

Experience in implementing effective programs of colorectal cancer screening for the development of an appropriate model in Ukraine – a literature review

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ABSTRACT

Aim: To explore the potential for preventing cancer development through CRC screening programmes.

Materials and Methods: A number of foreign articles, international guidelines were analysed using PubMed, Google Scholar, Web of Science, and information from national government websites about the aspects of CRC screening programmes in countries with high rates of participation of the average-risk population as well as the stages of their implementation for national colorectal cancer screening program development in Ukraine.

Conclusions: The final goal of CRC screening is to decrease mortality by detecting disease at an early stage, which increases treatment effectiveness and provides a better prognosis, as well as reducing incidence in the long term. This decrease in CRC incidence is the result of massive detection of early asymptomatic cases before they progress to later stages.

KEY WORDS: model, public health, colorectal cancer, screening, cancer prevention, fecal immunochemical test

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide. More than 85% of CRC cases occur in high- and upper middle income countries. However, in lower middle- and low income countries, there is an insufficient level of detection of CRC, as a result, there is a gradual increase of mortality rates from this disease.

However, CRC can be treated if detected at an early stage. By removing polyps and pre-cancerous lesions during colonoscopy it is possible to prevent the development and progression of the disease. The high incidence of CRC and its late detection is a threat to the public health that requires systemic solutions at the national level.

AIM

To explore the potential for preventing cancer development through CRC screening programmes.

MATERIALS AND METHODS

A number of foreign articles, international guidelines were analysed using PubMed, Google Scholar, Web of

Science, and information from national government websites about the aspects of CRC screening programmes in countries with high rates of participation among average-risk population as well as the stages of their implementation for the prospective design of a national CRC screening programme in Ukraine. Articles and reviews were selected which contained information of existing CRC screening programmes and their successful variants. The publications were analysed using a non-systematic review method with the aim of compiling a brief overview of the collected information.

REVIEW AND DISCUSSION

In 2022, CRC is the third most common oncological disease worldwide among men (1,069,446 cases, 10.4% of all cases) and women (856,979 cases, 8.9% of all cases) [1] (Fig. 1).

More than 85% of CRC cases occur in high- and upper-middle income countries (according to the World Bank classification): 41.9% in high income countries and 43.3% in upper middle income countries and 81.7% of deaths (37.1% in high income countries and 44.6% in

Rank	Cancer site	Number of cases	Percent	Rank	Cancer site	Number of cases	Percent	Rank	Cancer site	Number of cases	Percent
1	Lung	1 572 045	15,2%	1	Breast	2 296 840	23,8%	1	Lung	2 480 675	12,4%
2	Prostate	1 467 854	14,2%	2	Lung	908 630	9,4%	2	Breast	2 296 840	11,5%
3	Colorectum	1 069 446	10,4%	3	Colorectum	856 979	8,9%	3	Colorectum	1 926 425	9,6%
4	Stomach	627 458	6,1%	4	Cervix uteri	662 301	6,9%	4	Prostate	1 467 854	7,3%
5	Liver	600 676	5,8%	5	Thyroid	614 729	6,4%	5	Stomach	968 784	4,8%
-	Others	4 974 131	48,2%	-	Others	4 325 410	44,8%	-	Others	10 835 921	54,2%
Number of new cases in 2022, males, all ages				Number of new cases in 2022, females, all ages				Number of new cases in 2022, both sexes, all ages			

Fig. 1. Top 5 most frequent cancers. Number of new cases worldwide in 2022.

upper middle income countries). In contrast, 14.8% of CRC cases occurred in lower middle- and low income countries (13.2% in lower middle income countries and 1.6% in low income countries) and 18.3% of deaths (15.9% in lower middle income countries and 2.4% in low income countries)[1] (Fig. 2).

The incidence rates of CRC in high- and upper middle income countries are 30/100,000 and 20.1/100,000, while the mortality rates of CRC in these countries are 10.2 and 9.0/100,000, respectively. Meanwhile, the incidence rates in lower middle- and low-income countries are: 8.1 and 8.0/100,000, while mortality rates are 4.6/100,000 for lower middle income countries and 5.6/100,000 for low income countries. This reflects the limited access to healthcare services, absence of screening programmes in these countries, and low detection rates of disease, which leads to higher mortality rates[1,2] (Fig. 3).

