.

According to the WHO Regional Office for Europe, "digital health is a broad category encompassing electronic health, mobile health, telehealth and health data, among others. It offers solutions that can strengthen health systems, such as bringing health services directly to people's homes and to underserved communities, helping to map outbreaks of

disease, and integrating digital tools that make health care more responsive and productive" [10].

At the global level, digitalization of healthcare aims to find solutions to such pressing issues as quality and availability of medical care across vast geographical territories, in remote areas and for low-income populations. Here, systemic digital technologies play an important role.

The large-scale implementation of information technologies in medicine and the pharmaceutical industry was triggered by the approval of the Resolution on eHealth at the 58th World Health Assembly in 2005 [11]. Since then, the problems of digitalization and its ethical aspects have been discussed in medical communities and at international conferences, including those arranged by the International Society for Clinical Bioethics.

The WHO Symposium on the Future of Digital Health Systems in the European Region held in Denmark in 2019 was attended by 360 experts from 50 countries. Following the discussion on healthcare digitalization, its aspects and development strategies, 3 key conclusions were formulated:

"1. Digitalization is challenging our understanding of how and where healthcare can be delivered and is driving a transition to predictive and preventive models of care.
2. Digitalization of health systems is not simply a notion of continuing what we are doing now more rapidly and more efficiently but:
   – puts the individual at the center of their own health and well-being;
   – addresses how the rights and consent of the individual can be respected and acted on; and
   – harnessing the value of data for health.
3. Digital health is centrally important to achieving universal health coverage with more efficient and effective modes of providing quality and equitable access to health for all. However, innovating towards a safe future enabled by digital health requires specifically linking investing for digital health with achieving public health objectives" [12].

At the international level, the HIMSS Analytics models and services have long been used to optimize healthcare. They formalize the process of exploiting information technologies to improve patient safety by creating tools for elaborating strategies for healthcare digitalization [13].

In Russia, the primary facilitator of healthcare digitalization (more specifically, digitalization of the internal workflow of medical organizations) is the Unified National Health Information System (abbreviated as EGISZ) [14]. A good example of successful digitalization is the Public Services Portal (Gosuslugi), which offers information and access to public services provided by the state and municipalities; using this portal, a patient can book an appointment with a doctor [15]. Another example is popular regional medical information services [16] and digital professional communities [17].

Digitalization of healthcare has revived an interest in ethical dilemmas, which determine the avenues of development for end-to-end technologies in healthcare, including vast data arrays, AI, automation, and robotics. Among such ethical issues are patient rights, responsibility of healthcare professionals, data processing and equality in healthcare.

A study [18] has identified 8 major problems related to digitalization:

1) big data (digital doppelgangers and falsifications);
2) transformation of the doctor-patient relationship;
3) digital literacy of patients;
4) responsibility in complex systems;
5) changes to medical specialties;
6) increasing costs and risk of overtreatment;
7) digital footprint;
8) role of clinical data in treatment and their protection.

Obviously, the implementation of such technologies has significantly transformed medical diagnostics, the system of prevention and treatment, and the relationship between the doctor and the patient. At the same time, the use of big data for AI training can result in manipulation, discrimination and human rights violation. However, by trying to constrain healthcare digitalization, we are slowing the progress in the field of medicine and diminishing the competitive ability of the Russian healthcare system.

So far, taking a history from a patient has been the gold standard in medicine. But only due to digitalization the amount of patient data increased dramatically and new opportunities opened for its storing, collecting and processing. Obviously, data related to a person's health and physical condition can be collected in different ways and may not always be associated with delivering medical care. The following data sources can be used in medicine:

– electronic medical records;
– mobile applications for healthcare (databases);
– sensors and monitoring devices;
– data generated by laboratory tests and radiography;
– data on past vaccinations and results of PCR tests available from Gosuslugi;
– data obtained in the course of clinical trials involving groups of patients;
– information about medications and other medical products purchased by patients;
– data from social media, search results, etc. [19]

According to experts, in order to effectively use AI for the prevention and treatment of diseases, more data is needed, both medical and social. This brings up an ethical issue of personal data protection, because strictly speaking this data is not medical.

Such data is available from different platforms and storage systems that are not always compatible with each other. Compatibility of storage systems, data verification, standardization and unification, as well as elaboration of ethical guidelines regulating their use, are needed to use such information for healthcare purposes.

The general principles of bioethics related to personal autonomy, confidentiality, the risk-benefit ratio, equality and healthcare availability play a special role in developing ethical guidelines for digital healthcare [20]. These principles have been most exhaustively documented in the Universal Declaration on Bioethics and Human Rights (UNESCO, 2005) [21].

Another great concern associated with the use of information technologies is their impact on human behavior and attitude to health. Digital technologies have come forward as a gauge of ethical behavior during a public health emergency, such as the current COVID-19 pandemic. With regard to human rights protection, which was high on the agenda during the pandemic, this problem necessitated development of new approaches to prevent the abuse of ethical principles. For example, the UK's Nuffield Council on Bioethics, the leading research center of bioethics, convenes a small group, should circumstances arise, to develop a separate "ethical compass" for each life-or-death situation [22].

The Russian state policy for countering epidemics restricts civil rights and freedoms listed in Chapter 2 of the Constitution and recognized as the supreme value [23]. Such violation of constitutional rights is justified by public safety. However, restrictions should not extend beyond necessity, result in the termination of international obligations of the state or be associated with discrimination of any sort. The pandemic raised the need for control over the daily lives of citizens, who had to

give up some of their freedoms for the sake of public health. Following WHO's recommendations, many countries mandated testing for COVID-19, lockdowns, social distancing and other measures limiting physical interaction between individuals. That is when the unexpected controlling function of digital technologies came to light. This incited fear that digital technologies could be used as a coercion tool even after the current restrictions are lifted because digital technologies proved to be effective in controlling the safety of gatherings in public places, and this experience could be later applied to other activities. Opponents of strict measures disseminate false or misleading information and fake news via the Internet, which exacerbates the problem. This phenomenon became known as an infodemic, i. e. the fast spread of excessive information about the pandemic, often distorted or unreliable, through mass media and social networking services. The Internet itself is not the root of the problem, but through it rumors and fake news spread much faster and farther than ever before. At the same time, the Internet is an effective tool that governments, healthcare agencies and scientists should exploit to communicate important information to the general public. The Web Foundation has published a Covid Policy Brief containing guidelines for governments, companies and individuals on spreading accurate information, free exchange of opinions and knowledge sharing [24]. Based on the international standards in the field of human rights, these guidelines underscore the need for a thoroughly elaborated approach to balancing health protection, public safety, the freedom of expression and privacy [25]. Standardization of ethical practices in spreading information through different media sources could improve the situation.

Importantly, compliance with ethics is expected not only from healthcare professionals but also from the developers of software that utilizes AI, operators or other persons who gain access to personal data by virtue of their occupation; this involves the issues of patient confidentiality, the right for privacy and personal data protection [23, 26, 27].

Defining ethics and deciding on what ethical guidelines to follow may be a challenge for those involved in designing, developing and implementing digital technologies for healthcare. There are various guidelines and restrictions aimed at regulating the impact of digital technologies on society. Software engineers who develop products for healthcare should follow the code of engineering and software ethics that apply to their work. In turn, development and implementation of digital technologies and applications for healthcare will determine what ethics is and what ethical principles should be adhered to. Thus, there is a need for creating the codes of ethics and professional conduct for new specialties that would combine ethical requirements for software, elements of engineering ethics and standards of medical ethics.

There is a plethora of foreign literature on various aspects of digital medicine. For example, a systematic review has been conducted to analyze the impact of using digital tools on the informed consent procedure in clinical research and practice. The researchers searched Pubmed, EMBASE and Cochrane electronic databases. Studies were identified using MeSH terms and keywords. The review included studies published from January 2012 to October 2020 and focusing on the use of digital informed consent tools for clinical research or medical interventions. Digital interventions were defined as interventions involving the use of multimedia or audio and video to provide information to patients. Those digital interventions were broken down in 3 categories: video, non-interactive multimedia and interactive multimedia. The literature search returned 19, 579 publications. After their titles and abstracts were screened for relevance, there were 100 publications selected for full-text analysis; of them 73 were included in the review. The included publications focused on interactive multimedia (29/73), non-interactive multimedia (13/73) and video (31/73); the majority of the studies had been performed on adults (34/38). Innovations in informed consent had been tested for clinical/surgical procedures (26/38) and clinical trials (12/38). For informed consent, 21 outcomes were analyzed; a positive effect on at least one of the studied outcomes was reported in 8/12 studies. For clinical/surgical procedures, 49 outcomes were analyzed; a positive effect on at least one of the studied outcomes was reported in 21 of 26 publications. The authors of the review concluded that the use of digital technologies for informed consent had not produced a negative effect on any of the outcomes, and multimedia tools were regarded as desirable. The effect of multimedia tools was more pronounced than that of videos. At the same time, the studies included in the review were heterogenous in design, which compounded the assessment. So, a robust design and standardization would be needed to perform further assessment [28].

