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ORIGINAL SCIENTIFIC REPORT

# Colonoscopy Needs for Implementation of a Colorectal Cancer Screening Program in Ukraine

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## Abstract

*Background* In Ukraine, there is no established colorectal cancer screening program. We aimed to project the number of screening colonoscopies needed for implementation of various CRC screening strategies in Ukraine.

*Methods* We modified a previously developed Markov microsimulation model to reflect the natural history of adenoma and CRC progression among average-risk 50–74-year-olds. We simulated colonoscopies needed for the following screening strategies: no screening, fecal occult blood test yearly, FOBT yearly with flexible sigmoidoscopy every 5 years, FS every 5 years, fecal immunohistochemistry test (FIT) yearly, or colonoscopy every 10 years. Assuming 80% screening adherence, we estimated colonoscopies required at 1 and 5 years depending on the implementation rate. In one-way sensitivity analyses, we varied implementation rate, screening adherence, sensitivity, and specificity.

*Results* Assuming an 80% screening adherence and complete implementation (100%), besides a no screening strategy, the fewest screening colonoscopies are needed with an FOBT program, requiring on average 6,600 and 26,800 colonoscopies per 100,000 persons at 1 and 5 years post-implementation, respectively. The most screening colonoscopies are required with a colonoscopy program, requiring on average 76,600 and 101,000 colonoscopies per 100,000 persons at 1 and 5 years post-implementation, respectively. In sensitivity analyses, the biggest driver of number of colonoscopies needed was screening adherence.

*Conclusions* The number of colonoscopies needed and therefore the potential strain on the healthcare system vary substantially by screening test. These findings can provide valuable information for stakeholders on equipment needs when implementing a national screening program in Ukraine.

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## Introduction

The incidence and mortality of colorectal cancer (CRC) is increasing in low- and middle-income countries [1, 2]. CRC is the third most common cause of cancer-related deaths in Ukraine [3]. In 2019, over 14,500 people in Ukraine died from CRC, representing a rate of approximately 33 deaths per 100,000 persons [4]. Deaths from CRC in Ukraine have been steadily on the rise since 2014 [4]. In high-income countries, cost-effective CRC screening strategies have been introduced, which substantially reduced CRC-related mortality [1, 2, 5]. For instance, the implementation of CRC screening in the USA is thought to have contributed to a reduction in CRC mortality of greater than 50% [6].

In Ukraine, an Eastern European lower–middle-income country, there is no established CRC screening program [7]. Access to treatment is limited due to the significant financial burden placed on patients through high out-of-pocket costs and limited funding for health care [3, 5, 8, 9]. With the lack of a CRC screening program and the financial burden associated with treatment, it is not surprising that nearly three quarters of colon cancer patients and two-thirds of rectal cancer patients present with stage 3 or stage 4 disease [5, 10].

Despite strong evidence supporting the potential health benefits of CRC screening, Ukrainian policymakers have not implemented a formal CRC screening program. Although the country's political climate was a significant barrier to application of any meaningful healthcare policy changes, in 2014, a National Health Care Reform Strategy was introduced in Ukraine to improve the nation's public health, with preventative care as one of the reform's main areas of focus [11–14]. The law of healthcare reform was passed by Ukraine's Parliament in October 2017 [14–18]. Implementation of the reform included a focus on primary care and early detection of disease, including screening for diabetes, HIV, hypertension, and cardiovascular disease [14–18]. The country has also dealt with significant economic challenges, which have increased barriers to healthcare access and have amplified existing disparities [8, 9, 19, 20].

In 2014, per capita healthcare spending was estimated at $584, and in 2017, healthcare spending in Ukraine was just over 7% of the nation's gross domestic product [15]. The health system, the National Health Service Ukraine (NHSU), is funded by various forms of public taxation [15]. The healthcare reform has introduced "programs of medical guarantees (PMGs)" which describe the health services and benefits that are free to all citizens of Ukraine, and these PMGs represent approximately two-thirds of the country's healthcare budget [15]. Though the NHSU has seen an increase in governmental funding since the reform, governmental funding covers less than 50% of health costs, while the remaining of healthcare spending is largely out-of-pocket [15].

Overall, a CRC screening program would fit squarely into the National Health Reform's goals and would help provide a nationally accessible service to all eligible patients in Ukraine. The current study aimed to project the number of screening colonoscopies needed for five different CRC screening strategies compared to no national screening (i.e., the current situation) at 1 year and 5 years post-implementation of the screening program. These findings can provide valuable information for stakeholders on resource, personnel, and equipment needs when implementing a national screening program in Ukraine.