However, CRC can be treated if detected at an early stage. The overall 5-year survival rate for CRC diagnosed at stage I is 90%, and for metastatic stage IV, this figure drops to 10%. In Europe, on average, only 13-15% of patients are diagnosed with pre-cancer or at stage I, more than 55% of cases are diagnosed at stages III – IV, of which 24% are still diagnosed at late stage IV [3,4] (Table 1).

Polyps and precancerous lesions can be removed during colonoscopy, preventing the development and progression of the disease. The cost of screening is less than for treatment, ranging from 3,000€ for stage I treatment, to up to 170,000€ for a late stage treatment[4]. Overall, the average difference in the cost of treatment for early and late stages of CRC is tenfold between 4,000€ and 40,000€[5].

The high incidence of CRC and its late detection is a problem for public health that requires systemic solutions at the national level. Performing screening only for symptomatic patients do not provide the required results in the management of the disease burden, therefore, organised population-based screening is designated for population of certain age group with no

symptoms of the disease, which is a potential solution of this problem[6-11]. Screening programmes should be accessible, safe, and integrated into the healthcare system at an economically reasonable price. Thus, effectiveness, quality and accessibility are the key requirements for screening programmes[12,13]

The Council of the European Union (EU) recommends that CRC screening programmes have to be implemented with systematic monitoring of quality at all levels[14,15]. The programmes are financed from budget or by reimbursement through health insurance[16].

In Austria, a population-based screening programme has been implemented in the federal state of Burgenland since 2003. In the rest of the country, screening is opportunistic. As part of the opportunistic screening, gFOBT is offered annually, and colonoscopy is offered once every 10 years[16].

The population programme in the Wallonia-Brussels was launched in 2009 and in the Flanders in 2013. Since 2016 Wallonia-Brussels replaced gFOBT with FIT. Patients with a positive test result are informed through the treating physician to have colonoscopy [17].

In Lithuania, the population based programme started in 2009 in two regions, and became nationwide in 2014. Invitations are sent via primary healthcare centres[16].

In 2019, the Romanian Colorectal Cancer Screening Programme (ROCCAS) was launched, by the Ministry of Health and the National Institute of Public Health, funded by the European Social Fund, that lasted 60 months until the end of 2023 and consisted of two phases. The first phase was to create the organisational and legal framework to implement the CRC screening programme. The second phase consisted of the pilot testing of the programme in 4 of 8 regions of Romania. By September 2023, 169,052 people were invited to screening in all four regions. The preliminary results revealed a high rate of FIT acceptance, between 89% and 99%, with a good rate for FIT return ranging 79-95%. All the information about the patient (demographics, comorbidities, antithrombotic medication), the procedure (findings, preparation,