Some foreign authors indicate that digital health products hold great promise for improving the quality of medical measurements, diagnostics and treatment. While many fields have embraced the digital revolution, public healthcare is yet to experience improvements, better access and economic effectiveness. Public healthcare lags behind other sectors partly because of the legislation, which usually slows the process as healthcare agencies are very cautious about the adverse consequences of digitalization [29].

Outside Russia, digital health studies are becoming increasingly widespread, partly due to the emergence of new concepts like "digital clinical trial" which involves the use of digital technologies for making the trial more accessible for the participants, promoting their involvement, improving the accuracy of measurements, ensuring blind randomization, etc. Digital technologies have a potential for transforming clinical trials and reducing their costs [30].

Summing up, in the modern world of progressive digitalization of healthcare and social services, the primary vulnerable spots in terms of ethics are data confidentiality, safety, equality, availability and protection.

Healthcare professionals are not the only ones affected by the implementation of digital technologies in medicine and healthcare. More people not bound by the code of medical ethics or legal medical obligations, including software developers, public servants, social and law enforcement workers, are gaining access to health data. This raises the need for creating the codes of professional conduct and updating legislation in the fields other than medical.

It is necessary to further refine the terms *digital healthcare, digital medicine, digital medical services, digital clinical trial*, etc. associated with the implementation of digital technologies because they are not clearly defined in the legislation, which makes the regulation of digital healthcare difficult.

Development of effective digital healthcare tools is an intense and complex process requiring interdisciplinary effort from a wide range of specialists, from engineers and ethics experts to tax payers and suppliers. Many problems are exacerbated by the interdisciplinary nature of digital healthcare. The progress of digital medicine slows down when the participants involved speak different languages and have different standards, experience and expectations.

Ethical standards for digitalization in healthcare should not be prohibitory. Instead, they should seek to regulate the sector and offer opportunities for development and implementation of end-to-end technologies, aiming to improve the quality of people's lives.

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THE ROLE OF AN ETHICAL REVIEW IN PEDIATRIC CLINICAL TRIALS

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The article discusses the role of an ethical review in clinical research involving minors. It examines the historical aspect of the ethical component of clinical trials involving minors. The article analyzes the legislative regulation of clinical trials involving minors in Russia and internationally. Currently, the need in pediatric trials is not a point for dispute. It is the issues of optimization of planning and conducting pediatric trials concerning design and protection of minors' rights that are being discussed. A detailed examination of how clinical trials with the participation of children are conducted today is provided. Special attention is paid to the use of "off-label" drugs in clinical practice. The authors predict further progress in creating favorable conditions for the participation of children in clinical trials and provide practical advice for achieving it.

Keywords: clinical trials involving minors, ethical review, pediatrics, experimentation, legislative regulation of clinical trials

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КЛИНИЧЕСКИЕ ИССЛЕДОВАНИЯ С УЧАСТИЕМ ДЕТЕЙ: РОЛЬ ЭТИЧЕСКОЙ ЭКСПЕРТИЗЫ

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Статья посвящена роли этической экспертизы в клинических исследованиях с участием детей. Изучается исторический аспект этической составляющей клинических исследований с участием детей. Анализируется законодательное регулирование клинических исследований с участием несовершеннолетних в России и за рубежом. Поскольку сегодня потребность в педиатрических исследованиях уже не является предметом разногласий, и обсуждается в основном оптимизация планирования и выполнения педиатрических исследований с точки зрения дизайна и охраны прав несовершеннолетних участников, в статье подробно рассматривается то, как клинические исследования с учатием детей проводятся сейчас. Особое внимание уделяется использованию препаратов «off-label» в клинической практике. Авторы прогнозируют дальнейший прогресс в создании благоприятных условий для участия детей в клинических исследованиях и дают практические советы для его достижения.

Ключевые слова: клинические исследования с участием детей, этическая экспертиза, педиатрия, эксперимент, законодательное регулирование клинических исследований

Вклад авторов: Теплова Н. В. — разработка концепции и дизайна, редактирование, утверждение окончательного варианта статьи для публикации, ответственность за надлежащее изложение вопросов, связанных с достоверностью данных, целостность всех частей. Грацианская А. Н. — сбор, анализ, интерпретация материала, написание, языковое оформление текста, соответствие научной терминологии. Костылева М. Н. — офрмирование списка литературы по порядку упоминания источников в тексте.

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Clinical trials involving children as subjects are still the matter attracting a great attention of the society, especially as far as the ethical aspect goes. As an experiment is an essential part of any science development, experimental work in medicine has always been there, involving patients of any age. Edward Jenner (1798) conducted one of the first recorded medical experiments where children of different age groups had smallpox vaccination [1]. In the 19th century, when pediatrics has already become a separate branch of medicine, children in hospitals and orphanages have become a good resource for experiments. This didn't provoke any indignation in the society considering standards and norms of those times related to biomedical trials.

HISTORY OF PEDIATRIC CLINICAL TRIALS

During the World War II, children underwent mutilating experiments of the Nazi, who were convicted by the world community at the Nuremberg trial [2]. The resulting Nuremberg Code (1947) was the first document with provisions of biomedical research ethics. It requires compulsory informed consent to participation in any scientific experiment from a potential subject [3]. Thus, if a child can't consent to participation due to the limited legal capacity, involvement of children into biomedical trials was actually forbidden and the society had a deeply negative attitude to experiments involving children. However, until the 1960s

of the XX century, pediatric trials continued without any regulation.

In 1964, the World Medical Association developed and implemented the Nuremberg Code successor document, the Declaration of HelsinkiThe Declaration of Helsinki admits that clinical trials involving minors can be conducted in case when consent of parents or legally authorized representatives is provided [4].

Thus, in recent past, children were treated as a socially vulnerable group but at the same time pediatric clinical trials were understood necessary. Complexity of research pediatric activity, long-term lack of support at the state level and disinterest of pharmacological companies in pediatric trials caused a global shortage (or lack in some diseases) of registered (approved) pediatric dosage forms and the widely discussed issue of off-label (not according to the instruction) use of drugs among children [5]. By the close of the XX and at the dawn of the XXI century, international and national documents that regulate pediatric trials began to appear even in developed countries.

LEGISLATIVE REGULATION OF CLINICAL PEDIATRIC TRIALS

Guideline for Good Clinical Practice of the International Conference (Council since 2015) on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) has evolved since 1996. In 2001, ICH GCP E11 Guideline on Clinical Investigation of Medicinal Products in the Pediatric Population was developed [6]. The guideline determined basic provisions of drug development for children and approaches to safe, effective and ethically acceptable trials of drugs involving minors.

By 2007, the work related to implementation of ICH GCP E11 guideline provisions into regulatory documents of the European countries and USA consisted in the development of several important international and national documents for pediatric trials.

The EU pediatric legislation

- Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use [7];
- Regulation (EC) No 1902/2006, an amending regulation in which changes to the original text were introduced relating to decision procedures for the European Commission [8].

The USA pediatric legislation

- Pediatric Research Equity Act (PREA) [9];
- Best Pharmaceuticals for Children Act (BPCA) [10];
- Title V of FDA Safety and Innovation Act (FDASIA) [11].

In the EU and USA, provisions of the mentioned regulatory documents create conditions, where pharmaceutical companies can/have to carry out trials of their medicines among children and decrease 'the-off-label-use' in children in the future. At present, we already have reporting FDA (Food and Drug Administration, USA) and EMA (European Medicines Agency, European Union) documents based on the results of over ten years of work during execution thereof. They show that the course of pediatric trial stimulation is successful, as basic prescribing information of hundreds of medicines has acquired pediatric indications [12, 13]. Though from a legal point of view, a medicine approved for use in children from other countries, but not registered for pediatric indications in the Russian Federation, remains off label in national pediatric practice, the actual data from open sources make the use of these medicines less risky for a patient in our country as well.