## Methods

### Model overview

We modified a previously developed Markov microsimulation model [5] to simulate the natural history of adenoma and CRC progression and to compare competing strategies for CRC screening among average-risk individuals over a period of 1 year and 5 years. Based on Ukraine's age distribution, individuals aged 50–74 enter the model and are followed throughout their lifetime [21]. At model entry, individuals have normal mucosa, undetected adenomas, or preclinical CRC with an age-specific prevalence (Table 1). Transitions from low-risk adenoma to high-risk adenoma, to localized, regional, and distant CRC, occur with a constant yearly probability. Adenomas or subclinical CRC can be detected once an individual undergoes a screening test, depending on the sensitivity of the test, and adenomas are removed during colonoscopy. Individuals with subclinical cancers not detected by screening can progress to clinically symptomatic cancer and receive treatment. For the screening strategies including flexible sigmoidoscopy as a screening element, the model considers the probability that the proximal colon has a neoplasm at the time of sigmoidoscopy screening that is missed, and thus that some patients may progress to clinically symptomatic cancer. Furthermore, a patient with a cancerous polyp identified on screening flexible sigmoidoscopy would need a full colonoscopy in the model. Individuals in the model can die due to CRC, due to perforation from colonoscopy, or due to other CRC-unrelated causes. The values of the input parameters used in the model are listed in Table 1. Data for the model, including age-standardized rates of CRC, mortality from CRC with no screening, and transition probabilities between disease states, were specific to Ukraine and obtained from the National Cancer Registry of Ukraine [5, 22]. The model was validated by generating characteristics of a simulated population when no CRC screening strategy is in place [23], which is reflective of the current situation in Ukraine, and compared to current Ukrainian data [22]. The characteristics generated included: prevalence of CRC by age for average-risk 50–74-year-olds and the incidence of CRC conditional on survival for average-risk 50–74-year-olds.

### Screening strategies

The model was used to estimate the expected number of screening tests (number of colonoscopies, sigmoidoscopies, fecal occult blood tests (FOBTs), and fecal immunohistochemistry test (FITs)) needed for the six competing strategies at 1 year and 5 years after implementation of the strategy. We compared the following CRC screening strategies: no screening (i.e., the current situation), FOBT yearly, FOBT with flexible sigmoidoscopy (FS) every 5 years, FS every 5 years, FIT yearly, and colonoscopy every 10 years. We assume 80% adherence to screening, but vary this adherence rate from 20 to 80% in a sensitivity analysis. Patients who have polypectomy for a high-risk polyp or low-risk polyp undergo colonoscopy 3 years or 5 years following treatment, respectively, as per current clinical guideline recommendations [33]. Thus, the model was used to predict the number of screening colonoscopies for each of the screening strategies. The model did not estimate the number of diagnostic colonoscopies needed for patients with symptomatic colorectal cancer. Further, as in the real world, the model reflects the fact that individuals do not have perfect adherence to screening tests that they are eligible for under a given strategy. When individuals miss a screening test due to non-adherence, they remain eligible for it in the subsequent year with the same adherence rate, even if the screening strategy does not specify yearly testing.

Model estimates for screening tests needs are presented as the average number of screening tests per 100,000 average-risk 50–74-year-old persons in the general population in Ukraine.

### Mortality due to other causes

We used Ukraine life tables from 2013 from the World Health Organization to compute mortality due to other causes (unrelated to CRC) [5]. In order to eliminate CRC as a cause of death from the age-specific mortality risks, we used US cause-eliminated life tables to compute the proportion of death attributable to CRC and applied this estimate to the Ukrainian population [23].

### Sensitivity analyses

One-way sensitivity analyses were conducted to investigate the impact of varying model input parameters on the expected number of colonoscopies, sigmoidoscopies, FOBTs, and FITs needed to implement each program. For each screening strategy, we varied relevant screening test parameters (sensitivity for *low-risk polyp*, *high-risk polyp*, and *CRC* and specificity), screening adherence, and implementation proportion. The range of values used in the sensitivity analyses for each parameter are presented in Table 1. The implementation proportion per year describes how quickly the screening strategy is implemented (e.g., an implementation proportion of 0.5 means that 50% of the eligible population will be offered screening during the first year of implementation, and the remaining 50% will be offered in the second year.

### Statistical analysis

The model was developed in R version 3.6.3 (The R Foundation for Statistical Computing) [34]. Code is available to reproduce the model outputs (https://github.com/KerollosWanis/CRC_screening_Ukraine).

