CLINICAL AND ECONOMIC JUSTIFICATION OF SOFTWARE SCREENING PERFORMANCE OF COLORECTAL CANCER AT THE REGION LEVEL

Yu.Yu. Petukhova1,2, E.V. Eliseeva1, A.G. Petukhova3

1 Pacific State Medical University, 2, Ostryakov Ave., Vladivostok, Russia 690002
2 Primorsky Regional Oncological Dispensary 59, Russkaya Str., Vladivostok, Russia, 690105

E-mail: juliapetukhovavl@mail.ru

Received 01 Juny 2021 After peer review 20 Nov 2021 Accepted 24 Nov 2021

The aim of the study is to assess the clinical and economic effectiveness of the practical implementation results of programmed screening for colorectal cancer (CRC) in the Primorsky Territory using clinical and economic research methods.

Materials and methods. In the study, the following kinds of data were used: the statistical data from the regional clinic’s cancer registry on the structure of the morbidity and average life expectancy of CRC patients in the Primorsky Territory; the data on the cost of screening studies and the stages of anticancer therapy in accordance with the “Territorial Tariff Agreement on Payment for Medical Care (Medical Services) in the System of Compulsory Health Insurance in the Territory of Primorsky Krai”, 2021. Two methods of clinical and economic analysis with the corresponding calculation formulas have been applied. The cost of medical interventions were estimated in accordance with the screening standards and clinical guidelines for the treatment of malignant neoplasms of the colon and rectum, approved by the Scientific and Practical Council of the Ministry of Health of the Russian Federation, 2020.

Results. The evidence-based substantiation of screening clinical effects has been obtained: the structure redistribution of colorectal cancer incidence towards the prevalence of early forms by 16.81%; the average increase in the life expectancy of patients with the studied disease is 12.8 months. A natural consequence of these events is the predicted decrease in the mortality rate from CRC in the territory of the subject in the subsequent years. The economic justification of CRC screening software which guarantees a significant saving in health care resources amounting to 23% compared to an alternative strategy, has been demonstrated. It can influence the management decisions on the further strategy of the mass introduction of this medical technology.

Conclusion. Currently, CRC screening is the most effective way to reduce morbidity and mortality from this disease. The predominance of the early diagnosis of the disease is extrapolated to significant savings in public health care. A promising direction for further research in the field of CRC screening is the study of its long-term effects, in particular, a detailed clinical and economic analysis of the diagnostics effectiveness and the elimination of premalignant neoplasms.

Keywords: colorectal cancer; screening; clinical and economic analysis; morbidity; cost of treatment; resource saving; special pharmacotherapy; cost; pharmacotherapeutic interventions; effectiveness

Abbreviations: CRC – colorectal cancer; IARC – International Agency for Research on Cancer; ASCO – American Society of Clinical Oncology; WHO – World Health Organization; FIT – fecal immunochemical test; gFOBT – Guaiac fecal occult blood test; FCS – fibrocolonoscopy; CDI – cost difference indicator; CMA – cost/minimization analysis MN – malignant neoplasm; DC – direct cost; CER – cost-effectiveness ratio; Ef – effectiveness; DRG – Diagnosis-Related Group; CHIS – Compulsory Health Insurance System; WPT – willingness-to-pay threshold; LYS – life year saved; QALYS – quality-adjusted life-year saved; GDP – gross domestic product; CSAMIs – Central Storage Archive of Medical Images.

DOI: 10.19163/2307-9266-2021-9-6-465-475
КЛИНИКО-ЭКОНОМИЧЕСКОЕ ОБОСНОВАНИЕ
ЦЕЛЕСООБРАЗНОСТИ ПРОГРАММНОГО СКРИНИНГА
КОЛОРЕКТАЛЬНОГО РАКА НА УРОВНЕ СУБЪЕКТА

Ю.Ю. Петухова1,2, Е.В. Елисеева1, А.Г. Петухова1

1 Федеральное государственное бюджетное образовательное учреждение высшего образования «Тихоокеанский государственный медицинский университет» Министерства здравоохранения Российской Федерации
690002, Россия, г. Владивосток, пр-т Остякова, 2
2 Государственное бюджетное учреждение здравоохранения «Приморский краевой онкологический диспансер»
690105, Россия, г. Владивосток, ул. Русская, 59

Получена 01.06.2021                       После рецензирования 20.11.2021                       Принята к печати 24.11.2021

Цель. Оценить клиническую и экономическую эффективность результатов практической реализации программного скрининга колоректального рака (КРР) на территории Приморского края с использованием методов клинико-экономического исследования.

Материалы и методы. В исследовании использованы статистические данные канцеррегистра краевого онкологического диспансера о структуре заболеваемости и средней продолжительности жизни больных КРР в Приморском крае; данные о стоимости скрининговых исследований и этапов противопоказанной терапии в соответствии с «Территориальным тарифным соглашением по оплате медицинской помощи (медицинских услуг) в системе обязательного медицинского страхования на территории Приморского края», 2021. Применены два метода клинико-экономического анализа с соответствующими расчетными формулами. Затраты на медицинские вмешательства оценивались в соответствии с стандартами скрининга и клиническими рекомендациями по лечению злокачественных новообразований ободочной и прямой кишки, одобренными Научно-практическим Советом Минздрава РФ, 2020.