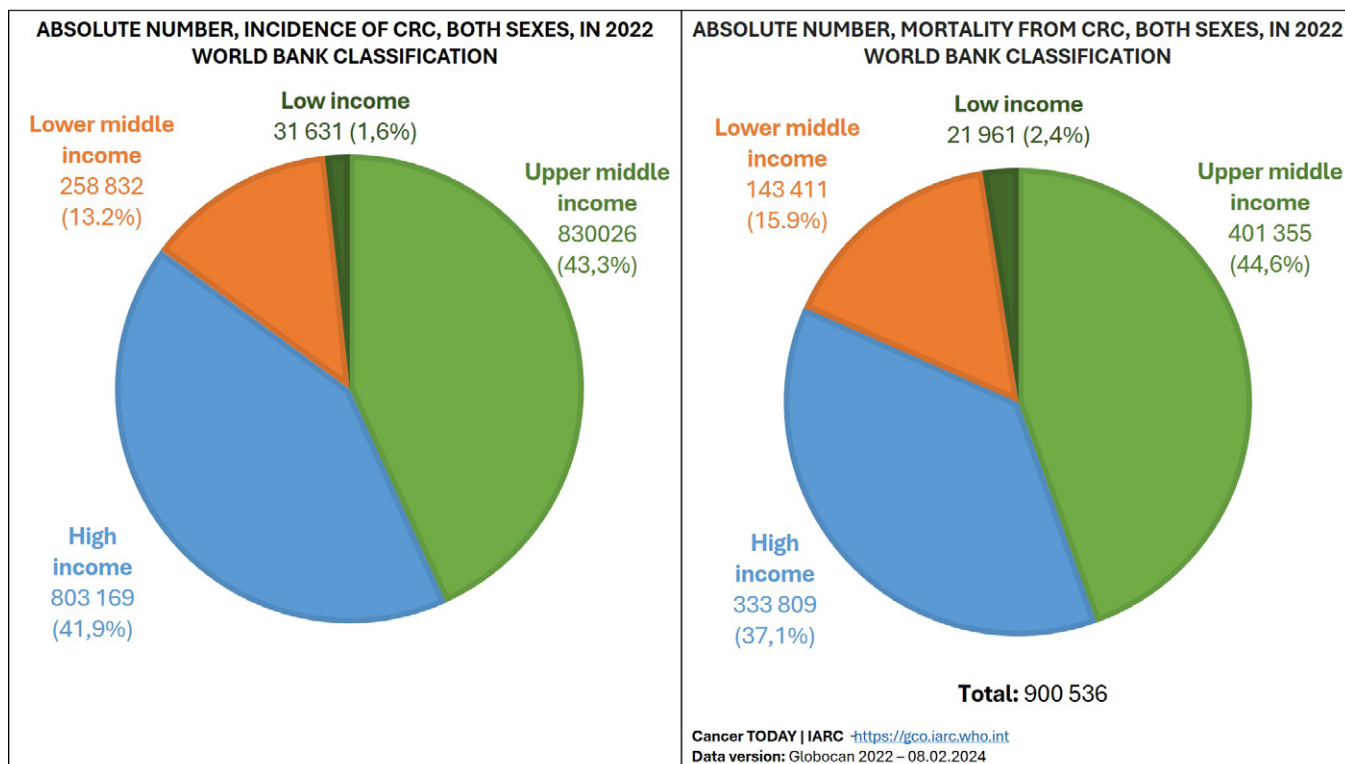


Fig. 2. Incidence and mortality data in countries according to their income levels _ World Bank classification_ in 2022.

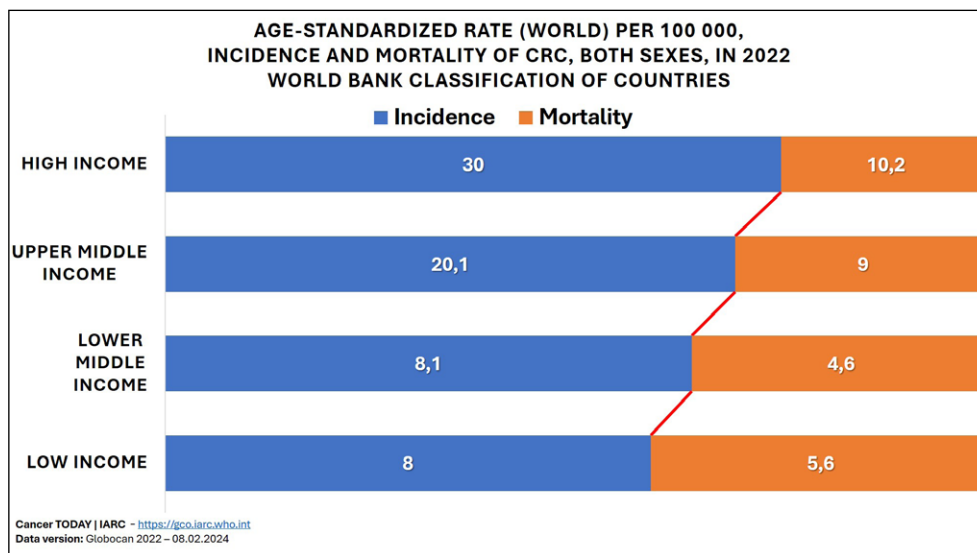


Fig. 3. Age-standardised incidence and mortality rates from CRC per 100_000_ both sexes_ in 2022 in countries according to their income (World Bank classification).

therapeutic approach, adverse events, sedation), histopathology results were collected in a standardized format in the Electronic Screening Record System according to the EU General Data Protection Regulation. The results of the ROCCAS programme have confirmed the effectiveness of CRC screening at the national level, and will be implemented in Romania in 2024[18].