## Results

### Population characteristics with no screening

For validation purposes, the model was used to generate characteristics of a simulated population reflective of the current situation in Ukraine with no CRC screening program in place. The prevalence of CRC by age for average-risk individuals in Ukraine with no screening is presented in Fig. 1a. Starting at age 50, prevalence of CRC increases linearly with increasing age, through age 74. The cumulative incidence of all-cause mortality for the population is presented in Fig. 1b and increases linearly with age from 50 through 74 years. The cumulative incidence of CRC conditional on survival for average-risk individuals from age 50–75 years with no CRC screening program increases linearly with age and is presented in Fig. 1c.

### Screening test needs

Table 2a presents the average number of screening tests needed per 100,000 persons in the population for each of the five screening strategies and for no screening at 1 year post-implementation, assuming 100% implementation and

**Table 1** Model parameters and range of values used in sensitivity analyses

| Ukraine population distribution (2021) | N | Reference | |
|---|---|---|---|
| Age 50–54 | 2,358,000 | [21] | |
| Age 55–59 | 3,049,000 | | |
| Age 60–64 | 2,946,000 | | |
| Age 65–69 | 2,668,000 | | |
| Age 70–74 | 1,870,000 | | |
| Disease prevalence | Prevalence, % | Range, % | References |
| *Low-Risk Polyp* | | | |
| Age 50 | 20 | 15–25 | [5, 24–26] |
| Age 60 | 40 | 35–45 | |
| Age 70 | 50 | 45–55 | |
| *High-Risk Polyp* | | | |
| Age 50 | 5 | 3–7 | [5, 24–26] |
| Age 60 | 9 | 7–12 | |
| Age 70 | 16 | 14–18 | |
| *Preclinical CRC* | | | |
| Local | 0.24 | 0.20–0.26 | [5, 24–26] |
| Regional | 0.12 | 0.08–0.14 | |
| Distant | 0.04 | 0.03–0.05 | |
| Age-Dependent Transition From *Normal Mucosa* to *Low-Risk Polyp* | Yearly probability | Range | References |
| Age 50 | 0.00836 | ± 0.10 | [5, 24–26] |
| Age 55 | 0.0099 | ± 0.10 | |
| Age 60 | 0.01156 | ± 0.10 | |
| Age 65 | 0.0133 | ± 0.10 | |
| Age 70 | 0.01521 | ± 0.10 | |
| Transition states | Yearly probability | Range | References |
| Low-risk polyp to High-risk polyp | 0.036 | 0.025–0.047 | [5, 24–27] |
| High-risk polyp to Preclinical local CRC | 0.042 | 0.03–0.051 | |
| Preclinical local CRC to Preclinical regional CRC | 0.17 | 0.12 – 0.22 | |
| Preclinical regional CRC to Preclinical distant CRC | 0.10 | 0.05–0.15 | |
| Preclinical local CRC to Clinical local CRC | 0.17 | 0.12–0.23 | |
| Preclinical regional CRC to Clinical regional CRC | 0.21 | 0.16–0.26 | |
| Preclinical distant CRC to Clinical distant CRC | 1 | N/A | |
| Screening test characteristics | Probability | Range | References |
| *Sensitivity:* | | | |
| *Low-Risk Polyp* | | | |

**Table 1** continued

| Screening test characteristics | Probability | Range | References |
|---|---|---|---|
| FOBT | 0.10 | 0.075–0.262 | [28, 29] |
| FIT | 0.17 | 0.159–0.186 | |
| FS | 0.85 | 0.80–0.92 | |
| Colonoscopy | 0.85 | 0.80–0.92 | |
| *Sensitivity:* | | | |
| *High-Risk Polyp* | | | |
| FOBT | 0.24 | 0.177–0.499 | [28, 29] |
| FIT | 0.42 | 0.387–0.462 | |
| FS | 0.95 | 0.931–0.995 | |
| Colonoscopy | 0.95 | 0.931–0.995 | |
| *Sensitivity:* | | | |
| *Colorectal Cancer* | | | |
| FOBT | 0.70 | 0.615–0.794 | [28, 29] |
| FIT | 0.92 | 0.84–0.97 | |
| FS | 0.95 | 0.931–0.995 | |
| Colonoscopy | 0.95 | 0.931–0.995 | |
| *Specificity* | | | |
| FOBT | 0.93 | 0.925–0.98 | [28–30] |
| FIT | 0.90 | 0.898 – 0.964 | |
| FS | 0.92 | 0.87 – 0.92 | |
| Colonoscopy | 1 | 0.86 – 1 | |
| 5-Year Mortality | % | | |
| Clinical local CRC | 10 | N/A | [5, 31] |
| Clinical regional CRC | 35 | N/A | |
| Clinical distant CRC | 92 | N/A | |
| Death from Colonoscopy Perforation | % | | |
| Diagnostic Colonoscopy | 0.08 | 0.06 – 0.5 | [5, 32] |
| Therapeutic Colonoscopy | 1.2 | 1–2 | |

