Current Developments and Innovations in Early Detection and Subsequent Treatment of Cancer

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Abstract: *Objective*: The study aimed to identify key trends in modern oncology by analysing developments and innovations in early cancer diagnosis and treatment methods. Using a comparative analysis of scientific and healthcare systems in Albania, Bulgaria, Kyrgyzstan, and Uzbekistan, the study examined innovative diagnostic approaches such as liquid biopsy, biomarker discovery, genetic testing, advanced imaging techniques, and artificial intelligence algorithms.

Methods: For treatment, it highlighted immunotherapy, personalised medicine, cellular, targeted, and combination therapies, as well as the development of radiopharmaceuticals and 3D modelling for surgical planning.

Results: Key findings revealed that the lack of economic support for research is the primary barrier to innovation in all four countries. Bulgaria, benefiting from European Union membership, demonstrated the highest potential for advancing oncology due to its stronger scientific, technical, regulatory, and social indicators. In contrast, Albania's transition economy and Kyrgyzstan's social and geographical challenges significantly hinder progress. The findings underline the need for enhanced economic investment, international cooperation, and regulatory support to address disparities and foster the implementation of innovative oncology practices globally.

Conclusion: This regional analysis provides insights into how tailored approaches can bridge the gap between low- and high-income countries in advancing cancer care.

Keywords: Oncology, radiopharmaceuticals, immunotherapy, personalised medicine, genetic testing, biomarkers.

1. INTRODUCTION

Cancer remains one of the leading causes of death in the world. The search for new approaches to their diagnosis and treatment is an urgent task, the successful implementation of which will significantly increase the survival rate of patients and improve their quality of life during and after treatment. As cancer is a global problem, the study of modern developments and innovations aimed at its early detection and subsequent treatment should cover the socio-economic, environmental and genetic factors inherent in different regions that affect the level of healthcare in the countries that belong to them. Even though the search for effective methods of early detection and treatment of cancer is one of the top priorities of modern medicine, the complexity of cancer biology, tumour heterogeneity and treatment resistance remains the main issue [1]. These challenges manifest in clinical settings through difficulties in identifying specific tumour subtypes, developing tailored therapies, and addressing variable patient responses to treatment due to genetic and molecular diversity. Moreover, treatment resistance often results in relapses and limited effectiveness of traditional therapies, demanding innovative approaches.

Based on the analysis of metagenomics, genomics, transcriptomics and clinical data from 4,160 biopsies of metastatic tumours, T.W. Battaglia *et al*. [2] investigated the presence and relevance of the microbiome in metastatic cancer. This approach identified organ-specific microbial tropisms and created a pan-organismal resource of the metastatic tumour microbiome. A.M. Tsimberidou *et al*. [3] deemed precision oncology medicine to overcome the complexity of tumour biology. The advantage of this approach over traditional therapies is that it focuses on the molecular characteristics of a particular tumour rather than on the type of tumour and stage of the disease. At the same time, this approach has certain problems, which were analysed by O. Pich *et al*. [4]. According to scientists, these problems are related to the biological complexity of tumourigenesis, which affects the processes of cancer initiation, prevention, early detection and resistance to treatment. To address these challenges, the authors propose the expansion of molecular profiling in clinical

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ISSN: 1929-2260 / E-ISSN: 1929-2279/24

practice and the introduction of a robust translation infrastructure.

Based on the analysis of the literature on the relevant topics, S.S. Senga and R.P. Grose [5] concluded that the understanding of the genetics and biology of cancer, which has expanded over the past decade, requires a revision of its characteristics. Therefore, scientists have identified four new signs of cancer: dedifferentiation/transdifferentiation, epigenetic dysregulation, altered microbiome, and altered neuronal signalling. The need to search for new characteristic features of cancer is also proved by D. Hanahan [6]. Hanahan’s findings highlight that beyond molecular markers, the tumour microenvironment and its dynamic interplay with host systems require greater emphasis to enhance early detection and tailored interventions. Among these features, the scientist identifies phenotypic plasticity, impaired differentiation, non-mutational epigenetic reprogramming, polymorphic microbiomes, and senescent cells of different origins in the tumour microenvironment. The possibilities of using high-dimensional single-cell technologies for the analysis of cancer immunotherapy were investigated by S.H. Gohil *et al*. [7]. The main advantage of such technologies is the ability to identify tumour heterogeneity by tracking individual T-cell clones using paired-end sequencing of T-cell receptor genes, which will provide the necessary resolution to create clinically relevant signatures in immuno-oncology.

The influence of risk factors on the early evolution of cancer was investigated by C.E. Weeden *et al*. [8]. To describe the process under study, the scientists analysed how early initiated cells are protected from further tumourigenesis and the risk factors that promote tumour growth, and based on this, they considered strategies for early detection of tumours and assessed the prospects for the development of molecular cancer prevention. The potential of artificial intelligence-based multiomics analysis in cancer medicine was discussed by X. He *et al*. [9]. According to scientists, innovative omics technologies make it possible to access information from the genome, epigenome, proteome, transcriptome, which can be used to determine the characteristics of different molecular layers and form a holistic view of tumour behaviour. These innovations for clinical practice are implemented by combining multiomics technology and artificial intelligence algorithms, contributing to the development of precision cancer medicine – early screening, diagnosis, prognosis and assessment of response to therapy. In general, the use of multi-omics technologies on the artificial intelligence platform will eliminate the existing problems of precision medicine, increasing its efficiency and, accordingly, the survival rate of patients.

The above studies analysed developments and innovations for the diagnosis and treatment of cancer, but given the global nature of the problem, did not address certain local features that may affect the development or implementation of these developments in the healthcare sectors of different regions. For this study, materials were selected based on inclusion criteria that prioritized publications from peer-reviewed journals, systematic reviews, and clinical trials indexed in databases such as PubMed, Scopus, and Web of Science. Articles were excluded if they lacked empirical evidence or region-specific data. The study aims to determine the effectiveness of modern approaches to the early detection and treatment of cancer. The rationale for choosing Albania, Bulgaria, Kyrgyzstan, and Uzbekistan lies in their unique healthcare dynamics, reflecting diverse socio-economic conditions and resource allocations. These countries represent regions with varying levels of scientific, regulatory, and infrastructural support, providing a comprehensive framework for understanding oncology’s development under differing constraints. The study objectives were to identify what factors can influence the different levels of development and implementation of such approaches and to analyse, in the example of Southern Europe and Central Asia, which regional features can facilitate and impede these processes.