In Poland, CRC is the third most common cancer among the population. In 2022, the estimated mortality rate in Poland was 30/100,000 women and 64.3/100,000 men, while the incidence rate is 53/100,000 women and 104.8/100,000 men [19].

The National CRC Screening Programme started in 2000 and is funded by the Ministry of Health of Poland and the National Health Fund within the framework of the National Cancer Strategy. The programme includes two types of screening: population-based targeted screening (through personal invitation letters) and opportunistic screening [20]. As part of the CRC screening, it is possible to undergo colonoscopy every 10 years. Participants are people aged 55-64 years (regardless the presence of clinical symptoms). Opportunistic screening includes four target groups: (1) people aged 50-65, regardless of family history; (2) people aged

Table 1. 5-year survival rates of patients with colorectal cancer per stage and the proportion of patients diagnosed per stage.

	Stage I	Stage II	Stage III	Stage IV
5-year survival rate	90%	75%	70%	10%
Rate of diagnosed patients	13%	31%	32%	24%

40-49 who have a first-degree relative diagnosed with CRC; (3) people aged 25-49 from a family with Lynch syndrome; (4) people aged 20-49 from a family with familial adenomatous polyposis syndrome. [20].

Despite improvements of CRC screening programme implemented by 2021, participation rate remains low. In 2018, less than 15% of those who received a personal invitation underwent a colonoscopy, which is lower than the 23-70% achieved in other EU countries[21,22].

To involve people to take part in screening tests, a national campaign called "Planning for a long life" was implemented as part of the National Cancer Strategy 2020-2030[22], which includes information campaigns promoting the importance of screening, including CRC, promoting people to participate and informing them about risk factors, symptoms and prevention strategies through media. In addition, the programme includes educational campaigns involving primary care physicians and nurses to inform the population at the local levels about the importance of screening and to spread information materials about screening programmes.

The results of a recent study in Poland demonstrated that the inclusion of primary health care staff in the organisation of a CRC screening programme was found to be a key factor in increasing the level of participation. Especially important factors were invitations in the form of a personal letter or phone call from primary care staff [21].

The programme improves the knowledge and skills of medical staff, with a particular focus on screening. The competence of medical staff is an irreplaceable element that allows for an early diagnosis of CRC. It is important to ensure continuous professional development by creation of training programmes of different levels of detalisation. Collaboration between oncologists and doctors of other specialties and precise detection of disease will speed up the diagnosis and treatment. By the end of 2024, the Public Health Centres would also invite Polish citizens to undergo screening. Due to the National Cancer Strategy, it is planned to increase the rate of the target population covered by CRC screening from 18% to 30%, and by the end of 2027, it is planned to increase this figure to 45%. From 2028, the use of high-definition endoscopes will become an obligatory technical requirement for colonoscopy. Improvements to the existing cancer data collection system have to ensure efficient data exchange, verification and access to the collected information for decision-making at

early stages of the disease [22].

The pilot programme "Prevention 40 PLUS", which started in July 2021 consists of a diagnostic package of tests that also includes a FIT. The purpose of this programme is to involve people over 40 years old to preventive examinations

Thus, thanks to the efficient organisation Poland has made significant progress in the early detection of CRC and prevention of its development in asymptomatic individuals.

Every year, about 13,000 people are diagnosed with CRC in the Netherlands, of whom about 5,000 dies. The 5-year survival rate for this pathology is 65%, but it depends on which stage the disease was detected. According to WHO data, the mortality rate from CRC in the Netherlands in 2022 was 30.3/100,000 women and 43.8/100,000 men, while the incidence rate was 79.2/100,000 women and 117.4/100,000 men [19].

In the Netherlands, the national CRC screening programme (Bevolkingsonderzoek Darmkanker) was launched in 2014, and the implementation process from pilot studies to full integration took about 13 years. Its phased realisations allowed to build the required capacity for screening and treatment within the healthcare system.

On behalf of the Dutch Ministry of Health, Welfare and Sport, the screening programme is funded by the Population Screening Centre of the National Institute of Public Health. The costs of diagnosis, treatment and surveillance are part of the insurance package. The legal framework of the screening programme are: the Public Health Act and the Population Screening Act.