*CRC* Colorectal Cancer; *FOBT* Fecal occult blood test; *FS* Flexible sigmoidoscopy

80% adherence. The average number of colonoscopies required for the first year of implementation of the different screening strategies ranges from 6,600 colonoscopies per 100,000 persons (FOBT alone) to 76,600 colonoscopies per 100,000 persons (colonoscopy every 10 years). At 1 year post-implementation, the estimated average number of sigmoidoscopies ranges from 0 per 100,0000 persons (FOBT alone, FIT, colonoscopy every 10 years) to 76,600 per 100,000 persons (FOBT with FS and FS alone). Likewise, the estimated average number of FOBTs needed ranges from 0 per 100,000 persons (FS alone, FIT, colonoscopy every 10 years) to 76,600 per 100,000 persons (FOBT alone and FOBT with FS). Finally, the estimated average number of FITs ranges from 0 per 100,000 persons (FOBT alone, FOBT with FS, FS alone, colonoscopy every 10 years) to 76,600 per 100,000 persons (FIT).

Table 2b presents the average number of screening tests needed for each of the five screening strategies and for no screening at 5 years post-implementation, assuming 100% implementation and 80% adherence. The average number of colonoscopies required for the first 5 years of implementation ranges from 26,800 colonoscopies per 100,000 persons (FOBT alone) to 101,000 colonoscopies per 100,000 persons (colonoscopy every 10 years). The average number of sigmoidoscopies needed ranged from 0 per 100,000 persons (FOBT alone, FIT, colonoscopy every 10 years) to 94,500 per 100,000 persons (FS alone). The average number of FOBTs ranged from 0 per 100,000