In the Russian Federation, there is no separate legislative document to regulate pediatric trials. That's why pharmaceutical companies decide whether they need to conduct pediatric trials to register children's indications, taking their own considerations into account. As state registration of a pediatric dosage form doesn't cause a significant growth of sales and is associated with certain technical difficulties and expenditures (clinical pediatric trials in Russia, state fee, etc.), a pediatric dosage form isn't most commonly registered even in its presence.

The significance of an ethical review is increased multiple times due to the lack of detailed legal regulation of many issues involving pediatric trials. Ethical standards of the trials with vulnerable patients are recorded in the Helsinki Declaration of the World Medical Association and ICH GCP Guideline.

'…19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm. All vulnerable groups and individuals should receive specifically considered protection.

20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research…'

Common legal requirements/limitations regarding inclusion of children in clinical trials are cited in Federal Law No. 61-FZ 'On Circulation of Medicines' [14], which takes all children as a vulnerable group, prohibits to treat orphaned children, children left without parental care and some other individuals (compulsory-duty servicemen, prisoners, law enforcement officials) as subjects of clinical trials.

Though GCP requirements to pediatric protocols do not differ from those for other groups of patients as far as relevance for obtaining valid results goes, it is erroneously to believe that a pediatric trial can use the same design as in adults [15]. It is known that a pediatric trial is often terminated prematurely due to a bad design (wrong determination of endpoints, non-applicability of a dosage form, unacceptability of some invasive procedures and/or their number, etc.) [16]. A prematurely terminated trial without significant results is not valuable for practical pediatrics. However, children already included into such an incomplete trial, have underwent the risk, and estimation of any trial perspectives can be an object of interest for an ethical review. Considering the protocol, experts of ethics committees compare the number and duration of planned visits, number of suggested procedures (particularly tender ones, such as vein puncture or intramuscular injection, or deep nasal or pharyngeal smears) and justify the necessity to estimate effectiveness and/or safety of the examined intervention.

For instance, when a locally acting treatment (i. e., throat spray) has been examined for 10 days, you can hardly explain the need in a biochemical blood assay sample, taken twice from a vein of 3–5-year-old children. Though the Ethics Committee doesn't estimate the scientific value of a trial, it determines whether the risk of inclusion of children into the trial is justified. Thus, in several cases, the committee can also pay attention to the scientific aspect of the trial. Ethics committees, that regularly deal with pediatric protocols, usually include a pediatrician and/or pediatric psychologist on a constant basis or can obtain an independent external opinion given by respective specialists.

From a legal point of view, a child is an individual from birth to adulthood (from 0 to 18 years old). Thus, another frequent matter of discussion is whether a clinical trial can be approved simultaneously in all age-specific subgroups or consistency

is better: approve inclusion first of 6–11-year-old children and then of 2–5-year-old children only after good results in 12–18-year-old adolescents have been obtained. This means that we need to shift to trials involving very small children only after data on effectiveness and safety for elder children have been collected. Followers of the subsequent approach are commonly not willing to approve simultaneous trials for all pediatric subgroups because they wish to protect those who are the most vulnerable, i. e., the youngest children, from risks of the trial until the examined intervention isn't proven effective and safe in elder children.

The approach is definitely reasonable. However, it is necessary to remember that delayed approval for inclusion of younger children remotes 'legalization' of practical use of the medicine among younger children. It is also necessary to take into account that it is more ethical and safe to use any medicine within a clinical trial (according to frequently checked/approved protocol by an experienced clinical investigator with exhaustive data about the examined medicine, with accompanying monitoring of the sponsor, with regular interim analysis results, under surveillance of the Ethics Committee and sometimes of a special Safety Committee), than to continue using the medicine off label in routine practice. The more serious an indication is, the more important it is to start trials in all age groups as early as possible. This is how the off-label period is reduced.

Apart from key features of a protocol design, a pediatric trial presents special requirements both to the process of gaining, and to the form of informed consent.

International documents and national legal instruments provide a unique solution stating that it is necessary to obtain consent of a potential subject's legal representative and consent of the minor (child) (Declaration of Helsinki, Federal Law No. 61-FZ). Unlike consent in a standard medical intervention, consent of a legal representative is always required when a child is included in a clinical trial. In the last case, the Russian legislation admits independent consent or refusal of medical intervention for adolescents elder than 15 years old [17].

In accordance with the legislation of the Russian Federation, legal representatives include parents, adopters, guardians and trustees [18]. However, only parents or adopters can sign consent to a child's participation in a clinical trial (No. 61-FZ). One parent's signature is usually enough only in case of no serious interventions when consent of both parents/adopters is deemed necessary. However, even in this case conditions when one parent is deemed to be 'substantially unavailable' must be determined.

The age when a child can take a conscious decision about participation/non-participation in a clinical trial is most frequently discussed. On the one hand, the principle of children's respect appeals to mobilize a child around taking important decisions about his/her own well-being as early as possible. On the other hand, can it be ethical to ask a small child to take such complicated decisions as participation in a clinical trial making him/her responsible for the consequences of refusal? There always exists a probability that a child can refuse to give consent due to mental peculiarities of his/her age because he/she is not able to understand how useful trial participation can be for his/her health or due to some other immediate considerations (acting against a doctor's/parent's will, because of poor health, fatigue, etc.). What will be the parental actions in this case? There exists a high probability that parents will make the child give such consent as they are aware of the advantages of trial participation. Then they will violate the basic principle of GCP about voluntary participation. A regulatory document determining the age when a child's consent is obligatory is currently lacking. As children of the same age can have different psychological and mental development features, every ethics committee decides upon the issue on an individual basis. For example, the issue can be solved by using the analogy of law [19] concerning the age of partial legal capacity, i. e., since 14 according to the civil code of the Russian Federation [20], or since the age of providing independent consent for/refusal of standard medical intervention set in 'The Fundamentals of the Legislation of the Russian Federation on the Protection of Citizens' Health' (15 years old) [21].

In the USA, many ethics committees (IRB — Institutional Review Board) suggest that a child's consent must be required since the age of 7 [22].

An ethics committee can discuss this issue and record the decision in the respective standard operation procedure (SOP) [23].

If the committee defines the age of compulsory consent in accordance with the abovementioned recommendations, the matter of including small children in a trial and their participation in the process of gaining informed consent is still open. Refusal of consent requirement for children who are too small to provide obligatory consent doesn't exclude the requirement to inform a child. Young children should be given information in an accessible form, for instance, as graphic novels or large-print texts with pictures depicting study procedures (MRI, blood sampling, examination by a doctor, etc.). The texts can also describe impressions experienced during the procedures (for example, 'an injection feels like an insect's bite', 'one needs to wear headphones while inside the MRI system as it is noisy', or 'you will be sleeping during gastroscopy and feel nothing', etc.). In this case, the data must not contain a consent request, but are intended for information only. Children are commonly fine with a doctor's recommendation to take part in a clinical trial, they like to have respectful conversations with medical investigators and the process of signing a consent form; later they will treat the research procedures in a responsible way.

CLINICAL PEDIATRIC TRIALS: MODERN TIMES

Discussing the issues of biomedical trials, we usually mean the clinical trials conducted by pharmaceutical companies to provide for state registration of their products (or other purposes), but where investigators perform only the function of collecting data as per the approved protocol. However, expertise of academic trials (including thesis research) has always been a separate challenge for Ethics Committees (particularly academic ones). In an academic trial, an investigator doesn't only collect data, but also acts as a sponsor, a documentation developer, a safety committee and a pharmacovigilance officer. A researcher is also responsible for the scientific aspect of an academic trial.

In our country, clinical trials have been arranged in accordance with international standards for over 20 years. An extensive cohort of experienced investigators, including a vast deal of supervisors of scientific divisions, Ph. D. thesis mentors and external Ph. D. students, has been formed in Russian centers (comprising the clinical basis of medical universities). Participation in international trials displays an example of a proper attitude to ethical and legal aspects of scientific activity. Paradoxical as it may sound, even experienced researchers are usually not aware that neither GCP rules, nor legislation of the Russian Federation make any differences between the requirements to trials conducting by pharmacological companies and initiative academic research involving human subjects [24].