2. METHODS

The study of modern developments and innovations in the early detection and subsequent treatment of cancer involved an analysis of relevant scientific sources in oncology, immunology, genetics, molecular biology and epidemiology. References were collected from publications in PubMed, Google Scholar, Web of Science, and Scopus databases using keywords: “cancer”, “oncology”, “tumour”, “new technologies in cancer diagnosis/treatment”, “personalised cancer medicine”, “precision medicine”, “genetic analysis”, “epigenetics”, “bioinformatics”, “multiomics”, “gene sequencing”, “T-cells”, “artificial intelligence in cancer diagnosis/treatment”, “nanotechnology in cancer diagnosis/treatment”. Following the specifics of the research, the search was limited by the year of publication – materials from 2020 to 2024 were selected for review. A total of 24 publications were selected.

To determine the factors that may influence the processes of scientific development and implementation of certain developments and innovations in clinical practice, a literature search was conducted: “ways to introduce innovations in oncology”, “stages of development/implementation of new cancer treatments”, “barriers/obstacles to the development/ implementation of new cancer treatments”, “factors influencing the development/implementation of innovations in early cancer detection”, “stages of clinical trials”, “technical/economic/ethical issues of clinical trials”, “financing of cancer research”, “cost-effectiveness of cancer research”, “access to cancer treatment”, “grants for cancer research”, “commerciali-sation of cancer research”, “economic/environmental/ epidemiological factors affecting cancer research”. A total of 5 scientific sources were selected for further analysis.

The impact of regional peculiarities that may facilitate or impede the development and implementation of modern developments and innovations in early detection and subsequent treatment of cancer was determined based on the analysis of the healthcare profiles of the Southern European countries of the Balkan region – Albania and Bulgaria and the Central Asian countries – Kyrgyzstan and Uzbekistan. To this end, the epidemiological situation of cancer was assessed in each country separately, in the region to which it belongs, and globally. For this purpose, statistics from the International Agency for Research on Cancer [10-16] World Health Organization [17-20] were used. The current level of technical, scientific and economic capabilities of these countries was also assessed. Based on descriptive statistics, socio-economic, climatic, demographic and genetic factors were identified and the level of their influence (facilitating or hindering) on the development and implementation of innovative approaches to the detection, treatment and prognosis of cancer in the countries of these regions was assessed. The obtained metrics were compared between these countries, between the general indicators of the region and the world. Based on these comparisons, the influence of regional aspects on the level of development of innovations in the field of cancer control was assessed.

3. RESULTS

Modern oncology is in a period of active development due to the complex influence of many factors that interact with each other and contribute to constant changes in approaches to the diagnosis, treatment and prevention of cancer. The most effective new developments that facilitate the early detection of cancer include liquid biopsy, new imaging methods, the use of artificial intelligence, the discovery of new biomarkers, and the use of genetic tests to identify a patient’s genetic predisposition to cancer.

Liquid biopsy is an innovative method of cancer diagnosis that analyses blood for DNA fragments of cancer cells that contain information about genetic mutations of the tumour – circulating tumour DNA (ctDNA); RNA molecules that encode proteins necessary for the growth and survival of cancer cells – circulating tumour RNA (ctRNA) and whole cancer cells circulating in the blood – circulating tumour cells (CTCs). The analysis of these components was used to identify tumours at early stages when they are still small and traditional methods cannot always diagnose the disease. Compared to other types of biopsies, such as surgical biopsy, liquid biopsy is a minimally invasive method, which greatly simplifies the diagnostic procedure and allows for an increase in the number of biopsies, which makes it possible to monitor the dynamics of the disease, the effectiveness of treatment, and to detect relapses and resistance to therapy. In addition, liquid biopsy can detect even a small number of cancer cells and provide detailed information about the genetic characteristics of tumours, which characterises it as a highly sensitive and informative diagnostic method [21]. Currently, efforts to develop liquid biopsy technology are aimed at developing new cancer markers, expanding the range of tumours for which this method can be used, and reducing the cost of the procedure. Thus, the advantages of this method make it possible to consider it in the future as a routine procedure for diagnosing and monitoring cancer, which will significantly improve treatment outcomes and improve the quality of life of patients.

Advances in imaging have improved the resolution of magnetic resonance imaging (MRI), positron emission tomography with computed tomography (PET-CT) and ultrasound and made it possible to detect the smallest changes in tissue, which is critical for early cancer diagnosis. Modern MRI devices can assess functional activity in different parts of the organs and, thanks to the use of special contrast agents, better visualise tumours and determine the level of their blood supply [22]. The high sensitivity of PET-CT makes it possible to detect tumours at early stages, when they are still invisible to other imaging methods, to determine the presence of distant metastases and to assess the metabolic activity of tumours (growth rate and metabolic features) [23]. Ultrasound can be used to assess the mobility of organs and tissues in real time, while Dopplerography allows to assessment of blood flow in blood vessels [24]. Even though this method is less sensitive and informative than MRI and PET-CT, its advantage is the low cost of the procedure. Advances in computer technology, the search for new contrast agents and the development of more accurate image processing algorithms are expanding the prospects for further improvements in oncology imaging, which will increase diagnostic accuracy and expand access to more patients.

Artificial intelligence, especially machine learning algorithms, is revolutionising medical diagnostics in general and cancer diagnostics in particular. This technology can analyse large amounts of medical information (MRI, PET-CT, ultrasound, X-rays) and detecting the smallest fragments that are identified as signs of cancer [25]. The use of artificial intelligence in oncology significantly reduces the possibility of error, as the analysis of machine learning algorithms is free from human error. Therefore, such algorithms provide highly accurate, objective and fast diagnostics, which allows for early detection of cancer when treatment is most effective. Before artificial intelligence can be fully involved in the process of diagnosing cancer, important issues related to this technology need to be addressed. Among them, the main ones are ensuring the quality of data used to train algorithms; interpretation of results (it is important that the doctor understands how the algorithm makes decisions and, in case of a contradictory result, can analyse it); addressing ethical issues, for example, the extent of the doctor's responsibility for making decisions based on the results of artificial intelligence. Despite these challenges, artificial intelligence technology has great potential in cancer diagnostics, as it can make it more accurate, faster, and more accessible to patients.