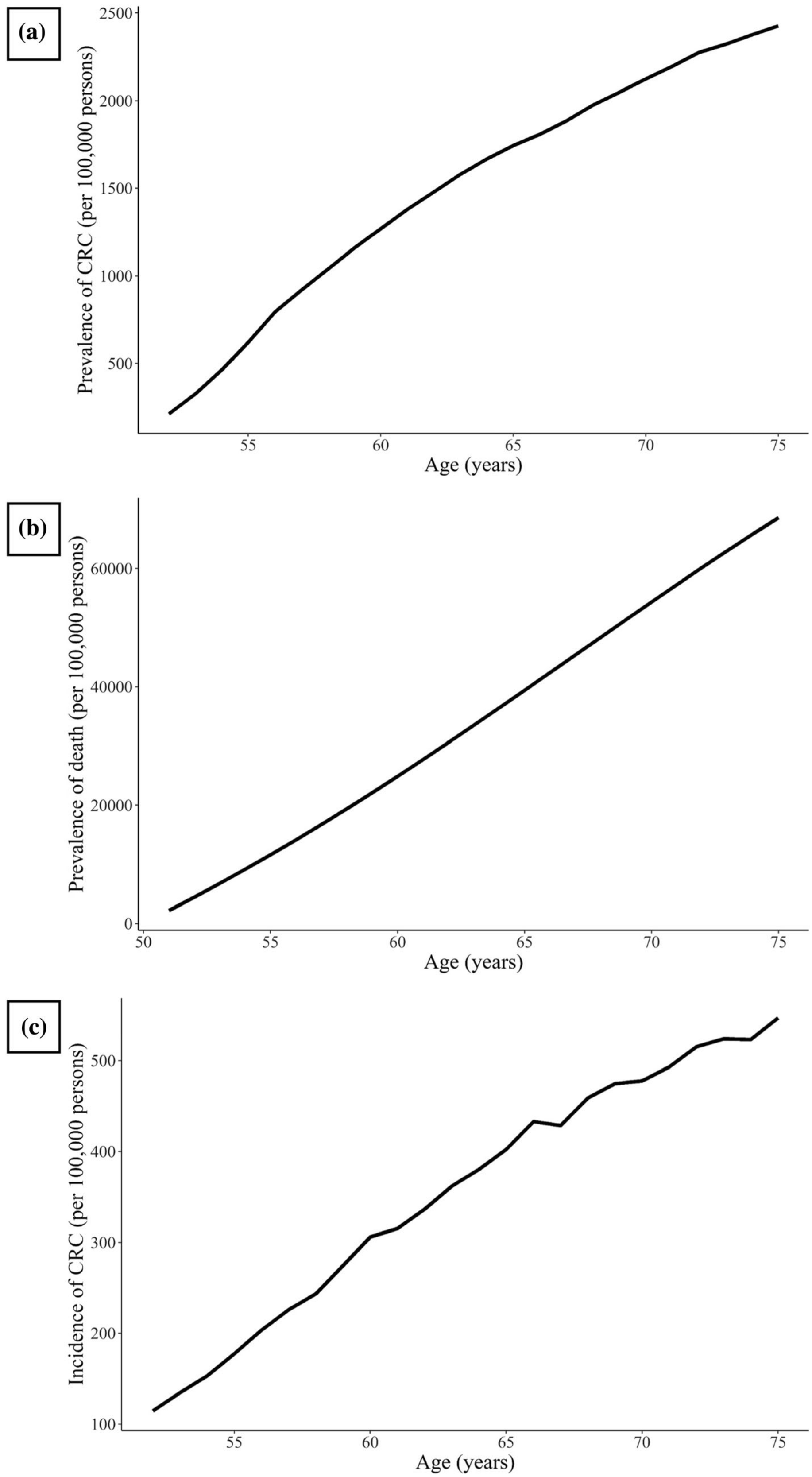



**Fig. 1** **a–c** Microsimulation model-generated characteristics of a simulated population reflective of the current situation in Ukraine with no CRC screening program in place. **a** Prevalence of CRC (per 100,000 persons) by age for average-risk individuals with no screening. **b** Cumulative incidence of deaths due to all causes (per 100,000 persons). **c** Cumulative incidence of CRC (per 100, 000 persons) by age for average-risk individuals with no screening. *CRC* colorectal cancer

**Table 2** a–b Screening test needs per 100,000 persons for average-risk individuals following program implementation (assuming 100% implementation in the first year)

| Screening strategy | Number of colonoscopies per 100,000 persons | Number of sigmoidoscopies per 100,000 persons | Number of FOBTs per 100,000 persons | Number of FITs per 100,000 persons |
|---|---|---|---|---|
| *a. 1 year Post-Implementation* | | | | |
| No screening | 0 | 0 | 0 | 0 |
| FOBT | 6,600 | 0 | 76,600 | 0 |
| FOBT with FS | 27,800 | 76,600 | 76,600 | 0 |
| FS | 23,900 | 76,600 | 0 | 0 |
| FIT | 10,500 | 0 | 0 | 76,600 |
| Colonoscopy | 76,600 | 0 | 0 | 0 |
| *b. 5 years Post-Implementation* | | | | |
| No screening | 0 | 0 | 0 | 0 |
| FOBT | 26,800 | 0 | 300,000 | 0 |
| FOBT with FS | 49,000 | 93,100 | 241,000 | 0 |
| FS | 33,300 | 94,500 | 0 | 0 |
| FIT | 39,000 | 0 | 0 | 280,000 |
| Colonoscopy | 101,000 | 0 | 0 | 0 |

*FOBT* Fecal occult blood test; *FS* Flexible sigmoidoscopy; *FIT* Fecal immunohistochemistry test

persons (FS alone, FIT, colonoscopy every 10 years) to 300,000 per 100,000 persons (FOBT alone). Finally, the average number of FITs ranged from 0 per 100,000 persons (FOBT alone, FOBT with FS, FS alone, colonoscopy every 10 years) to 280,000 per 100,000 persons (FIT).

## Sensitivity analyses

Tornado diagrams illustrating the results of the one-way sensitivity analyses are presented in Fig. 2a–e. The model input parameter that had the biggest impact on the number of colonoscopies per 100,000 persons was screening adherence. In the case of FOBT alone and FOBT with FS as screening strategies, the sensitivity of FOBT for low- and high-risk polyps as well as the specificity of FOBT had the biggest impact on the number of colonoscopies needed, after screening adherence. For FIT as a screening strategy, the specificity of FIT impacted the number of colonoscopies needed the most, after screening adherence.

The estimated number of colonoscopies needed for each of the five screening strategies and no screening as a function of implementation proportion per year at 1 year and 5 years post-implementation is presented in Fig. 3a and b, respectively.

## Discussion

We modified a previously developed Markov microsimulation model to estimate the number of screening tests required for implementation of five CRC screening strategies and for no screening in an average-risk population of 50–74-year-olds in Ukraine. We found that at both 1 and 5 years following CRC screening implementation, the number of colonoscopies needed was lowest for FOBT alone (6,600 per 100,000 persons), and it was highest for colonoscopy every 10 years (76,600 per 100,000 persons). For all screening strategies, the biggest driver of the number of colonoscopies needed was screening adherence. Otherwise, the number of colonoscopies varied most with changing sensitivity or specificity of FOBT and specificity of FIT, for the relevant screening strategies that use these tests. Although the numbers changed while varying key model input parameters, the ranking of the screening strategies remained the same.

