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Colonoscopy Quality Performance: Evaluations of the Early Introduction of FIT-based Population Screening for Colorectal Cancer in Romania and Lessons Learned

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Abstract

Background: Organized population-based colorectal cancer (CRC) screening using fecal immunochemical testing (FIT) followed by diagnostic colonoscopy is the recommended standard across the EU. In 2019, Romania started the ROCCAS pilot screening program in 4 administrative regions in South Muntenia. We evaluated pilot key performance indicators (KPIs) to inform evidence-based decisions for the upcoming national rollout.

Methods: From January 2021-December 2023 50,000 average-risk individuals aged 50–74 years were invited to participate in a biennial FIT-based CRC screening program (cutoff for test positivity≥20 µg/g). FIT-positive participants received colonoscopy at the regional screening centre. Prospectively collected registry data were analysed. Multivariable logistic regression analysis was used to identify predictors of adenoma, advanced adenoma (AA), sessile serrated lesion (SSL), and CRC detection.

Findings: FIT completion rate was 89%, with 6% positivity (n=2576). Colonoscopy uptake was 40% (n=1038). Caecal intubation (96%) and adenoma detection (55%) rates reached/ exceeded international benchmarks. Advanced adenomas, SSL and CRC were diagnosed inx 29%, 4% and 11% of scoped cases respectively. Multivariable analysis showed that male sex predicted adenoma (OR 2·72, 95%CI 2·11–3·51) and AA detection (OR 1·85, 95%CI 1·41–2·44), and was protective against right-sided SSLs (OR 0·34, 95%CI 0·14–0·81). FIT values correlated with lesion severity and independently predicted CRC (aOR 1·53 per 100 µg/g, p<.001).

Interpretation: Our ROCCAS pilot screening program provided promising evidence of high-quality colonoscopy performance and clinically relevant detection rates. Nevertheless, colonoscopy uptake improvement should be prioritized before national rollout. We are currently scaling up awareness efforts and tailored communication strategies to maximize program's outreach and effectiveness.

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Introduction

Cancer affects half of the European Union (EU) citizens during their life time, and among them only one in two survives. [1,2] Colorectal cancer (CRC) is responsible for more than 10% of cancer related mortality in Europe, being the third most common cancer among men and the second most common in women. [3] Countries with high human development index are experiencing a decline of cancer mortality rates partly due to effective prevention and early detection interventions. [4] The European Council recommends all Member States implement and continuously improve accessible population-based cancer screening programs in accordance with the European guidelines and the national law. [1]

In Romania CRC causes around 12% of cancer related mortality and approximately 12 000 individuals receive this diagnosis every year. [5] In 2019 ROCCAS – the Romanian Colorectal Cancer Screening

Program was started with European funding support. The program comprised two sequential stages i.e. development of the infrastructure and personnel training followed by pilot implementation.

ROCCAS is in accordance with the EU guidelines for CRC screening. [6] It consists of biennial faecal immunochemical test (FIT) followed by colonoscopy in positives, in average risk individuals aged 50-74. To ensure an effective implementation ROCCAS was piloted in four of the eight administrative regions of Romania on 200 000 screening participants before national level roll-out. [7]

We performed a population-based cohort analysis to evaluate the key performance indicators of the ROCCAS colorectal cancer screening program, piloted in approximately 50,000 individuals from the South Muntenia region of Romania. ROCCAS was designed as a regional, population-based pilot screening initiative, undertaken with the explicit intention of informing future national rollout. In line with internationally accepted criteria for population-based pilot screening programs, the initiative incorporates defined organizational structures responsible for participant invitation, primary screening using fecal immunochemical testing (FIT), and secondary diagnostic assessment by colonoscopy, alongside service monitoring and outcome evaluation(8,9). While certain elements—most notably an explicit national screening policy and a fully consolidated quality assurance framework—remain under development and require further testing, this pilot fulfills the core operational characteristics of a population-based screening program [8,9].

The primary objective of the present analysis is to report program performance and identify critical strengths and areas requiring optimization, in order to guide refinement of the screening pathway and support evidence-based transition toward nationwide implementation.