Many modern developments related to early cancer detection prioritise the search for new biomarkers as important indicators of health and disease. The main technologies used for this purpose include the analysis of biological fluids (blood, urine, cerebrospinal fluid) to detect abnormal proteins, genes or other molecules associated with cancer; tissue biopsy to examine the tumour and surrounding tissues using mass spectrometry, microarray hybridisation and other instrumental methods; and omics technologies that allow for the simultaneous analysis of thousands of genes, proteins or metabolites [26]. An important tool for improving the accuracy and speed of each of these technologies is artificial intelligence, whose machine learning algorithms can analyse large amounts of data and identifying complex relationships between various biological parameters. Given the complexity of cancer biology and the diversity of its types, the search for biomarkers is a lengthy process that yields important results. Examples of discovered biomarkers include prostate-specific antigen (PSA), a biomarker for prostate cancer [27], CA-125, a biomarker for ovarian cancer [28], carcinoembryonic antigen is a biomarker for colon and other cancers [29], and human epidermal growth factor 2 is a biomarker for breast, ovarian and gastric cancer [30]. The search for cancer biomarkers is developing dynamically, as, in addition to the possibility of early detection of tumours, it can help establish new targets for therapy and develop effective medicines based on them.

The development of genetic tests is important for cancer prevention, as it can be used to identify the risks of cancer before the first symptoms appear. This method cannot be considered diagnostic in the literal sense, as it determines the presence of gene mutations that increase the risk of developing cancer [31]. Genetic tests are important for people who have a family history of cancer or who belong to ethnic groups with an increased risk of certain types of cancer, as well as for patients with a diagnosed disease to predict the course of the disease and select the best treatment. The most analysed genes are those associated with an increased risk of breast, ovarian, colon, pancreatic and prostate cancer. The development of genetic cancer tests is important in modern oncology, so the search for new genes whose mutations increase the risk of cancer is a key objective of this area. The most promising areas of research aimed at developing effective cancer treatments include immunotherapy, targeted therapy, combination therapy, personalised medicine, cell therapy, 3D printing, and the development of radiopharmaceuticals [32].

Unlike traditional treatments (chemotherapy or radiotherapy), which often affect healthy cells, immunotherapy, as an innovative area of oncology, aims to stimulate the body's immune system to fight cancer cells, so it is more specifically targeted at tumour cells [33]. This ability of immunotherapy is realised due to the ability of immune cells, in particular T-lymphocytes, to recognise cancer cells as foreign and attack them. The natural immune mechanism can be inhibited, as some cancer cells produce substances that suppress the immune system, while the use of immunotherapy helps to neutralise these substances and activate an adequate immune response. Immunotherapy has several ways of affecting tumours through checkpoint inhibitors – drugs that block molecules on the surface of cancer and immune cells that can suppress the immune response; through monoclonal antibodies – proteins that recognise specific proteins on the surface of cancer cells and mark them for destruction by immune cells; through cellular immunotherapy, a method that involves the extraction of a patient's immune cells, their modification in the laboratory to increase their effectiveness in destroying cancer cells and returning the already modified cells to the patient's body; through the use of immunomodulators, substances that stimulate the immune system, helping it to fight cancer cells more effectively. The advantages of immunotherapy over conventional cancer treatment, in addition to high efficacy and fewer side effects, are the long-lasting therapeutic effect, which is ensured by the ability of the immune system to "remember" cancer cells and activate them in response to their occurrence even after treatment. Currently, improvement of immunotherapy method is being carried out in several areas: identification of tumour treatment, resistance to immunotherapy, reduction of the cost of immunotherapy drugs and reduction of side effects, including autoimmune reactions, symptoms resulting from massive cancer cell death, neurological disorders, heart and kidney disorders.

The innovation of the targeted therapy approach is related to the fact that it targets specific molecular changes in cancer cells, blocking their growth, unlike traditional chemotherapy, which affects all rapidly dividing cells in the body. Targeted therapy has several mechanisms of action. It can block the signalling pathways that stimulate cancer cell growth, suspending their proliferation; inhibit tumour angiogenesis, depriving the tumour of a source of resources for growth; enhance the immune response to recognise and destroy cancer cells; and induce apoptosis. The main advantages of targeted therapy are specificity, which minimises side effects on healthy tissues, low toxicity, which allows for long-term therapy, and the possibility of combining with other treatments to achieve a synergistic effect [34]. Research into this therapeutic approach is still ongoing to address its limitations, which include the likelihood of cancer cells developing resistance to targeted drugs and their high cost.

A method of utilising a stem and immune cell from a patient, known as cancer cell therapy, is one of the most promising approaches to treating cancer. The immune and stem cells of the patient involved in cell therapy, when returned to the body after modification, perform important functions: immune cells effectively recognise and destroy cancer cells, while stem cells restore damaged tissues and organs and create a microenvironment unfavourable to tumour growth. Both types of cells can be used to transport drugs directly to the tumour, increasing the effectiveness of treatment and reducing the risk of side effects. According to the type of cell involved, there are several types of therapy. In chimeric antigen receptor-T (CAR-T) cell therapy, the patient's T cells are genetically modified by adding a CAR to them, which recognises specific antigens on the surface of cancer cells. In the process of adaptive cell transfer, the patient's T cells are multiplied in the laboratory and introduced back into the body to fight the tumour [35]. Stem cell therapy involves the use of the anti-inflammatory and regenerative effects of mesenchymal stem cells and the differentiation ability of induced pluripotent stem cells, which are used to repair damaged tissues [36]. Current research in the field of cell therapy technology is aimed at creating personalised immune cells for each patient, using new cell types, such as natural killer cells and gamma-delta T cells, and developing new methods for modulating the immune response.