Результаты. Получено доказательное обоснование клинических эффектов скрининга: перераспределение структуры заболеваемости КРР в сторону преображания ранних форм на 16,8%; среднее увеличение продолжительности жизни больных КРР на 12,8 мес. Закономерным следствием данных событий является прогнозируемое снижение уровня летальности от КРР на территории субъекта в последующие годы. Продемонстрирована экономическая целесообразность программного скрининга КРР, что гарантирует существенную экономию ресурсов здравоохранения, составляющую 23% по сравнению с альтернативной стратегией, и может повлиять на принятие управленческих решений по дальнейшей стратегии массового внедрения данной медицинской технологии.

Заключение. В настоящее время скрининг КРР является самым эффективным направлением в снижении показателей заболеваемости и смертности от данного заболевания. Преобладание диагностики ранних стадий заболевания экстраполируется в значимую экономию средств системы государственного здравоохранения. Перспективным направлением дальнейших исследований в области скрининга КРР является изучение его долгосрочных эффектов, в частности, детальный клинико-экономический анализ эффективности диагностики и элиминации предраковых новообразований.

Ключевые слова: колоректальный рак; скрининг; клинико-экономический анализ; заболеваемость; стоимость лечения; экономия ресурсов; специальная фармакотерапия; затраты; фармакотерапевтические вмешательства; эффективность

Список сокращений:
КРР – колоректальный рак; скрининг; клинико-экономический анализ; заболевания; стоимость лечения; экономия ресурсов; специальная фармакотерапия; затраты; фармакотерапевтические вмешательства; эффективность

INTRODUCTION
Colorectal cancer (CRC) is one of the most commonly diagnosed cancers worldwide. According to the information provided by the International Agency for Research on Cancer (IARC), colorectal cancer is the third most common cancer among men after lung and prostate kinds of cancer (10.6% or 1,065,960 cases in 2020). Among women with cancer, colorectal cancer ranks second in prevalence after breast cancer (9.4% or 865,630 cases in 2020) [1]. According to the Global Cancer Observatory (GCO) [2], the global burden of CRC...
is expected to increase by 60% (more than 2.2 million new cases and 1.1 million deaths) by 2030 [2]. Morbidity and mortality from colorectal cancer show wide geographical differences around the world: the highest rates are recorded in Australia and New Zealand, the lowest - in West Africa [3]. In Russia, in 2019, colorectal cancer (CRC) took the fourth place in the structure of the incidence of malignant neoplasms. Most of the cases are people aged 50 and over, but according to ASCO forecasts, 12% of colorectal cancer cases will be diagnosed in people under 50 years of age [4]. At the same time, an early diagnostics provides a 50–60% 5-year survival rate, while at stage IV it is less than 10% [5, 6].

The multistage theory of colon carcinogenesis explains the development of carcinoma through the stage of adenoma [7–9]. Depending on the evolution path of a malignant intestinal tumor [10], its manifestation can be realized from 4–5 to 20 years after its onset [11, 12]. This confirms a long asymptomatic course of this disease with the absence of active complaints in the patient [5]. Thus, a timely diagnostics and removal of colon and rectum adenomas are a priority to reduce not only mortality, but also the incidence of colorectal cancer [3, 13, 14].

There are two most effective screening strategies for colorectal cancer [15, 16]. First, colonoscopy is to be performed every 10 years, that provides the highest long-term clinical results, and it is the least expensive. Second, it is the annual fecal immunochemical test (FIT) [17]. This strategy is considered the best as well as the most cost-effective screening option, with a willingness-to-pay threshold more than €15,000 for each acquired life year [18]. Currently, a generalized 2-step screening standard for CRC is the examination of persons aged 50 to 75 years. The first stage is a laboratory determination of occult blood in feces (hemocult test, gFOBT, or, preferably, an immunochrom method – FIT). The second stage is fibrocolonoscopy (FCS) [13, 19, 20].

In the context of age restrictions for CRC screening, it should be notified that, in contrast to the decline in the incidence of colorectal cancer among the elderly, this indicator has almost doubled among young people since the early 1990s [21]. These are people younger than 50 years old who do not meet the screening recommendations [4, 22]. On the other hand, it has been proven that endoscopic resection of colon polyps is safe even for elderly patients aged 80 and older [23]. In this regard, nowadays, the optimal age for CRC screening is being revised [21]. Taking into account the growing economic burden of CRC, the cost of program screening and the economic effects of its implementation, a number of experts proposed the age of 32 years as the minimum threshold for screening studies [24].

**THE AIM** of the study is to assess the clinical and economic effectiveness of the practical implementation results of programmed screening for colorectal cancer (CRC) in the Primorsky Territory using clinical and economic research methods.