Materials and methods

Study design and setting

We report the analysis of participants enrolled in the pilot colorectal cancer screening program (ROCCAS) in the South Muntenia administrative region of Romania (January 2021–December 2023). The ROCCAS methodology has been described previously [10,11]. Briefly, ROCCAS is a biennial FIT-based screening program targeting average-risk individuals aged 50–74 years (Fig. 1). Invitations were issued by general practitioners (GPs); individuals from remote areas or without access to a GP were enrolled with support from non-governmental organizations (NGOs). Eligibility was assessed by GPs using a standardized risk questionnaire (Supplementary Annex 1). Participants completed a fecal immunochemical test (FIT OC-SENSOR®, Eiken Chemical, Tokyo, Japan) at home. FIT-positive individuals (≥20 μg/g) were contacted by the regional screening center team and invited for colonoscopy at the Digestive Disease and Liver Transplant Centre, Fundeni Clinical Institute (Bucharest); NGOs facilitated transportation when needed. Colonoscopies were performed in the ambulatory setting by experienced endoscopists under propofol sedation administered by anesthesiology specialists; complex lesions requiring advanced resection were scheduled for a subsequent therapeutic procedure. Individuals classified as high risk by the GP were referred directly to colonoscopy and were not included

in the present analysis. (12,13) Before launching the pilot phase, multi-layer training sessions were provided to healthcare professionals involved in the screening pathway (general practitioners, gastroenterologists/endoscopists, pathologists, and the screening center team). Training focused on standardized program implementation, including colonoscopy quality assurance, risks and complications, early CRC detection and diagnosis, hereditary CRC recognition/management, and hands-on endoscopic resection workshops.

Participants and study size

The regional pilot's target was 50 000 screened individuals of whom 50% belong to a disadvantaged group. The eligibility criteria, disadvantaged group and CRC risk definitions are detailed in Annex 1 of the Supplementary Material.

Data sources/management

All data about the participants undergoing follow-up colonoscopy were prospectively recorded in a standardized manner in the Electronic Screening Record System that was developed before enrolment initiation. It comprised – general data about the participants – demographics (county of origin, age, sex – physician assessed, socioeconomic status – self reported), comorbidities, antithrombotic treatment; FIT value, sedation information – medication type and dose, sedation related incidents; colonoscopy findings – preparation, evaluated segments, detected lesions (type, number, location, management, incidents). Subsequently, histopathology results were added to the registry if applicable.

Outcomes

Our primary outcome was to measure the main performance indicators of the pilot screening program – colonoscopy uptake rate and key performance indicators for the colonoscopy procedures. The definitions for the colonoscopy KPIs are detailed in Annex 1, Supplementary materials. Furthermore, we are reporting predictors of adenoma, advanced adenoma (AA), right sided sessile serrated lesion and CRC detection in our population.

Statistical methods

Continuous variables are reported as mean and standard deviation (mean ±SD) or median and inter-quartile range (mdn, IQR) as suitable. Categorical variables were reported as frequencies and percentages (%). Independent sample *t*-test, Mann-Withey U or Chi-square were used as appropriate to compare groups. Multivariable logistic regression was performed to identify independent predictors of adenoma, advanced adenoma, right sided sessile serrated lesion detection and CRC detection. Results were reported as odds ratios and 95% confidence intervals (OR, 95%CI). Two tailed $P < .05$ defined statistical significance. The statistical analysis was performed with SPSS (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 26.0. IBM Corp, NY, Armonk, United States) and Jupyter Notebooks [12].

We are reporting our data according to the STROBE guideline [13]

Results

Of the 50 000 invited screenees, 89% completed the FIT. Among the screenees undergoing FIT - 62% were females and 63% were younger than 65. FIT positivity rate was 6% (2576 screenees - 51% females and 52% below 65 years- Fig. S1). The colonoscopy uptake rate among the FIT positives was 40% (1038 screenees). (see Table S3, Fig. S1). The characteristics of the patients undergoing colonoscopy in the South Muntenia ROCCAS pilot are summarized in Table 1 and Figure S2. There was a slight dominance of participants residing in rural areas and belonging to disadvantaged socioeconomic groups. About 20% of participants had moderate to severe comorbidities, with a higher prevalence in males than females aged 50–64 years (22% vs. 14%, $p < .01$) (Fig. S2). All other characteristics were similarly represented in both sexes.