Therapy with radiopharmaceuticals – drugs containing radioactive isotopes that are directed directly to cancer cells, destroying them from the inside. The drug is administered intravenously. A radioactive isotope is combined with a carrier (often an antibody or small molecule) that has a high affinity for specific molecules on the surface of cancer cells. It transports the radioactive isotope to the tumour, where it accumulates in cancer cells and emits energy that damages the DNA of these cells, leading to their death [37]. Important research is currently underway in the field of radiopharmaceutical therapy. Scientists are developing new radioactive isotopes with shorter half-lives and greater efficiency and are working on new carriers to deliver radioactive isotopes to tumours faster and more accurately. 3D printing technology has become a revolutionary not only in the field of prosthetics but also in other areas of medicine, including oncology. This technology makes it possible to create exact replicas of organs, tissues and tumours for treatment planning and the creation of personalised implants. Creating a 3D model involves several stages. At the first stage, a three-dimensional image of the tumour and surrounding tissues is built using CT or MRI images; at the second stage, the data is processed using special software; at the third stage, the model is printed on a 3D printer using biocompatible (non-toxic, bioinert and bioactive) materials, such as polymers or metals [38]. 3D models in the fight against cancer allow for the planning of surgical interventions, enabling surgeons to study the patient's anatomy in detail and determine the optimal access to the tumour, develop individual implants, adjust the accuracy of radiation targeting the tumour while minimising damage to healthy tissues, and create training models for surgeons to learn from. Scientists are currently working on the development of bioprinting technologies that allow the creation of tissues and organs from living cells, which will open prospects for the creation of personalised transplants, and the search for new biocompatible materials that will have improved properties and allow for the creation of more functional implants.

Despite the existence of many innovations in cancer treatment, none of the developed methods is universal and has certain drawbacks and limitations. Therefore, along with their improvement, research is being conducted on combination therapy as a means of achieving a synergistic effect, overcoming tumour resistance to certain types of treatment and reducing the likelihood of disease recurrence. The most promising areas of this therapeutic approach are the combination of immune therapy with other treatments and the search for new effective combinations of chemotherapeutic, targeted and immunotherapeutic drugs [39]. The field of personalised medicine is currently being actively developed in all areas of medicine. It has great prospects of becoming a leading treatment method in oncology, as it can be used to consider all the unique genetic characteristics of each patient, which is highly relevant given the complex anatomy of cancer. Genetic analysis of a tumour sample can be used to identify mutations in the genes that lead to its growth and development and to select the type of treatment that will most effectively affect these mutations and stop the development of the disease [40]. The main advantages of personalised medicine are the high efficiency of therapy, reduction of side effects and expansion of treatment options for patients with rare forms of cancer. Among the current developments in this area, an important place is occupied by the development of faster and cheaper DNA sequencing technologies, the development of immuno-oncology and the creation of tumour biobanks to compare genetic data of different patients as a basis for using machine learning technology for diagnosis and treatment.

There are currently many examples of developments used in clinical oncology. CAR-T cell therapy, which uses genetically modified T-cells to recognise and destroy cancer cells, is carried out using axicabtagene ciloleucel, a drug approved for the treatment of large B-cell lymphoma and diffuse large B-cell lymphoma, and tisagenlecleucel, a drug approved for the treatment of acute lymphoblastic leukaemia in children and young adults [41]. The use of checkpoint inhibitor drugs that block the mechanisms that allow cancer cells to evade the immune system (nivulumab, pembrolizumab, atezolizumab – inhibitors of programmed cell death protein 1 (PD-1) and Programmed cell death ligand 1 (PD-L1) molecules, ipilimumab – cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) inhibitor) [42]. The development of drugs that inhibit angiogenesis has led to the development of bevacizumab, a drug that blocks the action of the vascular endothelial growth factor protein, which stimulates the formation of new blood vessels; sorlafen, a broad-spectrum drug that inhibits not only angiogenesis but also other processes necessary for tumour growth; sunitinib is a drug with multikinase activity that inhibits tumour growth by blocking several signalling pathways; pazopanib is a tyrosine kinase inhibitor that blocks tumour growth [43-45]. The study of the possibility of blocking the expression of genes necessary for the survival of cancer cells accelerated the development of patisiran, the first RNA interference-based drug approved for clinical use and currently used to treat hereditary transthyretin amyloid polyneuropathy [46].

The most relevant factor that directly affects the development and implementation of innovative methods of early detection and treatment of cancer is the epidemiological situation. However, this process also depends largely on the influence of a combination of other factors, among which the main ones are the scientific, technical, regulatory, economic, social and infrastructural levels of the subject of scientific activity. Innovations in oncology, such as artificial intelligence and personalised medicine, have the potential to bridge disparities between high- and low-income countries. While high-income nations focus on refining these technologies, low-income countries could benefit from cost-effective applications that enhance early detection and treatment accessibility. Global collaboration, including knowledge sharing and subsidising technological implementation, is essential to ensure that these advancements contribute to reducing the global cancer burden and improving healthcare equity. The scientific and technical level is determined by the speed of scientific discoveries, technological capabilities and strength of ties in international cooperation; the regulatory level – by the level of legislative and state support for scientific activity, as well as the effectiveness of regulatory bodies; the economic level – by the level of financing of the industry, the price of drugs and the level of competition; the social level – by the availability of treatment, public awareness and ethical aspects; the infrastructural level – by the availability of modern At the level of individual countries, the combination of these factors creates potential opportunities and limitations, the balance of which determines the state of scientific development in the field of oncology. The impact of these factors on the development and implementation of new approaches to early detection and treatment of cancer should be considered in the example of the countries of Southern Europe and Central Asia, addressing the regional and global epidemiological situation (Figure **1**).