People aged 55-75 years are invited to participate in the screening programme every two years. Each participant receives an individual FIT test kit to take a stool sample at home. This test uses antibodies against human globin, which allows for quantitative measurement of haemoglobin in the material[23]. The advantage of FIT over gFOBT is its higher sensitivity and specificity, and its use does not require dietary or medication limitations [24,25]. The sample is sent by mail to the designated laboratory in a return package.

Implementation of the CRC screening programme at the local level is entrusted to five regional screening organisations that are responsible for programme execution, coordination and quality. These organisations have signed agreements with:

- laboratories;
- colonoscopy centres;
- the national postal operator of the Netherlands (PostNL);
- the FIT-kit packing centre;
- a transport company;
- FIT manufacturer;

The screening organisations are responsible for:

- selecting and reviewing the list of the target group;
- inviting and reminding the target group to undergo the screening;
- sending the FIT to the participants;
- informing about the results and guiding the patient for further diagnostics, if necessary;

Laboratory diagnostics specialists, endoscopists and pathologists undergo accredited learning and advanced training to be allowed to work within the CRC screening programme. According to the protocol, the laboratories and its employees are audited every three months. There is a programme of continuing professional development for GPs on the basic principles of the screening programme. The content of the educational programmes is updated every two years [26].

Individuals of the target group are invited biennially, resulting in approx. 2.2 million invitees each year. The personal data is obtained from the Personal Database (Basisregistratie Personen). Citizens receive an invitation package, which contains invitation letter, information folder, reply envelope, FIT test kit with instructions for use. If the invitee didn't respond, the screening organisation sends reminder per invitation set. If the invitee remains unwilling to participate, a new invitation is sent after two years, unless they have reached age 75. They may also unsubscribe from the current round or the entire program via phone, email, or the client portal [27].

The participant sends a sample of the material in a reply envelope by post to the laboratory, which is the starting point for the screening. The laboratory receives and performs analysis of the sample and sends the results digitally within 48 hours. If the screening laboratory determines the stool sample as unsuitable for the test, the Screening Organisation sends a new invitation set to the participant. If the result is negative, the participant is informed of this and will be invited to participate in the screening programme again in two years. If the FIT test is positive, the participant will be informed and scheduled for a colonoscopy. The participant can change or cancel his/her previous visit (time and/or place) via client portal or by phone. If a colonoscopy is cancelled for medical reasons, this is recorded in the ScreenIT system, indicating when the examination will take place (from 2-10 years, till the age of 75) or will not at all, depending on the reason for not having it [27].

If a patient refuses to undergo colonoscopy a CT colonography can be performed and the results will be sent to the GP and the patient. After a positive CT colonography, it is recommended to undergo colonoscopy. When pathology is detected during colonoscopy, histological samples are sent to a certified laboratory. The results are registered in ScreenIT via nationwide network and registry of histo- and cytopathology to monitor the results of the screening programme and are provided to the participant in written form within 15 working days after the procedure. In case of a cancer diagnosis, treatment is usually started within four weeks [27].

Before the screening programme was launched, 17% of patients were diagnosed at stage I, and thanks to screening, this figure increased to 48% [27]. In 2017, a study was performed in the Netherlands, where among people from the target group 55-75 years old – 42% had adenomatous polyps – people who had absolutely no complaints about their health and considered themselves to be absolutely healthy. 70% of those who were invited took part in the primary screening with FIT, which is the highest rate in the world for screening programme [28-31]. 97.6% of patients with a positive FIT wanted to be consulted before having a colonoscopy. After consultation, they agreed to undergo the procedure, which confirms its importance.

In 2022, 2102881 people were invited to participate in the CRC screening programme. The coverage rate of the target group was 93.2%. 67943 people (4.7% of invited) had a positive result of FIT and were sent for colonoscopy. Out of them, 56847 people (83.7%) underwent the procedure. The participation rate in colonoscopy was higher among those who were first invited to the programme (86.5%), compared to those who participated in the programme again (83.3%). Perhaps this is due to the lower age of first-time participants. During colonoscopy, 2243 cases of CRC (3.9%) and 14373 of advanced adenomas (25.3%) were detected. In 29.2% of patients with a positive test result, colonoscopy revealed colorectal pathology – the indicator of positive predictive value[32].