Table 1. Characteristics of the included patients

Participants	1038
Age	63±6·4
Aged 50-64	56%
Male sex	49%
Living in urban area	41%
High education level	13%
Disadvantaged socioeconomic group	59%
Associated comorbidities	77%
ASA score	
1	5%
2	75%
3	20%

Footnote: Variables are reported as mean±SD, or as percentage from total count (%); **Abbreviations**: ASA: American Society of Anesthesiologists;

Key performance indicators

The evaluated key performance indicators (KPIs) are summarized in Table 2. The clinico-demographic and colonoscopy related parameters were evaluated in association with detection of several lesion types (see Table S2-3, Fig S2). Multivariate analysis was performed correcting for sex, socioeconomic group, preparation adequacy, associated comorbidities and FIT value to reveal independent predictors for the

investigated lesions. Older age (≥65 years) was associated with higher odds of adenoma detection (OR 1·30, 95% CI 1·01–1·68, p = .045). Male sex independently predicted both adenoma (OR 2·72, 95% CI 2·11–3·51, p < .001) and advanced adenoma detection (OR 1·85, 95% CI 1·41–2·44, p < .001), and had lower odds of right-sided SSLs detection (OR 0·34, 95% CI 0·14–0·81, p = .015 male vs female). Advanced adenomas were also more likely in participants with higher FIT values (OR 1·13, 95% CI 1·02–1·25, p = .023). Of note, 59% of participants belonged to disadvantaged socioeconomic groups. While adenoma and SSL detection did not differ significantly, advanced adenomas were less frequently detected in disadvantaged socioeconomic group (23% vs. 33%, OR 0·69, 95% CI 0·53–0·92, p=·011). The distribution of cases by the most severe lesion detected at colonoscopy is shown in Figure S4. Advanced adenomas and colorectal cancer together accounted for 38% of all lesions. In addition, FIT values increased progressively with lesion severity in this cohort. (Fig. S5, Table S4). In total, 2012 polyps were resected, of which 258 (13%) were sessile serrated lesions (SSLs). Dysplastic serrated lesions were uncommon, with an overall rate of 0·3% (n=7, one <10 mm). Among small polyps (<10 mm), the prevalence of advanced histology was 0·05% (6/1292), indicating that advanced histologic features were rare in diminutive/small lesions in this screening cohort.

Table 2. Colonoscopy results and key performance indicators (1038 colonoscopies)

Variable	Results
Colonoscopy waiting time • ≥6 months	60 (42-77) days <2% (18 cases)
Cecal intubation rate	96%
Withdrawal time • Adequate withdrawal time (≥6 minutes)	8 (7-11) minutes 80%
Adequate preparation	81%
Adverse events rate *Bleeding* *Sedation-related* *Examination suspended*	<2% of all colonoscopies *14 cases* *3 cases* *3 cases*
No lesions	21% (216 cases)
Adenoma detection rate • female vs male	55% (581 cases) 43% vs 67%*
Adenoma per positive colonoscopy	2 (1-3)
Proximal adenoma detection rate	29%
Advanced adenoma detection rate	29%
Multiple adenoma detection rate	32%
Sessile serrated lesion detection rate • Right sided SSL detection rate	4% 3 %
Mass suggestive of malignancy	7%

Footnote: Variables are reported as median (IQR), or as percentage from total count (%); **Abbreviations**: BBP: Boston bowel preparation scale; ASA: American Society of Anesthesiologists; *p<.05

Cases of colorectal cancer detected during colonoscopy

The characteristics of the patients diagnosed with CRC are summarized in Figure S6. In total 114 cases (11% of cases) (65±6 years old) were identified with malignant lesions, accounting for 11% of the scoped population (24% pT1 -27 lesions, 8% pT2 – 9 lesions)). When compared with patients without malignant lesions, patients with CRC were slightly older (MD=1·87, 95% CI 3·02,·589, p=.03), had higher FIT values (168·1 µg/g, IQR: 54·5-538·4 vs· 50·2, IQR:29·9-147, p<·001), worse preparation quality (adequate BPPS 62% in CRC vs. 79% in non-malignant, p<.001) and presented more comorbidities (ASA>2 in 15% vs. 9% in non-malignant cases, p= .011). Age, FIT value, and ASA score, were independently associated with CRC detection (Table 3).

Rate of. A quarter of the detected CRCs were removed endoscopically while the rest were referred to surgical resection or oncologic treatment as needed. R0 endoscopic resection rate was 68% (19 cases).