According to statistics, the problem of cancer morbidity and mortality is quite acute, especially for countries in the European region. The morbidity and mortality rates in Europe are twice as high as the global average and more than 3.5 times higher than in Central Asia. There are several probable reasons for this situation. Given that the risk of developing cancer increases with age, an important reason for the high incidence rates in Europe is the ageing of the population. A more developed cancer registration system allows for a more accurate assessment of cancer prevalence. In other regions, especially in low- and middle-income countries, the registration system may be less effective, leading to underestimation of the number of cases. A focus on prevention and early diagnosis, as well as greater public awareness, allows for early detection of the disease, which can lead to an increase in the number of reported cases, but also improve the prognosis for patients. This is also evidenced by the percentage ratio between morbidity and mortality, which is 45% in Europe and 53% in Central Asia [47-49]. This epidemiological situation creates a demand for and at the same time depends on the development of new effective treatments, contributing to the involvement of scientific, technical, economic, regulatory, social and infrastructure resources in this process.

Analysing the state of modern developments and innovations in the early detection and treatment of cancer in Albania, it is worth identifying limitations and assessing positive trends that affect this process. The unfavourable factors that hinder its development include insufficient funding for oncology; restricted access to the latest technologies, including modern equipment, software, and reagents required for complex research and development in the field of oncology; insufficient funding for scientific research; and shortage of qualified personnel – a lack of scientists with experience in working with modern technologies; weak integration into international scientific networks – limited participation of Albanian

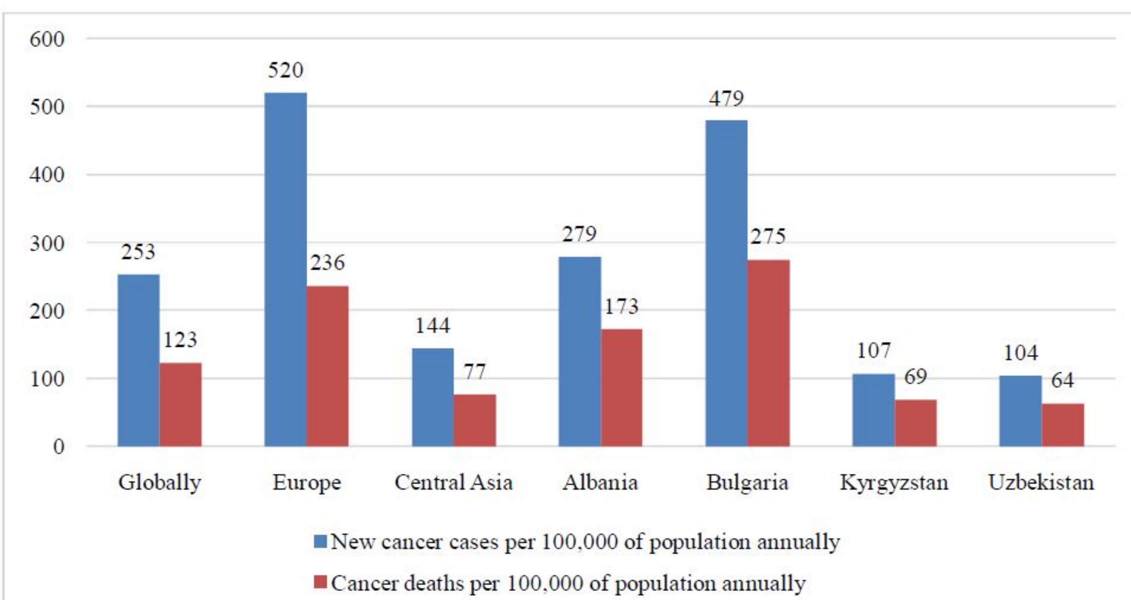

Figure 1: Global and regional cancer incidence and mortality statistics for the year.

Note: due to the lack of up-to-date statistics, the data used is for 2022.

Source: compiled by the authors based on International Agency for Research on Cancer [10-16].

scientists in international research projects; complications in conducting clinical trials and registering new drugs due to bureaucratic restrictions; lack of efficiency and transparency of regulatory bodies, which hinders the development and implementation of innovations in the field of oncology; problems with the logistics of medicines and medical devices, especially in the regions; uneven distribution of modern clinic equipment between large cities and regions. Potential development paths for cancer research and innovation include cooperation with international organisations, which facilitates the transfer of knowledge and technology, attracts additional funding, and allows countries to use the experience of other countries with more developed healthcare systems, which will help avoid some mistakes and accelerate the development of domestic cancer service [50]. Positive trends towards improving this situation are the increase in modern clinics with high-quality equipment in large cities and the rise in public awareness of the importance of early cancer diagnosis.

The factors affecting the decrease in the effectiveness of scientific developments in the field of oncology in Bulgaria have both similar and more specific limitations to those in Albania. These include underfunding of research projects in the field of oncology, outdated equipment in some medical and scientific institutions, limited integration into international scientific networks, uneven distribution of modern equipment across regions, and a shortage of highly qualified personnel due to the emigration of scientists and doctors to countries with more developed economies. Another important factor in slowing down the process of scientific development in oncology is the ongoing problems with corruption and inefficiency, which, despite the development of the regulatory system, have not yet been resolved. Nevertheless, the presence of many positive trends indicates Bulgarin's high potential in the field of cancer control. These include close cooperation with international organisations, attracting investment and assistance from European funds to increase the number of modern equipment in clinics and research centres, developing private clinics to stimulate competition and promote the introduction of new technologies, and raising public awareness of the importance of early cancer diagnosis, stabilisation of the supply of medicines and medical devices between the regions of the country and opening up new opportunities for funding research, more harmonised legislation and implementation of European standards in healthcare through integration into the European Union [51]. The challenges faced by Bulgaria, such as underfunding, outdated equipment, and uneven resource distribution, mirror similar obstacles in other low- and middle-income countries. However, Bulgaria's integration into the European Union offers a unique advantage through access to international funding and regulatory frameworks, which may accelerate the adoption of modern technologies. Compared to Central Asia, where geographic and infrastructural barriers are more pronounced, Bulgaria's primary focus on harmonising with EU standards demonstrates a different pathway to addressing shared challenges in oncology innovation.