**MATERIALS AND METHODS**

This study was carried out in the area of diagnostics and treatment of colorectal cancer in the Primorsky Territory as a retrospective analysis of the data from 2016 to 2018. The choice of the period is due to the following facts: in 2016, screening for colorectal cancer was not carried out in the region; in 2017, the gradual introduction of screening began but did not have a regulatory basis; in 2018, in accordance with the Order of local health authority [5], the implementation of the CRC screening program began.

The practical foundation of the research, implemented in specific spatial-temporal conditions, made it possible to exclude the need to build a conceptual model of the initial stage implementation of the medical technology under consideration. By CRC, a set of malignant neoplasms of the colon and rectum corresponding to the C18-21 ICD-10 codes [6] is meant. The study is based on two methods of clinical and economic analysis: a cost/minimization analysis (CMA) and a cost/effectiveness analysis (CEA) [25]. In the first case, the cost difference indicator (CDI) was calculated using the formula:

\[
CMA = DC1 - DC2,
\]

where: DC1 is the cost when applying the 1st method; DC2 is the cost when applying the 2nd method.

In the second case, the cost/effectiveness ratio was determined:

\[
CER = DC/EF,
\]

where: DC is the cost; EF is the effectiveness (in this study, the unit of effectiveness is a month of life after making the diagnosis of colorectal cancer).

The resulting CER values corresponding to the study periods were compared. The optimal (smallest) cost-effectiveness indicator has been identified.

---

1. Kaplan AD, Starinsky VV, Shakhzadova AO. The state of cancer care for the population of Russia in 2019. – M.: MNIOI them. P.A. Herzen is a branch of National Medical Research Center of Radiology. 2020: 239 p. Russian
2. American Society of Clinical Oncology (ASCO). Available from: https://www.asco.org/.
3. International classification of diseases 10th revision (ICD-10). Available from: https://mkb-10.com/. Russian
4. Order of November 13, 2017 No 977-o “On the introduction of centralized screening of malignant neoplasms in the Primorsky Territory” (as amended on December 20, 2019). Available from: http://docs.cntd.ru/document/446638102/. Russian
5. GOST R 57525-2017. Clinical and economic research. General requirements Available from: http://protect.gost.ru/v.aspx?control=8 &baseC=6&page=2&month=&year=2017&search=&RegNum=1&Do cPageCount=15&id=210129&pagek=270D5A13-9BFF-4EE4-B026-A43760F3E20F/. Russian
In order to conduct this doublet of complementary clinical and economic studies, the average diagnostics cost and treatment of one CRC patient, depending on the stage of the disease, was determined, as well as the average predicted life expectancy of these categories of patients after the diagnosis had been made. The data obtained were converted into averages for each patient array identified in 2016, 2017, and 2018 and used to perform the corresponding calculations. As a result of the application of the above-listed research methods, the analysis of “the impact on the budget” of the implementation of the considered treatment and diagnostics strategies was carried out and presented in the study. Besides clinical and economic methods, the following additional research methods were used: statistical (summary and grouping of statistical observation materials) and sociological (collection and analysis of quantitative documentary information).

The statistical information used is provided by the databases of the Cancer Registry and the Software Department of the Primorsky Regional Oncological Dispensary. To obtain and process the data necessary for the research work, Microsoft Office Excel 2007 software was used, as well as medical information systems (DOKA+, Oncor and the Centralized Storage Archive of Medical Images (CSAMIs). The analyzed treatment strategy corresponds to the current clinical guidelines approved by the Scientific and Practical Council of the Ministry of Health of the Russian Federation. The calculations estimated the direct costs of medical interventions: screening studies and an anticancer treatment program. The expenses were accounted for in accordance with the current Territorial Tariff Agreement on Payment for Medical Care (Medical Services) in the Compulsory Health Insurance System in the Primorsky Territory. Inflationary expectations had not been considered.

Thus, the analysis eliminated the impact of changing price conditions on medical interventions during the period covered by the study. There is an assumption in the work: the patients with an unknown stage of the disease were not taken into account (their share among the identified patients in 2016 was 5.4%, in 2017 – 5%, in 2018 – 2.8%). The clinical and economic effects of detecting precancerous diseases were not the subject of this study and were not used to carry out the corresponding calculations.

**RESULTS**

In Primorye, CRC screening was set up in 2017. At that time, it did not have a regulatory framework and was opportunistic in nature. The implementation of centralized screening for colorectal cancer began in 2018 after the approval by the local health authority of the corresponding Order dated November 13, 2017 N 977-o “On the introduction of centralized screening of malignant neoplasms in the Primorsky Territory” (as amended on December 20, 2019).

Despite the absence of the screening program in 2017, 641 laboratory fecal occult blood tests were carried out as the first stage of CRC screening and subsequent FCC in the amount of 104 manipulations. The price expression of one hemostest is 846 rubles/$12, colonoscopy – 1,283 rubles/$18. The cost of performing blood tests was 542,286 rubles/$7,474, of endoscopic examinations – 133,432 rubles/$1,839. As a result, in 2017, the cost of a 2-stage CRC screening amounted to 675,718 rubles/$9,313.