The Dutch government set clear goals, expecting that by 2031 the screening programme will save 2,400 lives per year, with the estimated cost of the screening programme at €2,200 per year of life gained, which shows that the cost of screening is reasonable for the healthcare system by increasing life expectancy and reducing healthcare spendings [3,26].

In Slovenia, CRC is the second most common cancer by incidence and mortality. In 2022, the mortality rate from CRC in Slovenia was 36.2/100,000 women and 79.3/100,000 men, while the incidence rate was

68.6/100,000 women and 136/100,000 men[19]. The change in CRC incidence in Slovenia is caused by the implementation of the national CRC screening programme Svit. Since 2010, the overall incidence of CRC has been decreasing annually by 3.0% among men and 2.1% among women. In contrast, before the introduction of the screening programme in 1999-2008, it increased by an average of 3.6% per year among men and 3.4% among women[33].

The screening programme reached participation rate of 64.63% (59.38% men and 69.60% women), with 5.9% of citizens having a positive test result, of which 92% underwent colonoscopy. Today, 49% of patients are diagnosed in stage I, which is a significant success [3,34]. Since 2011, Slovenia has recorded a decrease of new cases of CRC. This is mainly due to the removal of precancerous lesions during colonoscopies [33].

When the Svit programme started in 2008, a communication strategy based on the theory of planned behaviour and informed decision-making was implemented. The advertising agency created the programme's style and design, whose ideas and approaches proved to be successful. In particular, the materials avoided frightening messages, motivating the target group to participate in the programme. Attention was focused on a wide audience through communication activities, since the topic of digestion and excretion is still a delicate one for the society. Therefore, in order to increase the level of participation in the screening programme, it is crucial to stimulate an open discussion of the topic. The majority of the population needs to modify their behaviour, reconsider their attitude to health and acquire new skills[35].

The Svit programme was established by the Ministry of Health and organised as a Centre for Early Detection of Cancer at the National Institute of Public Health. The goals, structure and execution of the programme are described in the Rules for the Implementation of National Screening Programmes for the Early Detection of Pre-Cancerous Conditions and Cancer and in National Cancer Control Plan. The Svit programme is funded by the Health Insurance Institute of Slovenia. On the basis of the Health Care and Health Insurance Act and Health Databases Act, it obtains data on the target population from the Central Population Register and the Health Insurance Institute of Slovenia. The acquired information is protected in accordance with the Personal Data Protection Act [35].

The high quality of the Svit programme, its accessibility are the result of the involvement of a large number of specialists. The programme is organised by the National Institute of Public Health and consists of the following teams:

- in-house mailing service;
- laboratory;
- call centre;
- analyses and quality control;
- information technology.

The programme involves healthcare professionals throughout Slovenia: pathologists, endoscopists, GPs and healthcare professionals who provide consultations at Svit contact points. They cooperate with the regional units of the National Institute of Public Health, which are responsible for the promotion, implementation and coordination of the programme in their region. A special role is played by the media, which is an important partner in raising awareness and informing the public about CRC [35].

Presentation events are organised for citizens at the local level to inform them about the screening programme, boosting public awareness and prompting social discussion on off-limited topic. The population avoids talking about digestion, referring to existing stereotypes. This is one of the main reasons for late treatment. Therefore, attention is also paid to inform children and adolescents who are not burdened with various prejudices and taboos. School events promote open discussion of the problem and understanding of the importance of proper digestion, which will encourage the younger generation to pay more attention to their health [35].

Lectures and presentations with inflatable colon model and information materials are provided to employers and employees to promote health awareness and knowledge about prevention. These measures have been well accepted by employers, as they decrease the incidence of CRC among the workforce, providing economic benefits [35].

People aged 50-74 years who are covered by compulsory health insurance in Slovenia are eligible to participate in the Svit programme. About 600,000 residents are invited to undergo screening every two years. The process of engaging citizens is a step-by-step process: first, they receive an invitation to participate in the screening programme along with participating statement, which they have to sign and send to the central office. The Svit programme's internal post service processes an average of about 3,000 shipments per working day [35].

The difference in numbers between those who agree to participate in the programme and those who actually send samples for analysis after receiving the test kits is insignificant. In 2018, among those who were invited to participate in the screening programme, 64.63% agreed, of whom more than 92% sent samples. The participation rate of men is on average 10% lower than

that of women, therefore, additional informational campaign is being conducted to promote men's participation in the screening programme[35].