Despite the positive trends, the situation with the development of scientific achievements in the field of oncology in Albania and Bulgaria is still at a low level. This is confirmed by the epidemiological situation in both countries. In terms of the number of registered cases, they are lower than the European average, but in terms of the mortality-to-morbidity ratio, they significantly exceed it – in Albania by 17% (62% vs. 45%), in Bulgaria by 12% (57% vs. 45%), which may indicate the insufficient effectiveness of the methods used for early detection and subsequent treatment of cancer in both countries. The constraints affecting the development and implementation of innovations in cancer control in Kyrgyzstan include insufficient funding for scientific research in the field of oncology; a shortage of oncologists, radiologists and other qualified personnel, especially in the regions; outdated equipment in scientific and medical institutions; poor integration into international scientific networks; and difficult access for residents of remote regions due to the specifics of mountainous terrain; limited access to quality water and food, which increases the risk of cancer among the population; outdated and non-adapted legislation that hinders clinical trials and registration of new drugs; unstable government policies that lead to disruptions in the provision of medical facilities and complicate long-term planning; often inefficient regulatory authorities that lead to delays in registration procedures and bureaucratic issues. Positive trends that may have a certain impact on the overall situation with the development of this industry include cooperation with international organisations, the development of private clinics offering a wider range of services, including modern treatment methods, and a gradual increase in public awareness of the importance of early cancer diagnosis [52].

Similarly to Kyrgyzstan, limited funding for research, a shortage of qualified personnel, poor integration into international scientific networks and the lack of modern equipment in the regions are the main issues in the development of oncology research and innovation. Despite the compliance of the legislation with international standards and the satisfactory performance of the regulatory authorities, there are still certain bureaucratic obstacles in the country that slow down the process of scientific development and delay the registration of new medicines. Cooperation with international organisations, the development of private clinics, raising public awareness of the importance of early cancer diagnosis, efforts to remove bureaucratic obstacles that hinder the process of scientific development in oncology, certain state support for the oncology sector, and efforts to speed up the registration and implementation of scientific developments can help reduce the impact of such restrictions [53].

Currently, the imbalance between restrictions and positive trends in Kyrgyzstan harms the development of innovations in cancer control. This is evidenced by the epidemiological situation. Despite the lower incidence rate in the countries compared to the region they are part of, the mortality-to-morbidity ratio in Kyrgyzstan exceeds the regional rate by 11% (64% vs. 53%), the European rate by 19% (64% vs. 45%), in Uzbekistan the regional rate by 8% (61% vs. 53%), and the European rate by 16% (61% vs. 45%). A common problem in all four countries that affects the development of oncology R&D and innovation is the underfunding of the healthcare sector (Figure **2**).

Bulgaria currently has the highest potential, given the positive trends and the level of current healthcare expenditure, which can be explained by the expanding opportunities for economic growth and research and development available in the European Union (Figure **3**). Albania, as a country in transition that is not a member of this alliance, has certain difficulties with funding, legislation and regulatory factors that hinder the development of scientific developments in the fight against cancer. Bureaucratic restrictions arising from discrepancies between national legislation and European standards have a significant impact, making it difficult to conduct clinical trials and register new drugs. In addition to these limitations, the situation is worsened by the demographic factor, with a large population creating additional challenges for the organisation of an effective healthcare system, and the diversity of climatic conditions, which can affect the spread of certain types of cancer. Unfavourable social and geographical factors in Kyrgyzstan complicate the development and implementation of innovations in the field of oncology and affect the quality of life of patients with cancer.

The results of the complex and long-term development of effective cancer treatment methods have already made it possible to transform cancer from an incurable disease into a disease that can be successfully controlled, ensuring long-term survival and improving the quality of life. However, the high mortality rate, which accounts for about half of all cases, requires increased efforts and stronger international cooperation between scientists and doctors around the world to accelerate the solution to this common problem.

4. DISCUSSION

When studying modern developments and innovations in the early detection and treatment of

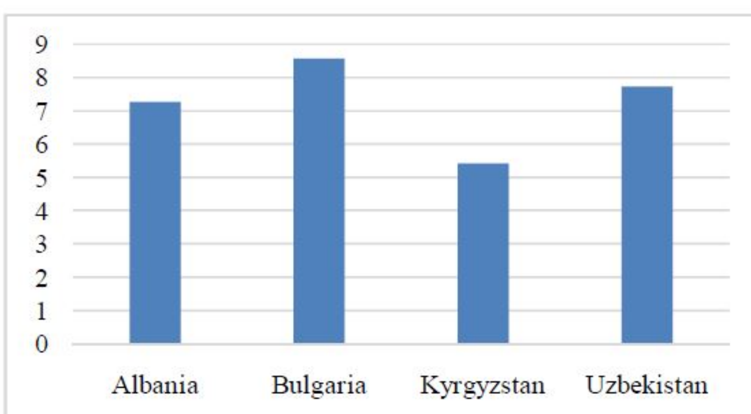

Figure 2: Current healthcare expenditure (% of GDP) in Albania, Bulgaria, Kyrgyzstan and Uzbekistan.

Note: due to the lack of up-to-date statistics, the data used is for 2021.

Source: compiled by the authors based on World Health Organization [17-20].