In 2018, as a result of the introduction of centralized CRC screening, 13,245 laboratory occult blood tests were performed. The second, endoscopic stage of screening, was carried out by performing FCS in the amount of 1,045 procedures. The cost of performing hemotests was 11,205,270 rubles/$154,438, of carrying out endoscopic examinations – 1,340,735 rubles/$18,479. In 2018, the total cost of CRC screening amounted to 12,546,005 rubles/$172,916. Thus, the resource consumption of screening studies with the introduction of the Order on their planned implementation, increased by 11,870,287 rubles/$163,603.

In 2016, in the absence of CRC screening, 687 cases of CRC were diagnosed for the first time. In 2017, when screening appeared, there were 711 such cases, and in 2018, with the introduction of centralized screening, there were 769 cases. Therefore, taking into account the presented costs, the cost of screening corresponding to one case of a newly diagnosed CRC in 2017 was 950 rubles/$13, in 2018 – 16,315 rubles/$225, or 15,364 rubles/$212 more than before the screening program implementation (Fig. 3). The change in the structure of the CRC cases identified in 2016-2018, is presented in Table 1.

As it has been demonstrated, with the introduction of screening, the diagnostics of colorectal cancer improved. That was reflected in an increase in newly diagnosed cases of the disease, as well as in an increase in the number of patients diagnosed at stages I–II (Fig. 1).

---

8 Clinical guidelines. Malignant neoplasms of the colon and rectosigmoid section 2020. Association of Oncologists of Russia. Russian Society of Clinical Oncology. Available from: https://oncology-association.ru/files/clinical-guidelines-2020/zno_obodochnoj_kishki.pdf/, Russian

9 Territorial tariff agreement on payment for medical care (medical services) in the compulsory medical insurance system in the Primorsky Territory for 2021. Available from: http://omspk.ru/upload/iblock/701/TTC%20na%202021%20ru%20fa%20cafr).doc/, Russian

10 Order of November 13, 2017 N 977-o “On the introduction of centralized screening of malignant neoplasms in the Primorsky Territory” (as amended on December 20, 2019).

11 72.6022 RUB (rubles) for 1 USD (US dollar) – exchange rate of the Central Bank of the Russian Federation as of November 19, 2021.
Table 1 – Structure of CRC incidences in 2016-2018

| CRC localization          | Disease stage | 2016     | %   | 2017     | %   | 2018     | %   |
|---------------------------|---------------|----------|------|----------|------|----------|------|
| Colon malignant neoplasms | I             | 46       | 11.7 | 70       | 17.24| 98       | 21.8 |
|                           | II            | 85       | 21.7 | 129      | 31.78| 132      | 29.4 |
|                           | III           | 94       | 24   | 88       | 21.67| 102      | 22.7 |
|                           | IV            | 167      | 42.6 | 119      | 29.31| 117      | 26.1 |
|                           | Total         | 392      | 100  | 406      | 100  | 449      | 100  |
| Rectal malignant neoplasms| I             | 24       | 8.1  | 40       | 13.11| 45       | 14.06|
|                           | II            | 61       | 20.7 | 95       | 31.15| 96       | 30   |
|                           | III           | 84       | 28.5 | 80       | 26.23| 89       | 27.81|
|                           | IV            | 126      | 42.7 | 90       | 29.51| 90       | 28.13|
|                           | Total         | 295      | 100  | 305      | 100  | 320      | 100  |
| Total number of CRC cases | I             | 70       | 10.19| 110      | 15.47| 143      | 18.6 |
|                           | II            | 146      | 21.25| 224      | 31.5 | 228      | 29.65|
|                           | III           | 178      | 25.91| 168      | 23.63| 191      | 24.84|
|                           | IV            | 293      | 42.65| 209      | 29.4 | 207      | 26.91|
|                           | Total         | 687      | 100  | 711      | 100  | 769      | 100  |

Table 2 – Predicted life expectancy of CRC patients depending on the stage of the disease

| CRC stage | Average life expectancy of patients, months | Weighing coefficient of CRC contingent enrollment and corresponding average life expectancy, months | 2016 | 2017 | 2018 |
|-----------|--------------------------------------------|-------------------------------------------------------------------------------------------------|------|------|------|
| I         | 99                                         | 0.102                                                                                           | 10.1 | 15.4 | 18.4 |
| II        | 83                                         | 0.213                                                                                           | 17.7 | 26.1 | 24.7 |
| III       | 35                                         | 0.259                                                                                           | 9.1  | 8.3  | 8.7  |
| IV        | 13                                         | 0.427                                                                                           | 5.6  | 3.8  | 3.5  |

Figure 1 – Increase in diagnosed CRC cases and number of patients diagnosed at stages I–II of the disease in 2016–2018

Figure 2 – Costs of CRC treatment depending on the disease stage in 2016
According to the clinical guidelines approved by the Scientific and Practical Council of the Ministry of Health of the Russian Federation\(^\text{12}\) and the National Guidelines for the Drug Treatment of Malignant Tumors\(^\text{13}\), depending on the stage of the disease, a few worked out options should be used in the treatment of colorectal cancer. They are as follows: at stage I – surgical treatment; at...
stages II and III – surgical treatment followed by adjuvant drug therapy XELOX or FOLFOX for up to 6 months; at stage IV, as well as in the progression of the disease – sequentially prescribed lines of special pharmacotherapy (combined and independent modes of cytostatic and targeted agents). When the process is localized in the rectum, the treatment program, as a rule, includes radiotherapy or its combination with a pharmacotherapeutic component.