However, it often happens that the goals of academic investigators are even more inventive than the ones of

pharmaceutical companies, both in planning, and conducting pediatric trials. Thesis papers of pediatricians sometimes correspond to the third or even second phase of pre-marketing trials (for instance, estimation of effectiveness and safety in children of a drug approved in adults or in a not previously examined dosage or with a new method of administration). Researchers usually ignore that trial participants must be insured in accordance with the law, that an approval from a regulator has to be obtained and many other conditions registered in regulatory documents. This is most typically of doctoral thesis papers, as traditionally collection of data for the papers must be almost completed by the moment of the topic approval. Local Ethics Committees of the universities monitor thesis works very rarely: they demand and obtain annual reports, serious adverse event reports, and approval of amendments to the protocol and informed consent.

It is obvious that a clinical trial planned in accordance with GCP standards and not contradicting the legislation of the Russian Federation requires long-term preparation, participation by a large team of diversified specialists and massive budget, delivery of documents to the Ministry of Health for revision (in some cases) and obtaining an approval for the trial. Can a university provide a proper quality of trial preparation as a sponsor, particularly in pediatrics? Can a university obtain a regulator's approval for the trials of their employees? Will manufacturers of medicines consent to conduct a trial of a medicine with preregistration signs at a university in accordance with the requirement of the Ministry of Health?

Theoretically, some of the abovementioned conditions can be fulfilled, but it is hard to do so from a practical point of view.

At first glance, both GCP guidelines and a legislative standard are roughly violated within academic science: patients are not protected, their rights are violated, data validity is not controlled, risky trials are conducted without a regulator's approval and LEC observations.

Fortunately, the reality is not that terrifying. The main problem is that in the majority of cases investigators determine their trial type (design) in a wrong way. They present it as a prospective, controlled, parallel-group and sometimes even randomized trial, though it is actually a retrospective, non-interventional, case-control trial. Even a trial of a new indication or effectiveness/safety in a not previously examined age group (for instance, in children) is actually a retrospective analysis of off-label use of a medicine in clinical practice. In pediatric clinics, off label indications are currently closely controlled, properly traced, and based on the algorithm from regulatory documents [25–29] after the necessity of such an indication has been discussed at a consilium or by a medical board and if a child's legal representative signed an informed consent form that had been compiled at a clinic.

Clinical pharmacologists are commonly these patients. Thus, a medicine is indicated in the interests of a patient (but not within a trial), a patient is insured via obligatory medical insurance, adverse events are traced using the pharmacovigilance system of a therapeutic institution, the primary documentation is maintained according to the regulatory requirements accepted in a clinic. When a trial design is determined in a correct way, in the majority of cases a trial subject is not a patient, but his/her case history. At the stage of a completed selection of the necessary number of medical records, submission of documents to the LEC is thoroughly acceptable from the point of an ethical review. In this case, the LEC must make sure that a patient's personal data are held confidential, and request a model of an individual registration card. Then it is not necessary to approve the informed consent form.

Thus, to conduct an ethical review of thesis research and other research and development trials, it's most important to provide a correct definition of a trial type (intervention or non-intervention) and design (retrospective or prospective). The majority of thesis works, which are disturbing for experts of the Local Ethics Committee (LEC), are actually non-interventional and retrospective. Due to the lack of risk to patients' health and/or impairment of patients' rights in retrospective trials, no monitoring of these trials is required by the LEC on a constant basis.

Unfortunately, postgraduates are not taught how to draft documents. That's why it is difficult for them to differentiate between a trial proper, which is subject to an ethical review, from routine medical practice. To change the situation for the better, increase the literacy of young researchers in methodology of clinical trials and acquire correct understanding of the value of an ethical review, the lecture course for postgraduates from Pirogov Russian National Research Medical University in 2021 included lectures about the basics of good clinical practice and methodology of clinical trials involving humans.

CONCLUSION

Now it is difficult to imagine that quite recently any discussion of pediatric trials started with questions 'Do we need clinical pediatric trials at all?', 'Can't we use the data from adults not to expose children to risk of participation in medical experiments?' [30, 31]. Currently, the need in pediatric trials is not a point for dispute. It is the issues of optimization of planning and conducting pediatric trials concerning design and protection of minors' rights that are being discussed.

Compliance with ethical principles stated in international documents acquires significance, which can't be overestimated in the lack of distinct legislative regulation. However, ethical standards, which are stricter than legal norms, are advisory in nature and make high demands on an investigator's personal moral attitudes and determination of members of the Ethics Committee. Growing experience of experts, slow development of regulatory documents reflecting different aspects of research activity in pediatrics, accessibility of information and technical simplicity of communication between all participants of the research process allow to expect further progress in creation of favorable conditions for participation of children in clinical trials.

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INFORMATION TECHNOLOGY IN THE EVALUATION OF RWD / RWE (REAL-WORLD DATA/REAL-WORLD EVIDENCE)

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The features of evaluating data from real clinical practice are discussed. Approaches to material processing for decision support in medicine and health care are also given. The development of standardized methods of analysis with the possibility of obtaining a unified indicator for assessing data from routine clinical practice, combined with the development of information technology is the direction of development of the concept of result-oriented health care. The classification of information technologies used in medicine and public health is presented. The main characteristics and functioning features of the developed software modules for automated data evaluation of real clinical practice are presented: a program for the distribution of drugs on the levels of clinical efficacy, a program to assess the effectiveness of therapy for the specified period; a program to determine the interval of clinical efficacy of drugs.

Keywords: real clinical practice data, RWD/RWE, information technology, automated assessment, software module

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ИНФОРМАЦИОННЫЕ ТЕХНОЛОГИИ В ОЦЕНКЕ ДАННЫХ РЕАЛЬНОЙ КЛИНИЧЕСКОЙ ПРАКТИКИ

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Рассматриваются особенности оценки данных реальной клинической практики. Также приведены подходы к обработке материалов для поддержки принятия решений в медицине и здравоохранении. Разработка стандартизованных методов анализа с возможностью получения унифицированного показателя для оценки данных рутинной клинической практики в сочетании с развитием информационных технологий является направлением развития концепции результат-ориентированного здравоохранения. Представлена классификация информационных технологий, применяемых в медицине и здравоохранении. Приведены основные характеристики и особенности функционирования разработанных программных модулей для автоматизированной оценки данных реальной клинической практики: программа для распределения лекарственных препаратов по уровням клинической эффективности; программа для оценки эффективности терапии за расчетный период; программа для определения интервала клинической эффективности лекарственных препаратов.

Ключевые слова: данные реальной клинической практики, RWD/RWE, информационные технологии, автоматизированная оценка, программный модуль

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In different nosologies, medical aid is provided based on clinical recommendations. The conclusion about inclusion or non-inclusion of medicinal preparations (MP) into clinical recommendations is based on the principles of evidence-based medicine. Randomized controlled trials carried out at the pre-approval stage of MP registration constitute the framework of evidence-based medicine. They have an evidence level taken into account in clinical recommendations. MP effects are considered statistically significant here. However, it is not always possible to reproduce them in real clinical practice.

This occurs because when a medical technology or MP are widely applied, no estimate of effectiveness and safety of MP use is taken into account in patients with concurrent diseases and polypragmasy. The issue concerning principal and concurrent nosologies is unsolved in many cases. In the presence of many drug interactions which occupy a significant place in real clinical practice the values of MP effectiveness and safety can differ from those obtained in clinical research. The lack of long-term effects is a limitation for clinical trials. In its turn, this impacts on clinical and economic variables, as well as social and economic impact consequences. Thus, systematization of methods, development of methodologies and algorithms of complex estimation are essential in real clinical practice at the modern stage of healthcare development. The obtained outcomes can form a framework for introducing changes and additions into clinical recommendations and MP limited lists. Thus, non-interventional trials become significant now. The term ‘non-interventional trials’ was first mentioned in November 2016, when the Guidelines on Good Pharmacovigilance Practices and Guidelines on Good Clinical Practices of the Eurasian Economic Union (EEU) were approved [1, 2]. Due to the spread of coronaviral infection, the term has found a wider application at the federal level.