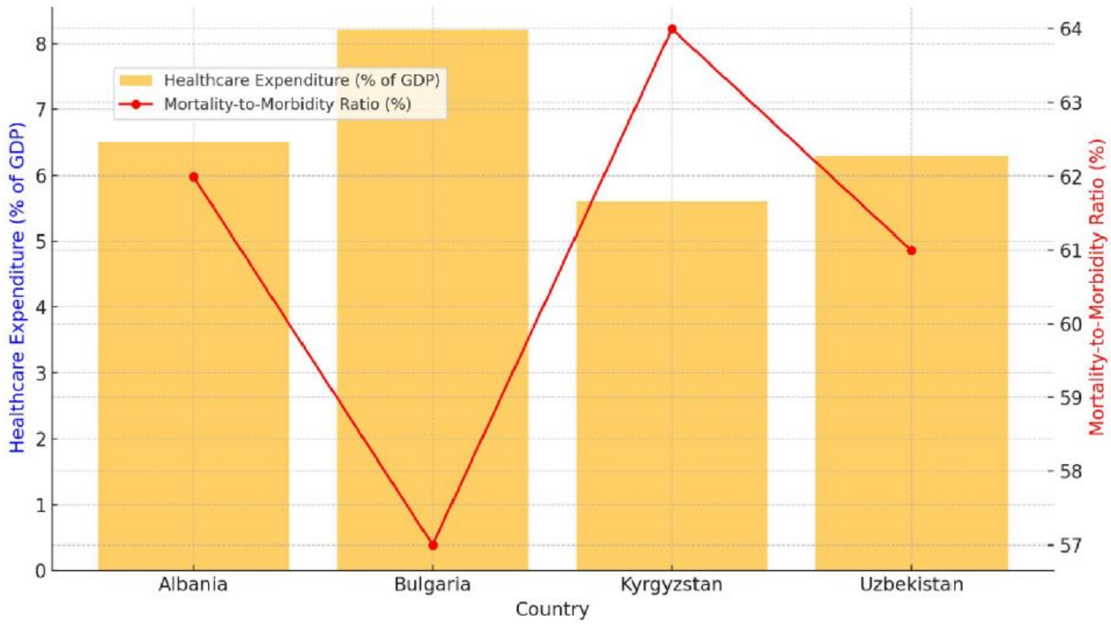

Figure 3: Healthcare expenditures and cancer outcomes across the regions.

cancer, it is difficult to assess the actual effectiveness of methods based on these developments. This is caused by some of them being at the testing stage, while others are just being introduced into clinical practice. Thus, the assessment of their effectiveness is based on an analysis of the available characteristics and mechanism of action. Therefore, it is necessary to compare the results obtained with the results of studies containing data on clinical trials of the diagnostic and therapeutic methods mentioned in this paper. This study is limited by several factors. First, the lack of comprehensive real-world clinical trial data on some innovations, such as liquid biopsy and advanced imaging technologies, restricts the ability to evaluate their long-term effectiveness. Additionally, financial constraints in low- and middle-income countries often delay the implementation of these developments, limiting their accessibility. Finally, disparities in healthcare infrastructure across the selected regions may introduce biases in assessing their applicability and success.

A clinical study of the effectiveness of CA19-9 as a reference marker for the early detection of pancreatic cancer was conducted by J.F. Fahrmann *et al*. [54]. Using the liquid biopsy method, the researchers evaluated 175 blood serum samples collected 5 years before the diagnosis of pancreatic cancer and compared them with samples from 875 patients obtained during screening for other cancers and samples from a control group of healthy individuals, patients with chronic pancreatitis and non-cancerous pancreatic cysts. Assessing the informative value of the CA19-9 biomarker, scientists concluded that it can be used as a reference marker for the early detection of pancreatic cancer and further monitoring of patients at risk. It is possible to partially agree with the conclusion of the scientists, but it is worth noting that there are certain limitations associated with this marker, such as insufficient specificity – elevated CA19-9 levels can be observed not only in pancreatic cancer but also in other diseases of the liver, pancreas and biliary tract. Therefore, despite the high sensitivity, it is advisable to confirm the results of diagnostics using this marker with MRI, PET-CT or ultrasound examinations.

The efficacy, safety and correlation of the toripalimab biomarker in the treatment of recurrent and metastatic nasopharyngeal carcinoma was investigated by F.H. Wang *et al*. [55]. In their paper, the researchers analysed the results of a Phase II clinical trial (POLARIS-02) evaluating the anti-tumour activity of a new PD-1 inhibitor for recurrent or metastatic nasopharyngeal cancer that is resistant to standard chemotherapy. At this stage of the study, toripalimab showed efficacy in terms of the duration of clinical response and safety in the treatment of recurrent and metastatic nasopharyngeal carcinoma. The results of a clinical trial conducted by scientists have virtually confirmed the benefits of immunotherapy over traditional cancer treatment. Toripalimab, as an innovative immuno-oncological drug belonging to the class of immune checkpoint inhibitors, targets the PD-1 molecule on the surface of T-lymphocytes [56]. It is this mechanism of action that ensures the long-term remission recorded in the study patients and the effectiveness in the treatment of certain types of cancer, in particular nasopharyngeal carcinoma, which does not respond to standard therapy. As of today, toripalimab has completed 3 phases of clinical trials and is approved for use in clinical practice for the treatment of melanoma, especially metastatic melanoma, non-small cell lung cancer, bladder, head and neck cancer [57-59]. This drug is not yet widely used for the treatment of nasopharyngeal carcinoma, which is due to the limited clinical trial data. Therefore, the study of F. H. Wang *et al*. may be useful in further trials to reach unambiguous conclusions about the feasibility of its use in the treatment of this type of cancer.

The impact of the introduction of a genetic test on the lifetime risk of prostate cancer in general practice was assessed by J. Fredsøe *et al*. [60]. A cluster randomised controlled trial determined that men who had undergone a genetic test for prostate cancer risk and were found to be at high risk had a higher propensity to undergo a second PSA test over the next two years compared to men with normal genetic risk. These results demonstrate the effectiveness of genetic tests as an effective tool for the prevention and early detection of cancer. Agreeing with the conclusions of the scientists, it is worth adding that a significant drawback of these tests is their high cost, which limits their use in general clinical practice. The authors of the publication also emphasise this, noting that among the study participants who underwent a genetic test, a large proportion were young men with high incomes.

The theoretical advantages of 3D printing technology are proved based on practical experience by Y. Chen *et al*. [61] published the results of a quasi-randomised clinical trial. During the study, 89 patients were divided into 2 groups: the first group included patients whose plan for localised thoracoscopic segmental lung cancer resection was based on preliminary positioning and simulated surgery performed using 3D reconstruction of the chest CT scan and 3D printing; the second group included patients whose surgery planning was based on improved 3D reconstruction images obtained during CT scanning. The quality indicators of the surgical intervention were the speed of the surgical approach, the frequency of the surgical method, the duration of the operation, intraoperative blood loss, and the incidence of postoperative complications. Significant differences in these indicators between the two groups were in favour of planning the operation using 3D printing technology, they had an advantage in the speed of approach switching by 10.5%, in the duration of the operation by 48 minutes, in the intraoperative blood loss by 53.43 ml, in the speed of switching the surgical method to lobectomy by 10.5%, but in terms of postoperative complications, the technology of using 3D reconstruction images from CT was superior by 9.3%. After analysing these results, the researchers concluded that planning an operation with 3D printing technology makes it easier for surgeons to identify nodules more accurately and generally improves the accuracy and safety of the surgical procedure. It is possible to agree with the authors' conclusions and add that the use of 3D models can be used to anticipate difficulties during surgery and find the best way to solve them at the preparation stage, reducing the impact of hidden risks and increasing the success rate of the operation.