Those who have responded to the invitation are sent a test kit for two stool samples by post. The samples are analysed in the Svit Programme laboratory to maintain quality standards, and the results are recorded digitally. Before carrying out the test, the applicant's data is cross-checked with the data in the information system. If the sample does not meet the criteria for the analysis, it is excluded and the person is informed of the type of error. Samples received by the laboratory must be analysed within 14 days from the date of sampling. During the implementation of the screening programme, only 3% of samples were collected incorrectly by participants. After phone call or counselling at the Svit contact point, in the chosen personal physician practice or during a visit from the community care nurse, the proportion of persons with inappropriate sent samples is approximately 0.3%. The samples are tested for the presence of antibodies to human haemoglobin. If the level of haemoglobin is exceeded in at least one of the two samples, the test is considered as positive[35].

The results are sent by mail directly to the participant and his/her GP. Individuals with a positive result are referred for a colonoscopy, which is carried out in accredited centres. The contact centre staff is responsible for communication with the target group and for giving information to participants about the following steps. They are the link between the accredited colonoscopy centres and participants, coordinating examination schedules and sending instructions on how to prepare for the procedure. The contact centre staff plays an important role in motivating people to undergo the examination, and as a result, 92% of people with a positive test result undergo colonoscopy[35].

The analysis of the questionnaires shows a very high level of satisfaction of the participants with the professionalism of the medical staff. Respondents rate the work on a scale from 1 to 5, with 1 being the worst and 5 being the best, with an average score of 4.7 for doctors and 4.8 for nurses. More than 91% of respondents agreed to undergo a colonoscopy again if necessary.

The Svit programme foresees the involvement of people with physical disabilities to the screening programme. For example, people with limited mobility are provided with home care by a nurse, most colonoscopy centres are equipped with ramps and lifts, and there is also an option of preparing for the examination in a hospital. People with cognitive disorders are provided with illustrated instructions of how to participate in the programme. Besides, a support is provided to involve them in the programme, through cooperation with

medical staff in various institutions. People with hearing disabilities are provided with instructions in printed form. In the media information about screening is available in sign language with subtitles, and people with visual disabilities can listen to the instructions in audio.

The role of GPs has a significant impact on increasing the level of engagement in the screening programme. Providing information to the population by GPs, recognition of potential obstacles and assistance in resolving them creates more possibilities for the patient, as GPs have the highest level of trust among citizens. To further involvement of the target group to participate, a communication algorithm (reminder system) was developed to ensure regular screening.

GPs are informed about the coverage rate and the results of their patients. Notification of a positive result is sent to the GPs one day before the result is sent to the participant, and notification of a negative result is sent to the GPs within a year. Three times a year, all GPs receive a list of people who did not participate in the programme.

The programme participants need not only the involvement but also the surveillance after receiving a result that confirms pathology. This can cause anxiety, so it is important to explain to them what this means and what their current cancer risks are. If colonoscopy is cancelled for medical reasons, the GP can choose an alternative method to determine the cause of hidden blood in the stool, such as CT colonography.

CONCLUSIONS

The ultimate goal of CRC screening is to reduce mortality by detecting pathology at early stages, which increases the effectiveness of treatment and gives a better prognosis, as well as reducing morbidity in the long term.

Countries that have implemented an organised population-based CRC screening programme have seen an increase in incidence (mainly due to the detection of early stages of CRC) in the first years after the implementation of the screening programme, followed by a gradual decrease (both in early and late stages of CRC) in the future [36]. Screening has increased the number of detected asymptomatic cases, which without screening might have been undetected until symptoms appeared, which may take years.

After the implementation of the screening programme, the incidence of CRC is reduced compared to its implementation before, by detecting and removing polyps and precancerous lesions, which leads to a decrease in the incidence of CRC in the long term [37-39]. This reduction in CRC incidence is the result of a

massive detection of early asymptomatic cases before they progress to advanced stages.

The implementation of a CRC screening programme is a task that requires the involvement of the state's resources and the creation of an appropriate informational and technical infrastructure, primarily an electronic

database of the target population, the development of the system of invitations and reminders about the stages of screening and results tracking, as well as continuous monitoring of each stage of screening to identify weaknesses within the healthcare system and make the necessary corrections.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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