Government regulation No. 441 dated April 03, 2020 ‘On the Peculiarities of Regulation of Drugs Intended for Use Under Threat of Emergency Occurrence and Management and to Provide Medical Aid to Persons Injured in the Result of Emergencies, Prevention of Emergencies, Prevention and Treatment of Diseases that Constitute a Danger to the Public, Diseases and Damages Obtained as an Effect of Unfavorable Chemical, Biological and Radiation Factors’ states that ‘drug

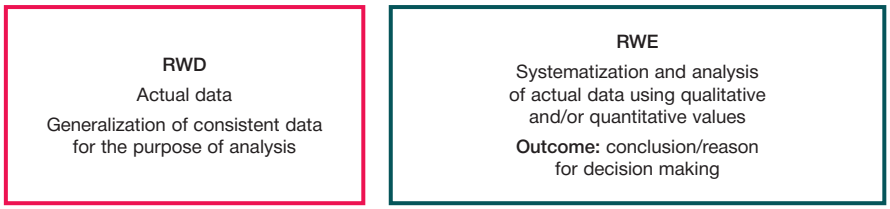


Fig. 1. Real World Data and Real World Evidence (RWD/RWE)

Table. Classification of information technologies applied in medicine and healthcare

Information technologies	Characteristics of information technologies
OLAP (online analytical processing) — technologies	Preparation of aggregate data based on big data structured following the multidimensional principle and their use to present the visualization means. Operates with retrospective archives with data stored for a long time.
Data mining technologies	Data analysis to find previously unknown values among numerical and text data. The key process of the ETL-technology (Extract, Transform, Load). ETL includes as follows: • extraction of data from external sources; • data transformation and clearance ensure their correspondence to the model requirements; • data upload to the repository.
SADT, RAD- and CASE-technologies	SADT (Structured Analysis and Design Technique) technology of structural analysis and design. It is the basis for CASE (Computer-Aided Software/System Engineering)-technology and RAD-(rapid application development) technology.
Simulation modelling	Computer technology to examine some real process parameters using a set of math tools, special simulation programs enabling focused research of a real complex process structure and functions stored in the computer in the mode of simulation.

effectiveness is examined during a low-interventional study following the principles of good clinical practice' [3].

Real World Data and Real World Evidence are estimated during the studies.

Real World Data (RWD) inform of a patient's condition and/or provision of medical aid. In the majority of cases, medical (primarily electronic) records, insurance company data, pharmacovigilance system data, patient registries are sources of RWD. RWD are collected beyond pre-approval clinical trials.

Real World Evidence (RWE) presents as an outcome of (qualitative/quantitative) use of a medical technology in a standard medical practice. RWE belongs to aggregate data obtained during the actual use of a medical technology/ MP (fig. 1).

RWD are actual data only. They carry no significant information about the use of a MP and form the basis for analysis, the outcomes of which enable to answer the questions about a routine usage of MP, and drug-drug interactions in polypragmasy (including long-term therapy effects).

In 2018, the FDA initiated the so-called Framework Program on Cumulative Evidence in Real Clinical Practice. This is the first step concerning systematization of real clinical practice data and algorithms of their estimation development in healthcare [4]. The approach can improve medical aid affordability and quality along with cost effectiveness in healthcare system. Implementing the principles of real clinical data analysis and development of information technologies must become a basis for healthcare system restructuring.

TECHNOLOGIES OF DATA PROCESSING FOR DECISION SUPPORT

Finding an optimal decision is the main task of using information technologies. The process of decision finding includes the system of decision support in the form of application programs and the controlling unit setting inputs and estimating the obtained result [5]. The widely used information technologies are as follows:

– OLAP-technologies (online analytical processing) or a data processing technology when aggregate data are prepared based on big data structured following the multidimensional principle;
– data mining technologies;
– SADT (Structured Analysis and Design Technique) methodology;
– RAD (Rapid Application Development);
– CASE (Computer-Aided Software/System Engineering) includes instrumental means used in system designing.

The information technologies mentioned embrace the entire range of works concerning creation and program maintenance (analysis and development, implementing project documents, system coding and testing) and technologies of simulation modeling (table).

SOFTWARE MODULES INTENDED FOR RWE AUTOMATED ASSESSMENT

1. **The program of MP distribution according to the levels of clinical effectiveness** (computer program). The program was developed using C++ Higher Level Programming Language in Borland Developer Studio (License Certificate Number: 24247). The software component is based on the methodology of weight coefficients calculation efficiency by the Fishburn's method (fig. 2).

MP names or schemes of pharmacotherapy are inputs recorded by users (can have code names such as 1, …, n); how many times every analyzed MP or scheme was prescribed (abs. number); number of positive outcomes obtained when a MP or pharmacotherapy scheme was used (abs. number). The values of clinical effectiveness defined as the ratio of positive outcomes with respect to the general number of prescriptions are calculated automatically. This is followed by clinical efficacy measures ranked from higher to lower values.

Then a user introduces a number of levels by which the available set of MP or schemes analyzed must be distributed into the 'Enter N' graph (fig. 3).

The program ranks a set of MP or treatment schemes from a higher to a lower level considering the value of weight coefficients.

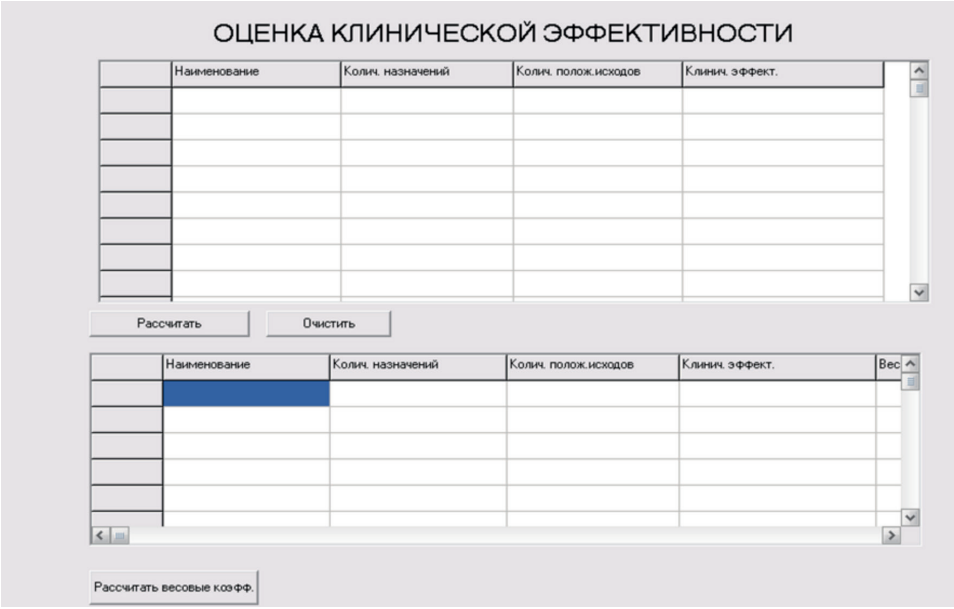


Fig. 2 Program interface to distribute MP based on the levels of clinical effectiveness

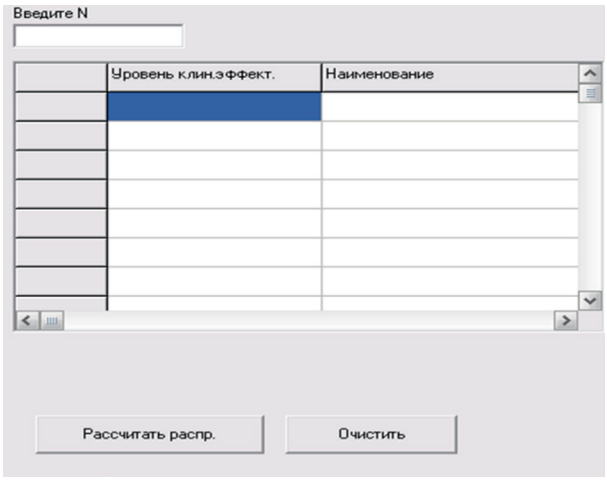


Fig. 3. Program interface to distribute MP based on the levels of clinical effectiveness when a number of levels is entered (N)