In a prior study by our group, colonoscopy every 10 years was identified as the most cost-effective strategy and showed the greatest potential to reduce mortality [5]. Specifically, colonoscopy every 10 years could reduce CRC mortality by 73% at an incremental cost-effectiveness ratio of $843 USD per quality-adjusted life year (QALY) compared to no screening, FOBT yearly, and sigmoidoscopy every 5 years with FOBT [5]. This is under the

**Fig. 2** **a**–**e** Tornado diagrams of one-way sensitivity analyses* estimating colonoscopy needs per 100,000 persons by screening strategy. **a** FOBT. **b** FOBT with FS. **c** FS. **d** FIT. **e** Colonoscopy. CRC = Colorectal Cancer; FOBT = Fecal occult blood test; FS = Flexible sigmoidoscopy; FIT = Fecal immunohistochemistry test. *Parameters varied as follows: adherence 20%–80% (20%, 40%, 60%, 80%); sensitivity *low-risk polyp*: FOBT 7.5%–22.5% (7.5%, 12.5%, 17.5%, 22.5%), FIT 15.5%–18.5% (15.5%, 16.5%, 17.5%, 18.5%), FS and colonoscopy 80%–95% (80%, 85%, 90%, 95%); sensitivity *high-risk polyp*: FOBT 20%–50% (20%, 30%, 40%, 50%), FIT 40%–46% (40%, 42%, 44%, 46%), FS and colonoscopy 93%–99% (93%, 95%, 97%, 99%); sensitivity *CRC:* FOBT 50%–80% (50%, 60%, 70%, 80%), FIT 80%–95% (80%, 85%, 90%, 95%), FS and colonoscopy 93%–99% (93%, 95%, 97%, 99%); specificity: FOBT 92%–98% (92%, 94%, 96%, 98%), FIT 90%–96% (90%, 92%, 94%, 96%), FS 86%–92% (86%, 88%, 90%, 92%); colonoscopy specificity set at 100%