Making use of Diagnostic Related Groups (DRGs) Decoding medical care and the Territorial Tariff Agreement on Payment for Medical Care (Medical Services) in the CHI system in the Primorsky Territory for 2021, the authors calculated the cost of treating a CRC case depending on the stage of the disease. So the cost of treating a patient at stage I of the tumor process was 187,718 rubles/$2,587; at stages II and III – 819,830 rubles/$11,299. Chemoradiation therapy as a part of the rectal cancer treatment program adds 154,488 rubles/$2,129 to its cost. Stage IV, like the progression of the disease, requires the use of the most expensive treatment option – palliative, including molecular targeted pharmacotherapy. Taking into account the average duration of its use (9–11 months), the costs of treating one patient ranges from 2,015,680 rubles/$27,781 to 9,163,500 rubles/$126,297, which is on average equal to the amount of 5,589,590 rubles/$77,039. Knowing the above-mentioned numerical structure of CRC detected in 2016-2018, the authors calculated the budget for treating the contingent of patients at stages I, II, III, and IV.

The costs of colorectal cancer treatment in 2016 (Fig. 2) were as follows: at stage I – 16,847,972 rubles/$232,209 (0.87%), at stage II – 129,118,948 rubles/$1,779,594 (6.65%), at stage III – 158,906,732 rubles/$2,190,146 (8.18%), at stage IV – 1,637,749,870 rubles/$22,572,436 (74.3%). The total costs of treating CRC patients in 2016 amounted to 1,942,623,522 rubles/$258,772; at stages II and III – 819,830 rubles/$11,299. The average cost of treating one patient is 2,827,691 rubles/$38,973.

The costs of colorectal cancer treatment in 2017 (Fig. 3) were as follows: at stage I – 26,828,500 rubles/$369,766 (1.75%), at stage II – 19,831,280 rubles/$2,733,340 (12.85%), at stage III – 150,090,480 rubles/$2,068,636 (9.72%), at stage IV – 1,168,224,310 rubles/$16,101,157 (75.68%). In 2017, the total costs of treating CRC patients amounted to 1,543,461,570 rubles/$21,272,899. The average cost of treating one patient is 2,170,832 rubles/$29,920.

In 2018, the costs of colorectal cancer treatment (Fig. 4) were as follows: stage I – 33,795,634 rubles/$465,791 (2.16%), stage II – 201,752,088 rubles/$2,780,666 (12.91%), stage III – 170,336,962 rubles/$2,347,685 (10.9%), stage IV – 1,157,045,130 rubles/$15,947,079 (74.03%). The total costs of treating patients with CRC in 2018 amounted to 1,562,929,814 rubles/$21,541,222. The average cost of treating one patient is 2,032,418 rubles/$28,012.

Thus, compared with 2016, after the introduction of screening advent in 2017, the average treatment cost of 1 patient decreased by 656,859 rubles/9,053$, and after the introduction of software screening in 2018 – by 795,273 rubles/10,961$. Taking into account the fact that, at the same time, the CRC diagnostics cost increased by only 950 rubles/$13 in 2017 and by 15,364 rubles/$212 in 2018, the authors show the amount of obvious savings in healthcare resources. They have justified their conclusions by applying one of the main methods of clinical and economic research – the analysis of “cost minimisation”. The amount of cost for the diagnostics and treatment of 1 CRC patient in the absence of screening (2016) averaged 2,827,691 rubles/$38973, and after the appearance of screening (2017) – 2,171,782 rubles/$29,933, in the first year of the program implementation (2018) – 2,048,733 rubles/$28,236.85. According to the formula for calculating the cost difference indicator, when comparing the expenses in 2016 and 2017, the authors show its value as 655,909 rubles/$9,040, and when comparing the expenses in 2016 and 2018, its value is proved to be 778,958 rubles/$10,736.

The presented calculations convincingly demonstrate the cost savings for each case of screened CRC (Fig. 5).

To obtain more convincing evidence of the economic justification of program screening, a cost-effectiveness analysis as the most objective of the methods of clinical and economic research was applied. For this purpose, the Cancer Registrar information on the average life expectancy of CRC patients after the registration, depending on the stage of the disease, was used. Taking into account the number and structure of CRC cases, the authors calculated the average predicted life expectancy of CRC patients identified in 2016, 2017 and 2018. The corresponding calculated data are presented in Table 2.

Thus, the average predicted life expectancy of CRC patients detected in 2016, is 42.5 months (3.5 years), in 2017 – 53.6 months (4.5 years), in 2018 – 55, 3 months (4.6 years). Applying the formula for calculating the cost-effectiveness ratio, the average of diagnostics and treatment costs for 1 patient is put in the numerator, the average predicted life expectancy of CRC patients,
months, is put in the denominator. The CER calculated by the authors in 2016, was 66,534 rubles/$197; in 2017 – 40,518 rubles/$558, in 2018 it was 37048 rubles/$111.