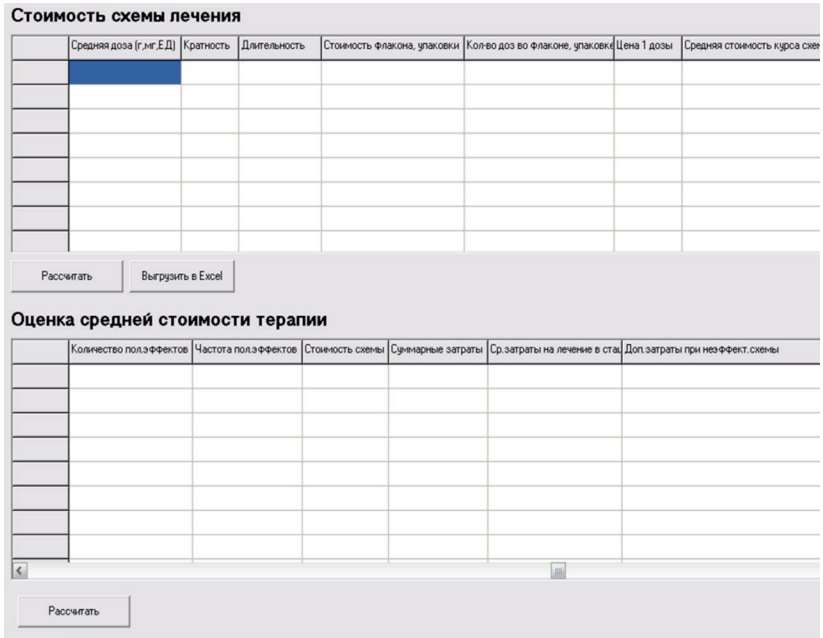


Fig. 4. Program interface to estimate therapy effectiveness

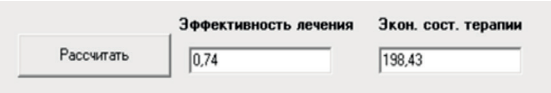


Fig. 5. Program interface to estimate therapy effectiveness when the analysis outcome is obtained

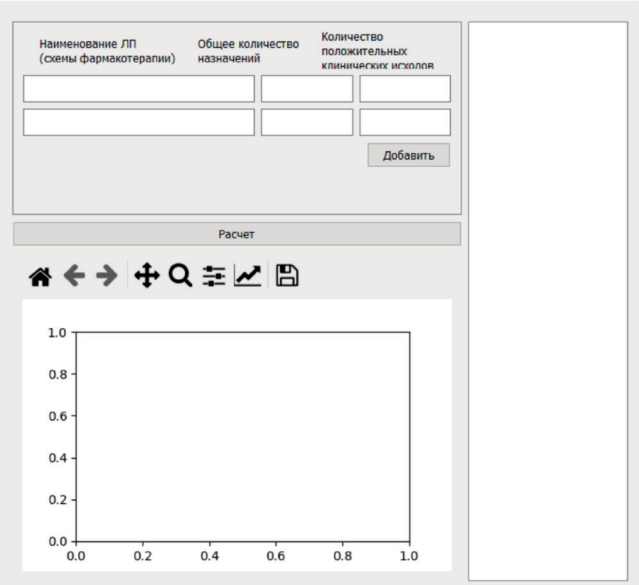


Fig. 6. Program interface to determine the interval of clinical effectiveness for MP

The program module can be used by clinical pharmacologists and health professionals when pharmacological support is planned. The module is optimal for comparison of outcomes of treatment with original and generic drugs.

2. **A program estimating the effectiveness of therapy for the specified period** (computer program) is developed to assess pharmacotherapy considering all MP used while treatment. The program is developed using C++ Higher Level Programming Language in Borland Developer Studio (License Certificate Number: 24247) (fig. 4).

13 subsequent mathematical operations form the basis for the algorithm of computer program implementation.

The user enters data on prescriptions (abs. number), positive clinical effects obtained when using MP (abs. number), expenditures for MP (RUB), additional expenditures associated with non-effectiveness of initially administered MP (RUB). The rest values are counted automatically.

This results in such values as 'Clinical Therapy Component' and 'Economic Therapy Component'. The Clinical Therapy Component is expressed as a percentage (%) and shows therapy effectiveness in a hospital, medical organization, city or region for the specified period. The economic component shows average expenditures per 1 case of the examined disease considering both positive, and negative clinical effects, the occurrence of which was associated with additional expenditure. This is how a patient's condition was improved. The economic effectiveness is expressed in rubles (fig. 5).

The program enables to compare MP or pharmacotherapy schemes in a medical organization; perform qualitative assessment of MP effectiveness, compare values obtained from different medical organizations in an objective way and find the best practice of MP prescription and usage (with the largest value of clinical therapy and the lowest value of economic therapy). The latter can be used by government health agencies during decision making.

3. **A program determining the interval of MP clinical effectiveness** (computer program) was developed. It was based on actual clinical practice to estimate the possibility to transfer the medical technology to another group of patients with this nosology. β-distribution was the program basis.

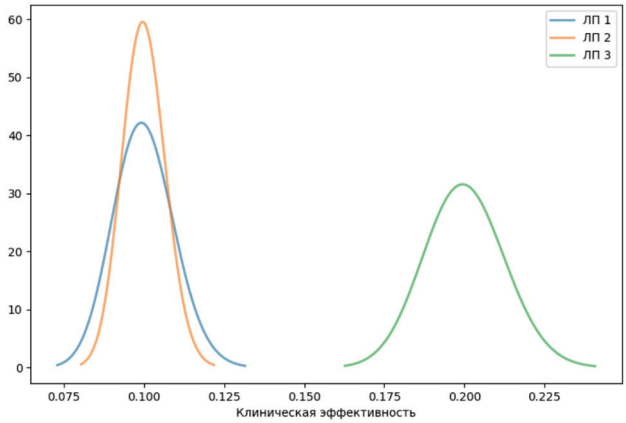
In theory of probability, it constitutes a two-parameter family of absolutely continuous distributions and is used when binomial probability distribution is described (for instance, 'ill-healthy', 'positive effect-negative effect'). It is limited by 0 to 1 interval and corresponds to the described occurrence of a clinical effect due to MP administration.

The values of effectiveness (average values) obtained in clinical practice can differ from those for another sample of patients. Beta-distribution allows to determine how significant the changes can be and which minimal intervals of values cover the actual exact values of the required clinical effectiveness with 95% probability. From a practical perspective, 95% confidence interval shows that 95% of all potential samples using the MP with the examined nosology will produce the values of clinical effectiveness within the set boundaries. In 5% of cases the values will go outside the found boundaries (fig. 6).

The user enters the MP or scheme name, a number of prescriptions for the specified period and a number of positive outcomes into the application. The analysis results are presented as a graph (curves of beta-distributions of clinical effectiveness with the probability of visual comparison) and a number (the interval of MP probable clinical effectiveness when it is transferred onto another group of patients with the same nosologies, 95% CI) (fig. 7).

CONCLUSION

The results obtained when the MP is used in routine clinical practice allow to obtain more exact data about its effectiveness and safety (considering polymorbidity and associated polypragmasy). It is necessary to develop methodologies and algorithms of non-interventional trials to improve validity of the obtained outcomes and for correct interpretation. Further development of standardized methods of analysis obtaining a unified value



(a)

label	a	b	mean	var	min	max
ЛП 1	100	900	0.1	0.0001	0.0822	0.1193
ЛП 2	200	1800	0.1	0.0	0.0872	0.1135
ЛП 3	200	800	0.2	0.0002	0.1758	0.2253

(b)

Fig. 7. Program interface to determine the interval of clinical effectiveness for MP when the graphical (**a**) and numerical (**b**) outcomes are obtained

to estimate the data of routine clinical practice combined with developed information technologies becomes an important step towards implementation and development of outcome-oriented healthcare. RWD/RWE are essential in acquisition, accumulation and analysis of data obtained while prescribing and using the MP and when an individualized approach to pharmacotherapy was developed. As a result, we deal with improved quality of rendered medical aid and optimization of expenditure on the system of pharmacological support.

Implementation of non-interventional trials into practice requires a more exact regulation of the legal part. The EAEU Guidelines regulate the trials with a human as a study subject presenting an ethical and scientific planning standard and conducting the trials. At the same time, they are not enough to organize non-interventional trials.