Table 3. Predictors of colorectal cancer detection among the 1038 average risk screenees undergoing colonoscopy within the South Muntenia ROCCAS pilot

Variable	OR	95% CI	***P***	aOR	a95%CI	***P***
FIT (µg/g)	1·53	1·34–1·74	<·001	1·53	1·34-1·74	<·001
Age 50–64 (vs ≥65)	0·65	0·44–0·95	0·02	0·63	0·42–0·95	·027
ASA > 2 (vs ≤2)	1·64	1·08–2·50	0·02	1·37	0·88-2·13	·16
Vulnerable group	1·20	0·80–1·79	0·37	■		
Sex (male vs female)	1·06	0·72–1·56	0·77			
Higher education	0·71	0·37–1·37	0·31			
Urban residence	0·85	0·57–1·26	0·41			

Discussion

The Romanian colorectal cancer screening program (ROCCAS) has been successfully piloted in the South Muntenia administrative region as a population-based pilot screening initiative, implemented on a regional scale with the explicit objective of informing future national rollout. In accordance with current European Union recommendations for organized screening programs, ROCCAS incorporates defined organizational structures responsible for identification and invitation of the target population through general practitioners, primary screening using fecal immunochemical testing (FIT), and secondary diagnostic assessment by colonoscopy, while also integrating non-governmental organizations to support participation among socioeconomically disadvantaged groups [1,8,9]. Although an explicit

national screening policy and a fully consolidated quality assurance framework are not yet formally established—elements that are commonly incomplete or under refinement at the pilot phase—ROCCAS fulfills the core operational characteristics of a population-based screening program, including service delivery and outcome monitoring. Within this framework, FIT return rates were high, and FIT positivity, advanced adenoma, and colorectal cancer detection rates were comparable to European benchmarks (Supplementary Table 5) [7]. FIT concentrations increased with lesion severity, supporting the biological and clinical validity of the screening pathway. Colonoscopy quality indicators were high; however, colonoscopy uptake remained suboptimal and waiting times were prolonged, highlighting key implementation challenges. Given that a substantial proportion of the target population belonged to disadvantaged groups—with likely barriers related to socioeconomic factors, health literacy, and competing priorities—these implementation challenges are not unexpected, and they underscore the need for targeted interventions that typically require time to translate into sustained changes in screening behavior. Collectively, these findings provide a structured evaluation of program performance and identify priority areas requiring optimization prior to transition toward nationwide implementation.(1)(7)The optimal screening program should be balanced between decreasing disease specific mortality and the potential negative effects like – overdiagnosis and overtreatment, false negative results and delayed diagnosis and the false positive results that may lead to psychological burden and additional futile tests and increased costs. [14–16] Romania is the 12th largest and 9th most populous of the 44 countries in Europe. ROCCAS results will be essential to characterize more comprehensively the profile of the individual at average risk for CRC in this region of the world and furthermore optimize screening strategies within the EU.

The efficacy of a FIT-based population screening program depends on the colonoscopy completion rate. [17–19] After a positive FIT, lack of colonoscopy is associated with increased risk of CRC related mortality. [20,21] Failure to undergo follow-up colonoscopy is most frequently patient driven. [21,22] Screening practices might not depend on cancer risk perception. [23] Instead they can be positively impacted by personalized communication adapted for each minority within the target group and community-based rather than health care facility-based screening invitation. [24] Screening adherence improvement strategies should rely on tailoring the programs to the particularities of the concerned population. To address colonoscopy uptake rate within ROCCAS several mitigation strategies were applied. We involved NGOs to identify, enroll and assist in screening participation those members of the target population belonging to disadvantaged groups with difficulties in accessing the healthcare system. A structured telephone interview is currently being conducted to explore reasons for refusal or non-attendance. Preliminary, unpublished, and incomplete data show that a proportion of invitees underwent colonoscopy in other centres.

FIT is more specific for colorectal disease than the previously used guaiac-based test. [25] Since it is a quantitative test, the positivity cut off can be adjusted to optimize the balance between false positive results and an acceptable positive predictive value, while maintaining optimal screening coverage without unnecessarily increasing colonoscopy burden. [26] The FIT value may aid the decision to prioritize colonoscopy invitation in patients with high values, or could be by included in risk stratification

scores aimed for improved follow-up strategies. [25,27] In our cohort the FIT value in patients with CRC was 300 units higher than in non-cancer participants. There is a tendency to screen based on the risk of CRC development rather than FIT value alone [28]. The MISCAN Colon microsimulation study revealed that at less than 3% risk of CRC development in 15 years, the benefits of screening are minor and similar to the associated screening harms. [28,29]

In our cohort, male sex was associated with lower right-sided SSL detection. The available literature remains inconsistent: while some cohorts have reported higher prevalence in women, particularly in the proximal colon, others did not confirm sex-based differences. [30,31] Further clarification is needed, as such patterns may influence colonoscopy quality benchmarks and risk-stratified screening strategies.