The optimal value is considered to be the lowest value of the ratio, which corresponds to the program screening strategy in this study (Fig. 6).

The results obtained make it possible to analyze “the impact of medical technology on the budget”. The cost of providing CRC patients with medical care in 2016, amounted to 1,942,623,522 rubles/$26,774,385 (specialized treatment cost), in 2018 – to 1,575,475,819 rubles/$21,634,376 (screening and specialized treatment costs). The reduction in the resource consumption of the whole diagnostics and treatment process of the entire CRC array, identified in the Primorsky Territory in 2018, amounted to 367,147,703 rubles/$514,009. Thus, the reduction in the financial support of medical care for the disease under study by 23%, compared with an alternative diagnostics and treatment strategy.

**DISCUSSION**

According to WHO principles, cancer screening is aimed at the early detection of the disease or its precursors [19]. Centralized CRC screening is currently actively used in most European countries, Canada, separate regions of the Americas, Asia and Oceania. The Netherlands showed the highest level of participation in the program (68.2%), and some parts of Canada – the lowest one (16%) [3].

A decrease in mortality from colorectal cancer observed in the latest 10 years, which is, in fact, a significant clinical achievement, is explained, first of all, by screening (53%) and, only second and third, by improved treatment (12%) and a controlled decrease in the influence of risk factors (35%) [4, 26]. It has been estimated that increasing the prevalence of CRC screening up to 80% in the next 2 years, will prevent 277,000 CRC cases which is more than 75% of the potential incidence rate, and 203,000 deaths by 2030 [4, 27]. The implementation of CRC screening programs is a rare example of effectiveness in oncological practice, yielding only to screening for cervical cancer in its clinical results [5].

At the same time, all over the world, more and more attention is paid to the cost and value of cancer treatment; among them, CRC is a nosological unit with a leading resource consumption. It is with this disease that the highest direct costs of the healthcare system of the Russian Federation are associated (52 milliard rubles per year), which are mainly attributable to anticancer pharmacotherapy [28–30]. Within the framework of the RF project “Combating Cancer”, in the period of 2019–2024, financing of the drug supply with anticancer preparations will be from 70 to 140 milliard rubles a year. However, the choice of a strategy for medical interventions is associated with an idea of a limited nature of the health care economic resources. This dictates the need for obtaining evidence not only of the clinical, but also of the economic justification of alternative medical technologies.

Professional oncological communities such as ESMO, ASCO are trying to analyze the cost-effectiveness of various treatment and diagnostic options for colorectal cancer. The complexity of this task lies in different costs of medical technologies in different countries. This fact does not make it possible to extrapolate the data on cost effectiveness from one country to another [31]. So, in Australia, thanks to the screening programs, the cost of the one year of life extension for CRC patients is $16,632, in the USA – up to $22,000, in Europe – up to $5,000 [17, 19, 23]. However, nowadays, the undoubted economic justification of colorectal cancer screening is beyond dispute among specialists in the United States and most European countries [16].

On the basis of two main methods of clinical and economic analyses, identical results, indicating a high clinical effectiveness of CRC screening were obtained. The presented data indicate that even opportunistic screening (2017), in comparison with the rejection of it, demonstrates a more optimal detection of the disease, both in quantitative and structural terms, as well as the predicted life expectancy of CRC patients at diagnosis. The number of patients with newly diagnosed CRC in 2017 increased by 3.49% (24 people) compared to 2016; the number of the identified at stages I–II of the disease – by 15.53% (118 people), the average predicted life expectancy of patients increased by 11.1 months. The very first year of the screening program implementation in the territory of the subject reinforced these advantages. The introduction of software screening in 2018, compared with its absence in 2016, provided an increase in the indicators under consideration by 11.9% (82 people), 16.81% (155 people) and 12.8 months, respectively (the expected consequence of these advantages will be a natural decrease in the mortality rate from CRC in the territory of the region in subsequent years).

These clinical effects are extrapolated into the cost reduction of expensive anticancer pharmacotherapeutic interventions, the most expensive among which are palliative drug regimens used in the treatment of advanced stages of colorectal cancer [28–30]. This economic advantage is confirmed by performing an analytical calculation of “the impact of medical technology on the budget”: a decrease in the level of the economic burden of the disease under study in the territory of the region in 2018 was 23% (367,147,703 rubles/$5,140,009) compared to the period not included in the screening program. Thus, the considered medical technology sig-
nificantly reduces the economic burden of CRC, avoiding excessive costs. This is consistent with the results of the screening programs in the United States and most of Europe. To assess the cost-effectiveness of CRC screening and other prevention strategies in these countries, a target willingness-to-pay threshold (WPT) of $30,000–50,000 is used, depending on the national health policy per life year saved (LYS) or per quality-adjusted life year saved (QALYS). The calculated cost-effectiveness ratio (CER) is on average $3,380/LYG, which makes it possible to consider a CRC program screening as the standard of the economic effectiveness [19]. Many countries, including the Russian Federation, comply with the WHO recommendations, adopting the formal threshold value of willingness-to-pay in monetary terms, equal to 1–3 level indicators of the gross domestic product (GDP) per capita. When applied to this criterion, the targeted implementation of CRC screening also demonstrates the results of a highly effective economic investment [17, 19, 23].