Expertise underwent by local ethics committees ensures an independent assessment of trial ethical aspects. It is considered by local ethics committees depending on standard operational procedures accepted. To simplify the organization of non-interventional trials, it is necessary to develop single approaches to planning and organization, as well as criteria to estimate the trial outcomes.

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COMPUTERIZATION OF EDUCATION. ETHICS IN INTERNATIONAL DISTANCE EDUCATION AT MEDICAL UNIVERSITIES

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The article deals with ethical aspects of psychological and pedagogical approach of teaching international medical students in the process of educational computerization at modern universities. Particular attention is paid to studying the basics of psychology and pedagogy and mechanisms of distance learning, taking into account cognitive and personal traits of students to develop their professional knowledge, skills and competencies.

Key words: distance learning, international students, computerization of education, ethical aspect, intercultural competency

Author contribution: Martinson ZhS has collected actual data. Krivosheeva NI has performed primary analysis of actual data. Podurueva-Miloevich VYu has detected characteristics of the basics of psychology and pedagogy and mechanisms of distance learning, conducted an empirical study (survey), and analyzed an ethical aspect, considering cognitive and personal traits of students.

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ИНФОРМАТИЗАЦИЯ ОБРАЗОВАНИЯ. ЭТИЧЕСКИЙ АСПЕКТ ДИСТАНЦИОННОГО ОБРАЗОВАНИЯ ИНОСТРАННЫХ УЧАЩИХСЯ В МЕДИЦИНСКОМ ВУЗЕ

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В статье рассмотрен этический аспект психолого-педагогического подхода в обучении иностранных студентов-медиков в процессе информатизации образования в современном вузе. Большое внимание уделяется изучению психолого-педагогических основ и механизмов дистанционного обучения, учитывающих когнитивные и личностные особенности обучающихся в целях формирования у студентов профессиональных знаний, навыков и компетенций.

Ключевые слова: дистанционное обучение, иностранные студенты, информатизация образования, этический аспект, межкультурная компетенция

Вклад авторов: Мартинсон Ж. С. — сбор фактического материала; Кривошеева Н. И. — первичный анализ фактического материала; Подуруева-Милоевич В. Ю. — выявление характеристик психолого-педагогических основ и механизмов дистанционного обучения, эмпирическое исследование (анкетирование), а также рассмотрение этического аспекта, учитывающего когнитивные и личностные особенности обучающихся.

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The path of development of domestic systems of higher education, as well as of entire pedagogy, is rather complicated and has its ups and downs. Its fundamentals were obviously deformed in the stages of the cult of personality and stagnation. The majority of pedagogical problems, which objectively occurred at the time of restructuring of all areas of public life and activity, couldn't be solved successfully. The task of the modern educational system is to raise a highly-educated, intelligent person with a holistic worldview who understands and comprehends the depth of the link between phenomena and processes forming the worldview.

In modern society, a computer is used almost in every sphere of a human life. Education is computerized to the largest extent. Computerization of education is treated as 'an objective and consistent process providing the educational sector with methodology and practice of development and optimal usage of information and communication technology (ICT) tools' [1].

It is of note that the principle of priority of a pedagogical approach during computerization is a feature of the modern Russian higher education system. Any implementation and use of ICT in education starts with pedagogical planning. The latter inevitably requires asking questions about who educates, who is educated, what and how is taught, etc. The pedagogical system embraces a purpose, contents, tools, methods, forms, the one who educates and the one who is educated. This is the reason why computerization and intensification of ICT implementation into the educational sphere don't modify a set of component data. 'It is obvious that educational tools are just transportation means used to deliver knowledge to students. However, the means do not influence acquisition of knowledge, just like a lorry, delivering products, produces no effect on the product nutritional value' [2].

Thus, ICT development gave rise to new conditions of learning and dealing with data in the educational system. Distance learning and ICT-rich educational environment are fundamentals of modern education. If, before the pandemic of 2020, distance education was widely used in the system of higher education as an additional offer as compared to traditional forms of teaching and learning, it, for now, becomes

almost the principal way of getting education. It can be asserted that being an educational core, learning undergoes certain modification, namely, its procedural component (the process of direct transfer of and gaining experience in the course of teacher-student interaction) is modified [3]. In other words, learning forms are changed, whereas its essential aspects stay unchanged. For example, transition of learning into electronic educational environment still requires targeted management aimed at the formation of professional knowledge, skills, competencies, and creative capacities in students.

Distance learning is 'a targeted process of interactive communication between those who educate, those who are educated and educational tools, which is indifferent to how all the participants are located in space and time, and which is implemented in the specific didactic system' [4].

Distance learning features are as follows:

- physical separation of teachers and students;
- physical separation of students and schools;
- asynchronous learning (diversity in time);
- interactive communication between teachers and students;
- interactive communication between students, and students and tools. In distance education, we always learn using tools;
- continuous academic activity of students;
- distance training course, selected educational materials;
- possible in-person learning.

A distance learner is usually isolated. Distance learning doesn't only lack motivating factors resulting from interaction or competition with other students during in-person lessons. It also lacks the necessary direct support from a teacher, who can motivate and pay attention to those needs and difficulties that arise in the course of the educational process. This means that students need to take personal responsibility for their learning process.

In distance learning, being independent (self-determined learning) is a high priority. As students are autonomous, independent learning has two meanings:

1) autonomy is a prerequisite for successful distance learning;
2) autonomy is an ultimate goal for distance learning.

Successful distance learning requires a high level of self-discipline and independence, as students have to rely on themselves and their motivation resources only, even more so than in in-person learning. This happens because many factors responsible for extrinsic motivation are available indirectly or lacking at all [5]. In in-person learning, intrinsic motivation is highly desirable. In distance learning, it is a necessary prerequisite.

Autonomous learning means that students need to cope with tasks that lack previously prepared answers. They are trying to solve the problems that seem relevant to them. Students' degree of self-sufficiency depends on the extent of their participation in research planning and conduction, and assessment of research outcomes. But as practice shows, not every student is ready for distance learning.

Direct or indirect influence on intercultural communication is commonly a decisive factor for previous motivation of international students. The importance of examining their emotions must be stressed as well. The emotional variable is a motivation language learning, whereas emotions are essential motivators. A. MacIntyre believes that relations by themselves are not enough to support motivation in learning, and that we need to take into account students' emotions during the process of learning to find the difference between the students who are interested in learning and those who are not [6].

We can conclude that emotional behavior of international medical students during the learning process can be comprehended the best, when they accept orientations of the studied discipline offered by their teacher, and when they are not stressed trying to accept them.

In this article, we report online survey results for medical international 1st year students. The survey shows that out of 100 students participating in the survey, the majority of those requested mentions a complex interaction of social and biographical variables in their perception of the Russian language and its use to express their emotions, and a mental effect obtained when one studies in an international language. Good emotional atmosphere can't be created by students only. 84% of those requested note that teachers are ultimately responsible for a positive learning environment; the students are concerned about emotions in class.

On the one hand, teachers need to structure their discourse so that it could be easily comprehended by international students. On the other hand, teachers have to create a true teaching environment using verbal and nonverbal tools, when international students believe in the value of education in Russian and understand that higher education is important.

Thus, distance learning requires high independence, self-discipline, good organization and time management. Consequently, based on modern realities, pedagogical activity must be aimed at development of these personal qualities in students. We need to concentrate on complex development of a model researching the basics of psychology and pedagogy and mechanisms of distance learning that could take into account both cognitive and personal traits necessary for distance learning, and effect of ICT on development of these traits in students.

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PHILOSOPHICAL ISSUES OF ARTIFICIAL INTELLIGENCE AND “SMART” ALGORITHMS’ TRUST IN MEDICINE

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In this article, the author examines the philosophical issues associated with the introduction of artificial intelligence (AI) systems in medicine. Currently, the use of AI technologies in the field of medical sciences is one of the most important trends in world of health. “Smart” AI systems are able to learn from their own experience, adapt in the environment and, according to the parameters of the assigned tasks, can make decisions that in the past belonged only to humans. These AI technologies provide an opportunity to take diagnostics, treatment and disease prevention to a higher level. Particular attention is paid to the ethics and moral obligations of AI developers and healthcare professionals in the transition to such digital medicine.