Analysing clinical trials on personalised cancer medicine, it can be noted that most of them publish the results of phase I trials. Currently, the pharmaceutical market does not have a single vaccine for personalised cancer treatment that has passed all three phases of clinical trials [62, 63]. The reasons for this delay may be related to the "youth" of the technology, the complexity and high cost of cellular research, and the length of time it takes to find the optimal combinations of different therapies [64, 65]. Nevertheless, this area has high potential and prospects, as evidenced by the number of scientific papers and the optimistic results of phase I trials. Such results were published by L.A. Rojas *et al*. [66] in a study of the effectiveness of personalised RNA-neoantigen vaccines that stimulate T cells in pancreatic cancer. The researchers used mutational T-cell neoantigens contained in pancreatic ductal adenocarcinoma as a target for the vaccine. In the Phase I trial of adjuvant autogenous cevumeran, an individual neoantigenic vaccine based on uridine mRNA lipoplex nanoparticles, scientists synthesised mRNA neoantigenic vaccines from surgically removed adenocarcinoma tumours. Postoperative treatment for patients included immunotherapy against PD-L1 (atezolizumab), autologous cevumera and a modified mFOLFIRINOX chemotherapy regimen of four drugs (folic acid, fluorouracil, irinotecan and oxaliplatin). The efficacy was determined by the induction of neoantigen-specific T cells by the vaccine and 18-month relapse-free survival. After therapy, the induction of high-amplitude neoantigen-specific T cells was observed in 50% of patients, with the number of T cells multiplied by the vaccine, including repeated multiplication after the booster, reaching up to 10% of all blood T cells. Relapse-free survival of patients was extended with the vaccine to 13.4 months but did not reach the expected 18 months. It is possible to agree with the authors' conclusions that the use of atezolizumab adjuvant, autologous cevumeran and mFOLFIRINOX induces significant T-cell activity, delaying the recurrence of pancreatic cancer, as this indicates the effectiveness of the developed vaccine, given the high mortality rate of this type of cancer [67, 68]. However, before the start of phase II trials, it is advisable to modify the vaccine to increase the recurrence-free survival rate to the planned 18 months.

As the results of the analysed studies show, the development and implementation of new approaches aimed at early detection and treatment of cancer is a technically complex, resource-intensive and lengthy process that brings scientists and doctors closer to overcoming the problem of high mortality from this disease with each step. Therefore, economic, regulatory, social and infrastructural factors must not slow down this process but rather contribute to its efficiency and acceleration.

5. CONCLUSIONS

The search for new methods for the early detection and treatment of cancer is a key area of development in modern oncology. Among the most effective innovative approaches to diagnosing this disease are liquid biopsy, the discovery of new biomarkers, improved imaging techniques, the use of artificial intelligence and genetic testing. Based on these approaches, methods have already been developed and continue to be developed to detect various types of cancer at an early stage, when treatment can be most effective. Given the shortcomings and side effects of traditional treatments, modern cancer treatment developments are aimed at targeting the tumour. The most promising of these are immunotherapy, targeted, cellular, combined and personalised therapies, the development of radiopharmaceuticals, and 3D printing.

The main factors affecting the process of developing and implementing innovative methods of cancer diagnosis and treatment include the scientific, technical, economic, social, regulatory and infrastructural levels of individual research centres or the healthcare sector of a particular country or region. Comparing the impact of these factors on the oncology R&D process in Albania, Bulgaria, Kyrgyzstan, the study determined that a common problem for each country is insufficient funding for R&D and innovation. Bulgaria, as a member of the European Union, currently has the greatest opportunities for the development of the oncology industry. The limitations that slow down cancer research in Albania are due to the shortcomings of economic and regulatory processes associated with the specifics of a transitional economy. The situation with research and development in Uzbekistan is complicated by the burden on the healthcare system due to the large population and climate, which can contribute to the spread of certain types of cancer. In addition to these limitations, the development of innovations in the fight against cancer in Kyrgyzstan is complicated by social and geographical factors that hinder scientific development and affect the quality of medical care for patients with cancer. Comparisons among the selected countries reveal shared challenges, such as underfunding and limited access to modern technologies, but also demonstrate differing approaches to addressing these issues. For example, Bulgaria leverages EU resources to modernise its oncology infrastructure, while Uzbekistan relies on bilateral cooperation with international organisations to enhance its capacity. Kyrgyzstan faces additional obstacles due to its mountainous terrain, which limits access to healthcare, whereas Albania's transition economy creates regulatory and financial hurdles that impede research progress.

Given that research into new areas of cancer diagnosis and treatment is developing under the influence of the aforementioned factors, which often hinder progress, the primary recommendation of this paper is to expand international scientific cooperation between researchers and healthcare professionals. Such collaboration can accelerate efforts to address the global burden of cancer by fostering the exchange of knowledge, technologies, and best practices. Policymakers should prioritise increased funding for oncology research and create incentives for private sector investment, while healthcare institutions must enhance training and capacity building, particularly in under-resourced regions. Researchers should focus on developing cost-effective diagnostic and therapeutic solutions tailored to regional socio-economic conditions. Future research should assess the ethical implications of clinical trials in oncology, particularly in regions with limited regulatory frameworks, and explore the cost-effectiveness of innovative approaches to ensure wider accessibility. Investigating region-specific interventions that address environmental, social, and economic factors influencing cancer incidence and treatment outcomes is also essential. Furthermore, studies should examine strategies to overcome logistical and infrastructural barriers to cancer care in remote areas and the role of public awareness initiatives in reducing stigma and promoting early diagnosis.

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Received on 08-11-2024 Accepted on 02-12-2024 Published on 31-12-2024

https://doi.org/10.30683/1929-2279.2024.13.12