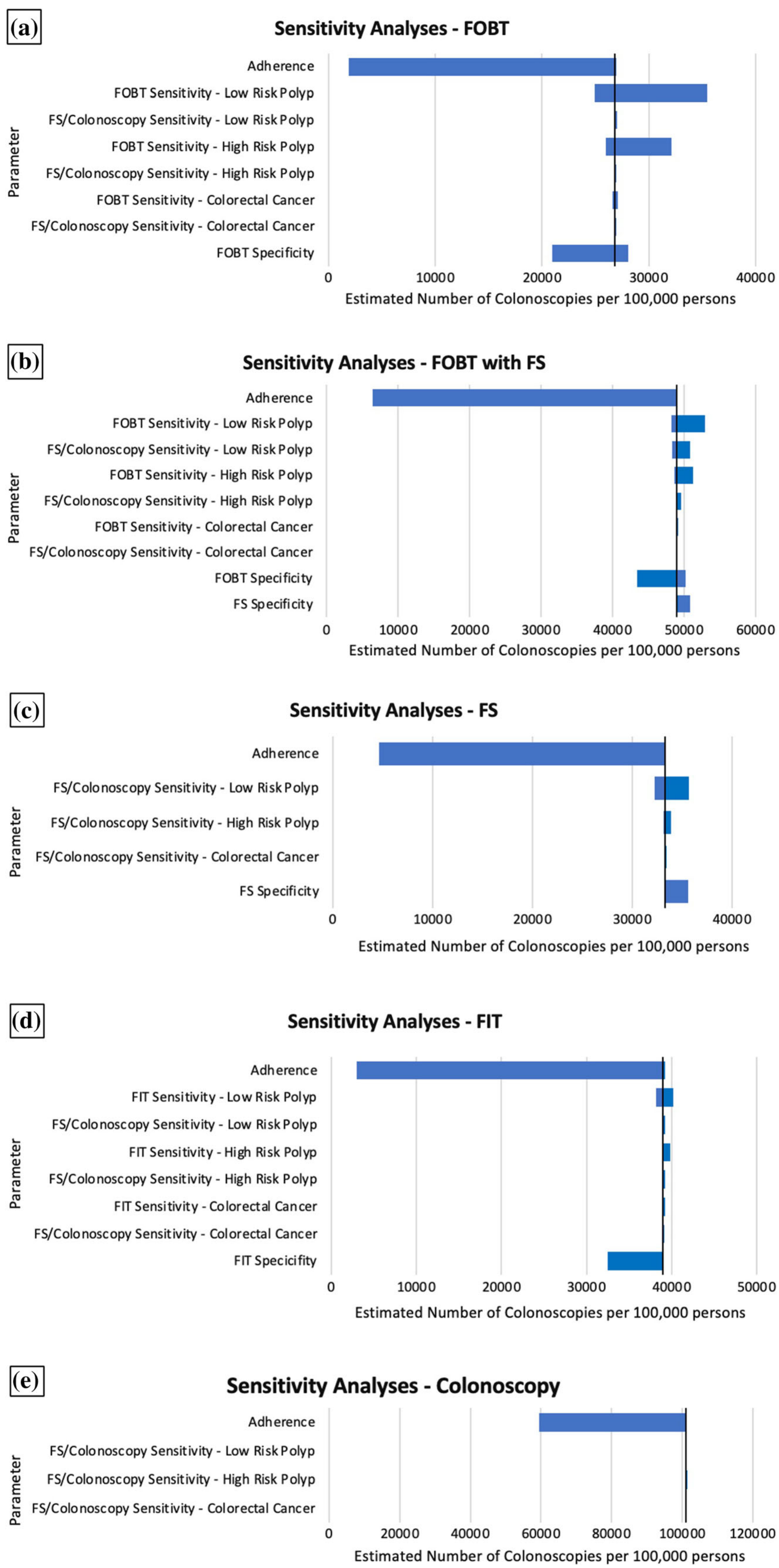
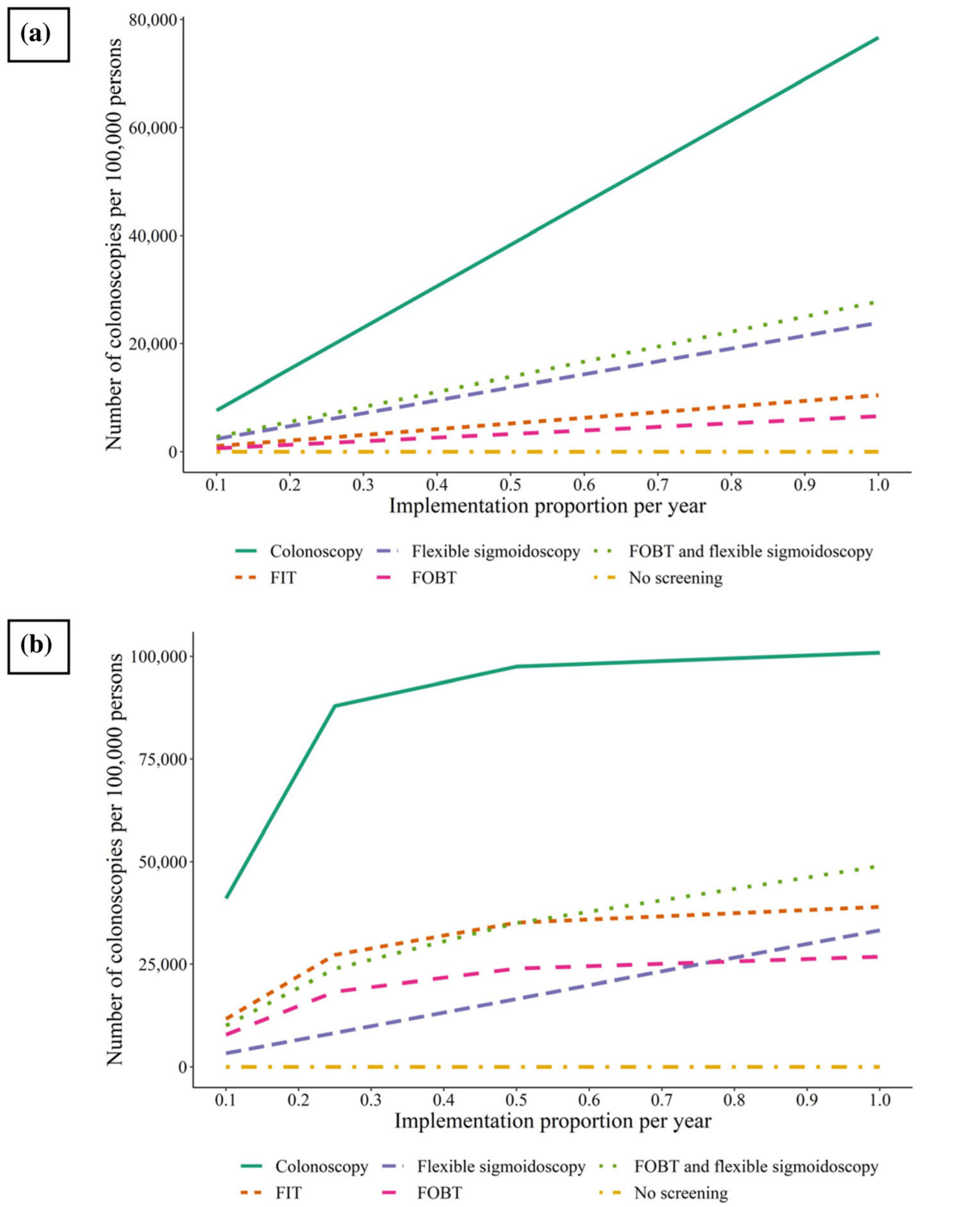