Keywords: artificial intelligence, machine learning, «smart» systems, medicine, bioethics, moral decisions, trust, safety

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ФИЛОСОФСКИЕ ВОПРОСЫ ИСКУССТВЕННОГО ИНТЕЛЛЕКТА И ДОВЕРИЯ «УМНЫМ» АЛГОРИТМАМ В МЕДИЦИНЕ

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В статье рассматриваются философские вопросы, связанные с внедрением систем искусственного интеллекта (ИИ) в медицину. В настоящее время использование технологий ИИ является одним из важнейших трендов мирового здравоохранения. «Умные» системы ИИ способны обучаться на собственном опыте, адаптироваться в окружающей среде и принимать решения, которые раньше мог принимать только человек. Эти технологии дают возможность поднять диагностику, лечение и систему профилактики заболеваний на новый уровень. Особое внимание уделено этике и моральным обязательствам разработчиков и пользователей — медработников при переходе к цифровой медицине.

Ключевые слова: искусственный интеллект, машинное обучение, «умные» системы, медицина, биоэтика, моральные решения, доверие, безопасность

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In modern society, artificial intelligence (AI) as a phenomenon covers the entire human life. It is associated with the fact that AI is an essential component of products and devices used in the daily life of humans. AI systems become an environment and participants of human social interactions [1].

Introduction of AI systems into medicine is one of the most important modern trends of world healthcare. AI technologies significantly alter the world healthcare system, form a revolutionary system of medical diagnostics, develop new medicinal preparations and generally improve the quality of healthcare services.

The term ‘AI’ is differently defined in literature, scientific magazines and on the Internet. According to many various scientists [2], AI is a group of rationally logical and formal rules developed and coded by humans. These rules simulate intellectual structures, reproduce goal-oriented rational actions with a subsequent coding and taking instrumental decisions without a preliminary set algorithm. This means that intellectual systems, called ‘smart’ systems in the market, can act in an autonomous way.

AI differs from traditional computer algorithms as it is capable of self-education based on the accumulated experience. Due to its unique function, AI can act differently in the same situations depending on the early experience.

Smart systems equipped with AI have such features as ‘intellectuality’, ‘logic’, ‘rationality’, ‘capability to think as a human’ under all or certain circumstances.

The term AI defined in such a way provokes disputes among scientists. Some say that it is impossible to simulate all functions of the human brain, others believe that AI can even surpass the human intellect. Thus, there are two types of AI: narrow and strong or general [3].

Strong AI is an ability of the intellectual system to think and be aware of itself as a separate personality and comprehend its own thoughts, in particular. The intellectual process is similar to human one.

Narrow AI means all the systems used to solve intellectual tasks aiding a human to achieve the set goals. Human intervention is necessary here and these applications became part of our lives as we are surrounded by equipment with weak AI and are their constant users. These AI technologies generate strong interest in medicine as well. They are widely applied in ‘smart’ healthcare systems.

The government of the Russian Federation is also interested in AI. Thus, according to the Decree of the President ‘On the Development of Artificial Intelligence in the Russian Federation’, ‘… creation of universal (strong) artificial intelligence capable

of solving different tasks, think, interact and adapt to the changing conditions is a complex scientific and technical issue. Its solution can be found at the junction of natural science, technical and socio-humanitarian scientific knowledge. When the issue is solved, it can result both in positive changes in key life spheres, and in negative consequences caused by social and technological changes which are concomitant with the development of AI technologies' [4]. In accordance with the Decree of the President mentioned above, use of AI technologies in the social sphere improves the quality of life due to the better healthcare services [4].

In modern medicine, AI is one of the most important constituents of medical activity. Intelligent analysis, expert systems, neural networks, evolutionary algorithms, and biocomputing are utilized to achieve the objectivesof modern medicine.

Healthcare has big hopes for AI. AI can make healthcare more effective and convenient for patients, speed up diagnostics and decrease the number of mistakes in diagnostics, help patients deal with their symptoms or cope with a chronic disease and avoid human prejudices and mistakes.

However, the use of such tools in healthcare requires to accumulate and analyze a vast amount of biological data from millions of patients, and compare them with clinical data. Expert systems are used to cope with non-formalized issues, and include tasks in medicine. Most importantly, no unique algorithmic solution of the tasks is available.

IBM Medical Sieve, IBM Watson supercomputer, AI-RAD Companion Brain MR for Morphometry Analysis, AI-RAD Companion Prostate MR for Biopsy Support, Russian Celsus Service program based on AI technology, World Well-BEING PROJECT, etc. belong to currently developed ambitious projects.

They aim at development of 'smart assistants' with multi-level analytical abilities. The assistants can have access to knowledge accumulated in clinical practice and can reason in such way to facilitate taking decisions in various areas (specialties) of medicine.

It is natural that use of big data and AI technologies rises diagnostics, treatment and system of disease prevention to a new level. However, such a use of AI in medicine, which requires trust in 'smart systems', raises serious philosophical issues. In transition to digital medicine, the issues of ethics became crucial. They determine the speed of technological progress in this sphere [5]. Thus, there is much concern about the extent of using health data to teach AI and extent to which the 'smart systems' can be trusted.

Self-learning is the basic feature of 'smart' systems. However, it must be noted that there are serious risks associated with a correct self-learning and the problem of its border determination. Overfitting is the main threat for effective treatment. It is of note that 'smart' systems are not smart by themselves. They are based on various AI technologies and depend on the set tasks for the purpose of effective implementation of required functions based on the developed algorithms. These technologies are developed by AI specialists.

That is why the Nuffield Council [6], which is an independent organization estimating a set of ethical issues in the area of biology and medicine, stresses the issues that must be taken into account in the first place:

- Who is responsible for the decisions taken by AI systems?
- Will the progressive use of AI result in the loss of contact with people while rendering medical aid?
- What happens when AI systems are broken?
- How can we trust the systems that can be uncontrolled at any time?

Moreover, the Nuffield Council doesn't exclude that AI can take an erroneous decision. And there is a question who is responsible for the decisions taken by AI [6].

The machine-learning algorithms are not transparent. They don't give people a chance to understand why AI makes some associations or conclusions and it is unknown when the system is down.

Neither science, nor medicine has absolute knowledge. However, there are different approaches to the object of cognition, different research results and outcomes. This results in a problem with the data used to educate AI. Moreover, trusting 'smart' system requires data protection, especially when it is about confidential data.

In 1931, a known Austrian mathematician Kurt Gödel has found out that any formal system, including mathematics, is incomplete and controversial. In other words, it means there are problems, assertions and issues that can't be solved, proved or contradicted while staying within the boundaries [7]. It is well known that mathematics forms the basis for AI algorithms. If everything is determined, a machine can't freely solve new and undetermined tasks. And if the system is able to solve tasks on its own, there are certain cases when unpredictable reactions can occur. In both cases, significant problems may arise. This is a serious challenge for medicine.

Thus, any 'smart' system can't take decisions independently without involvement of humans, especially when it is about moral acts [8], especially for medical purposes.

Some scientists believe that machine learning is an excellent instrument for AI agents. But it's difficult to explain how all this works and makes algorithms mysterious even for its creators. This limits the ability of people to understand this technology and undermines trust in AI technology and systems. Trust is of critical importance in all relations and is the precondition for approval in the society. Scientists and developers share an opinion about significant risks when AI is developed without human observation and surveillance. Trust and control are two basic aspects to construct safe and reliable AI [9].

People trust in 'smart' systems the most important things such as money, health and safety. It means that we don't just use the technologies, we depend on them. This is how we become vulnerable.

In this context, AI ethics determines moral obligations and duties of developers and users such as medical workers dealing with AI. AI bioethics concerns ethical issues with problems that may arise in designing and development of AI in medicine. Thus, we can say that there exist important aspects that endanger both medicine and entire society if these aspects are not agreed upon with bioethics [10, 11].

Gartner is the most well-known research and consulting company. It focuses on the markets of information technologies and often published tendencies in the area of technologies. Company specialists believe that almost all technologies that will produce a significant effect on business, people and society in the nearest decade are associated with AI [12]. There is no doubt that implementation of AI is a one-way road. The process will go on and embrace all parameters of personal, professional and social human activity. This is also true about medicine.

There is no doubt that AI technologies in medicine can be used for the benefit of humans. But absolute trust in the 'smart' algorithms can have devastating impacts. Thus, immense responsibility is imposed on medical scientists as they need to provide safety for humans and society considering obvious and latent risks, moral standards and principles of bioethics.

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