The experience of the US specialists also reports on significant long-term effects of screening, several times higher than the corresponding achievements at the initial stage of its implementation [3, 13]. So, after the initial growth in the CRC diagnostics rate, several years after the introduction of the program, there is a consistent decrease in the CRC incidences. At the same time, in the structure of the revealed CRC, the frequency of cases at stages I–II reaches 80%, at stages III–IV – no more than 25% [4]. Alongside with an early detection of malignant pathology, the aspect of premalignant neoplasms diagnostics is no less important in the CRC screening program. In this aspect, CRC screening, has obviously an even wider range of clinical and economic results, since the elimination of potentially malignant CRC neoplasms can reduce the CRC incidence by 20–90% according to the number of experts’ data [5, 8, 19]. These effects are expressed in an increase in the duration and improvement of patient QoL, as well as in significant savings in health care resources and costs of the population. This makes it possible to confidently expect the emergence of further evidence of a reduction in human and material losses due to the prolongation and mass implementation of screening software.

**CONCLUSION**

Accelerating progress in the struggle against colorectal cancer can be achieved by ensuring an access to high-quality precision health care for all patients and promoting healthier lifestyles to prevent cancer. Healthy behaviors such as a achieving normal body weight, being physically active, and avoiding excessive alcohol or smoking can reduce the CRC risk by at least one third. However, clinical and economic evidence of the widespread screening effectiveness states that even more cases of colorectal cancer and deaths from this disease could be prevented with its help. The steadily increasing burden of oncological pathology determines the perception of medical interventions aimed at the prevention and early diagnostics of malignant neoplasms as a necessary national strategy. For the full implementation of all the possibilities of CRC screening, the coverage of the population with research should be close to 80%. The principles of its application should be the universal availability and integrity of the health care system. If appropriate management decisions are made, a long-term prolongation of this technology in the territory of each constituent entity of the state can become a part of the practical implementation of the Federal project “Combating Cancer” (2019–2024). That will extrapolate to the implementation of its most important task: reducing the mortality rate from cancer by 6% (no more than 185 cases per 100 thousand people) until 2024.

**FUNDING**

This study did not receive any financial support from outside organizations.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**AUTHORS’ CONTRIBUTION**

Yulia Yu. Petukhova – study planning, data collecting and organizing, study conducting, analyzing and interpreting the results obtained, reviewing literary sources, manuscript writing, forming a list of references; Ekaterina V. Eliseeva – review of critical intellectual content, final approval of the manuscript for publication; Antonina G. Petukhova – participation in the development of the concept and design of the study, statistical processing of the results.