**Fig. 3** **a–b** Number of colonoscopies (per 100,000 persons) for each screening strategy as a function of implementation proportion per year. **a** 1 year post-implementation. **b** 5 years post-implementation. The implementation proportion per year describes how quickly the screening strategy is implemented (e.g., an implementation proportion of 0.5 means that 50% of the eligible population will be offered screening during the first year of implementation, and the remaining 50% will be offered in the second year. *FOBT* Fecal occult blood test; *FS* Flexible sigmoidoscopy; *FIT* Fecal immunohistochemistry test




established willingness-to-pay threshold (WTP) of three times Ukraine's annual per capita GDP (GDP 2017 = $3900 USD; WTP of $11,700 USD per QALY) and thus can be considered cost-effective [5]. However, in this study the costs of implementing the screening strategies were not considered. Colonoscopy every 10 years could become less favorable in terms of cost-effectiveness compared to the other strategies if, for example, the costs of obtaining equipment and training personnel to conduct colonoscopies is very high. Future cost-effectiveness studies comparing screening strategies in Ukraine should ideally include these implementation costs in the analysis.

Our study provides information regarding the number of screening tests needed in the initial implementation years of a national CRC screening program in Ukraine. Though the results of the current study indicate the highest number of colonoscopies is needed with a colonoscopy every 10 years strategy and the lowest with FOBT alone as a screening strategy, these estimates will need to be considered in light of possible benefits achieved with the various screening strategies. That is, the number of tests needed with each screening strategy will need to be weighted against the reduction in CRC deaths and the QALYs gained with a particular strategy. Though colonoscopy may be the most resource intensive strategy, a comprehensive cost-effective analysis may demonstrate that this investment is worthwhile when it comes to the established health benefits of colonoscopy.

Given colonoscopy every 10 years has been identified as the most cost-effective strategy in a previous study, this would be an important screening strategy to focus implementation efforts on if resources allow. However, the initial implementation costs, and thus budget impact, are an important consideration in implementing a national screening strategy. Ukraine may not be equipped to invest in expensive equipment or train additional skilled personnel to carry out the desired screening program. Despite these unknowns, our study provides a first indication of the potential initial equipment needs required for the implementation of a CRC screening program for relevant stakeholders and can inform a future budget impact and workforce analysis. The study can also guide stakeholders in determining an appropriate and feasible starting implementation proportion. Considering all these relevant components that inform decision making, a logical and important next step to the current study is to obtain information on the current colonoscopy capacity in Ukraine, to incorporate implementation costs in cost-effectiveness analyses, and to conduct a budget impact analysis [35]. Post-conflict in Ukraine, it will be particularly important to assess capacity and resources available to determine the optimal screening approach when rebuilding the healthcare sector. The information presented in this study will help inform screening implementation decisions post-conflict.

Our study has several limitations. First, as with other model-based analyses, we relied on several assumptions regarding model structure and model input parameter values. The natural history of adenoma and CRC progression applied in our model is a simplified version of the true structure and progression of disease. Parameter values were obtained from available published literature and several of these reference studies included data from populations besides the target population of Ukraine (Table 1). We had to rely on studies conducted outside of Ukraine given the lack of published literature specific to our population of interest. We did conduct extensive sensitivity analyses to investigate the impact of varying key model parameters on the outcome. Second, we did not consider the availability of equipment (e.g., colonoscopes), personnel, and histopathologic services in the hospitals in Ukraine. Thus, while we do not know how much equipment is currently available, we estimate how much equipment is needed to implement a national screening program. Third, we did not include implementation costs and a budget impact analysis. It is challenging to assess personnel costs and colonoscopy capacity in Ukraine, though this information should be the focus of future work in order to provide a comprehensive cost-effectiveness and budget impact analysis for implementing a national CRC screening program in Ukraine. Finally, this manuscript focuses on estimating the number of screening colonoscopies needed with each of the screening strategies, and does not consider diagnostic colonoscopies for symptomatic presentations of colorectal cancer. This decision was made given the variability inherent in symptomatic colorectal cancer presentation and diagnosis, including for example diagnoses made on imaging.

Despite these limitations, we conclude that the number of colonoscopies needed and therefore the potential strain on the healthcare system vary substantially by screening test. These findings can provide valuable information for stakeholders on equipment needs when implementing a national screening program in Ukraine. Future work will need to focus on costs and budget impact of implementation.

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**Declarations**

**Conflict of interest** None of the authors have any conflicts of interest to disclose.

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