**REFERENCES**

1. Soerjomataram I., Bray F. Planning for tomorrow: global cancer incidence and the role of prevention 2020-2070. Nat Rev Clin Oncol. 2021; 18(10): 663–72. DOI: 10.1038/s41571-021-00514-z.
2. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017 Apr;66(4):683–91. DOI: 10.1136/gutjnl-2015-310912.
3. Navarro M, Nicolas A, Fernandez A, Lanas A. Colorectal cancer population screening programs worldwide in 2016: An update. World J Gastroen-
terol. 2017 May 28;23(20):3632–42. DOI: 10.3748/ wjg.v23.i20.3632.
4. Siegel RL, Miller KD, Fedewa SA, Ahnen DJ, Meester RGS, Barzi A, Jemal A. Colorectal cancer statistics, 2017. CA Cancer J Clin. 2017 May 6;67(3):177–93. DOI: 10.3322/ caac.21395.
5. Nesterov PV, Ukharskiy AV, Kislov NV. Regional clinical and economic model of colorectal cancer screening. Research and Practical Medicine Journal. 2020;7(3):146–59. Russian. DOI:10.17709/2409-2231-2020-7-3-15
6. Brenner H, Jansen L, Ulrich A, Chang-Claude J, Hoffmeister M. Survival of patients with symptom- and screening-detected colorectal cancer. Oncotarget. 2016 Jul 12;7(28):44695–704. DOI: 10.18632/oncotarget.9412.
7. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell. 1990 Jun 1;61(5):1–7. DOI: 10.1016/0092-8674(90)90186-i.
8. De Palma FDE, D’Argenio V, Pol J, Kroemer G, Maiuri MC, Salvatore F. The Molecular Hallmarks of the Serrated Pathway in Colorectal Cancer. Cancers (Basel). 2019 Jul 20;11(7):1017. DOI: 10.3390/cancers11071017.
9. Cross W, Kovac M, Mustonen V, Temko D, Davis H, Baker AM, Biswas S, Arnold R, Chegwidden L, Gatenbee C, Anderson AR, Koelzer VH, Martinez P, Jiang X, Domingo E, Woodcock DJ, Fung Y, Kovacova M, Maughan T; S:CORT Consortium, Jansen M, Rodriguez-Justo M, Ashraf S, Guy C, Cunningham T, East JE, Wedge DC, Wang LM, Balanova YuA, Drapkina OM, Kontsevaya AV, Mukaneeva YVYu, Schepkin KV. Colorectal screening. First results. Pelvic Surgery and Oncology. 2018;8(4):11
10. Zobnina MV, Karasev IA, Cherkes LV, Tumanyan AO, Malikhov AG, Malikhova OA. The serrated neoplasms of the colon: endoscopic diagnosis, the role in colorectal carcinoma. Experience Clin Gastroenterol. 2018;4(4):4–8. Russian.
11. Nguyen LH, Goel A, Chung DC. Pathways of Colorectal Cancer. Experand Clin Gastroenterol. 2018;(4):4–8. Russian
12. Polyanskaya EA, Tryakin AA, Tjulandin SA. Preoperative biopsy in differential diagnosis of colon epithelial formations. Pacific Medical Journal. 2018;1:41–3.
13. Skouras T, Bond A, Agalia A, Bonnett L, Jiang Lim M, Sarkar S. Outcomes and adverse factors for endoscopic mucosal resection (EMR) of colorectal polyps in elderly patients. Frontline Gastroenterol. 2020 Feb 25;12(2):95–101. DOI: 10.1136/fl gastro-2019-101294.
14. Palant M, Smee MC, Passerini CS, Steer JG, Zborowski M, Allen J, Skidmore S, Todorovic J, Rochau U, Oberaigner W, Koffijberg H, Fischer T, Schiller-Freuhwirth I, Öfner D, Renner F, Jonas M, Hackl M, Ferlitsch M, Siebert U; Austrian Colorectal Cancer Screening Model Group. Effectiveness, benefit harm and cost-effectiveness of colorectal cancer screening in Austria. BMC Gastroenterol. 2019 Dec 5;19(1):209. DOI: 10.1186/s12876-019-1121-y.
15. Zobnina MV, Ukharskiy AV, Kislov NV. Colorectal cancer screening. Current techniques and recommendations review. Innovative Medicine of Kuban. 2018;1(1):5–6. Russian.
16. Stoffel EM, Murphy CC. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults. Gastroenterology. 2020 Jan;158(2):341–353. DOI: 10.1053/j.gastro.2019.07.055.
17. Kasi PM, Shahjehan F, Cochuyt JH, Li Z, Kolibasenau DT, Merchea A. Rising Proportion of Young Individuals With Rectal and Colon Cancer. Clin Colorectal Cancer. 2019 Mar;18(1):e87–e95. DOI: 10.1016/j.clcc.2018.10.002.
18. Yagudina R.I., Serpik V.G., Babiy V.V., Ugrekhelidze D.T. Criteria of efficiency in pharmacoeconomic analysis. Pharmacoeconomics: theory and practice. 2017; 5(3):11–15. DOI: 10.30809/phe.3.2017.7.
19. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. Nat Rev Gastroenterol Hepatol. 2019 Dec;16(12):713–32. DOI: 10.1038/s41575-019-0189-8.
20. Desyatov D.P. , Polovinkin VV, Puzanova I.A. Colorectal cancer screening. Current techniques and recommendations review. Innovative Medicine of Kuban. 2018;1(1):5–6. Russian.
21. Stoffel EM, Murphy CC. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults. Gastroenterology. 2020 Jan;158(2):341–353. DOI: 10.1053/j.gastro.2019.07.055.
of oncological diseases associated with modifiable risk factors. Health Risk Analys. 2020; 1: 133–41. Russian
30. Gretsova OP, Derkach EV, Dombrovskiy VV, Ignatieva VI, Omelyanovskiy VV, Stenina MB. Socio-economic burden of breast cancer in the Russian Federation. Medic Technol. Eval & Select. 2016;4:32–49. Russian
31. Goldstein DA, Chen Q, Ayer T, Chan KKW, Virik K, Hammerman A, Brenner B, Flowers CR, Hall PS. Bevacizumab for Metastatic Colorectal Cancer: A Global Cost-Effectiveness Analysis. Oncologist. 2017 Jun;22(6):694–99. DOI: 10.1634/theoncologist.2016-0455.

AUTHORS

Yulia Yu. Petukhova – 3rd year postgraduate student, Pacific State Medical University; Deputy Chief Physician for Medical Work, Primorsky Regional Oncological Dispensary. ORCID ID: 0000-0002-0724-9736. E-mail: julia-petukhovavl@mail.ru

Ekaterina V. Eliseeva – Doctor of Sciences (Medicine), Professor, Head of the Department of General and Clinical Pharmacology, Vice-Rector, Pacific State Medical University. ORCID ID: 0000-0001-6126-1253. E-mail: eliseeva@tgmu.ru

Antonina G. Petukhova – 5th year student of the General Medicine Faculty, Pacific State Medical University. ORCID ID: 0000-0002-0387-098X. E-mail: petukhova_antoninagl@mail.ru