Implications

Our pilot study revealed that colonoscopy uptake requires major improvement before national roll-out. This will be addressed through intensified campaigns for education and awareness on CRC. An evaluation of patient satisfaction after colonoscopy is ongoing, and results will be used to guide adherence strategies. Integration of pathology and immunohistochemistry data into the screening registry will further enable the identification of mismatch repair–deficient cases. In addition, the involvement of general practitioners in the screening invitation process creates the premises for establishing dedicated follow-up pathways for high-risk individuals. The lower detection of advanced adenomas in disadvantaged groups highlights potential disparities in risk or access, despite the support of NGOs. This finding underscores the importance of embedding equity-focused strategies into the national program, in line with EU recommendations for reducing inequalities in cancer prevention.

In terms of research implications, the prioritization of colonoscopy for patients with high FIT values remains under debate. Our data support the need for further investigation, either through retrospective propensity-score matched analyses across European CRC screening registries or through prospective learning screening programs comparing risk-stratified versus uniform invitation strategies. Such approaches could generate robust evidence on the optimal use of FIT values for prioritization and follow-up. [26,32]

Strengths and limitations

This is the first comprehensive report of the ROCCAS pilot in the South Muntenia region of Romania. We prospectively collected data using standardized reporting which is critical to building a robust national CRC screening registry. Nevertheless, several limitations should be acknowledged. First, the study reflects a single administrative region, and approximately half of the screened population belonged to disadvantaged groups, which may limit the generalizability of the findings to the entire country. To address this, we plan to reassess key performance indicators and outcomes after the national rollout to evaluate whether results differ across regions and population structures. Second, the follow-up period was relatively short, and interval canceranalysis could not yet be performed. However, the program is ongoing and longer follow-up will allow interval cancer assessment and more mature outcome

evaluation in subsequent analyses. Finally, colonoscopy uptake was lower and waiting times longer than recommended, which may have led to underestimation of the true detection yield. To mitigate this, structured training and continuing medical education for professionals involved in the screening pathway were implemented and are planned to continue before and during wider rollout; in parallel, CRC awareness campaigns are continued both locally and through social media to support participation. Being among the most recently initiated screening programs in the EU, ROCCAS benefited from an established European framework that has been continuously refined and updated, which likely contributed to the overall good results of the pilot. Beyond improving colonoscopy participation, the program should further develop a robust recall system to ensure adherence to repeated screening and surveillance examinations.

Conclusion

The ROCCAS was successfully conducted in the South Muntenia, Romania. The quality of the colonoscopies was high, however the colonoscopy participation rate needs improvement. The detection rates of advanced adenomas and CRC was similar to other FIT based screening programmes addressing the same age group in Europe. Our results reveal the screening program is ready for roll-out, while the target group may not be. Continuous awareness raising strategies application and education about the colorectal cancer screening implications are be fundamental for the implementation of the program at national level.

Declarations

Author contribution according to CRediT criteria: Cristian Gheorghe and Mircea Manuc conceived and supervised the study. Bogdan Cotruta, Stefania Bunduc, Razvan Iacob, Adrian Ionut Saizu, Anca Dimitriu, Dan Pitigoi, Cosmin Ciora, Bancila Ion, Mircea Diculescu, Gabriel Becheanu, Mona Dumbrava, and Silvia Sanduleanu contributed to data acquisition, interpretation, and critical revision of the manuscript. Stefania Bunduc performed the statistical analyses and drafted the initial manuscript. Cristian Gheorghe, Mircea Manuc, Silvia Sanduleanu and Bogdan Cotruta critically revised the manuscript for important intellectual content. All authors read and approved the final version and agree to be accountable for all aspects of the work.

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Ethical approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Fundeni Clinical Institute, approval number SMIS: 136828. All participants provided written informed consent for data collection and publication of aggregated results.

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Data sharing: deidentifieddata used for the current analysis can be made available upon reasonable request from the corresponding author

Clinical trial number: not applicable.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process: During the preparation of this work the author(s) used Genspark.AI in order to improving language and readability of the manusript. After using this tool/service, the authors reviewed and edited the content as needed and takes full responsibility for the content of the published article.

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Figures

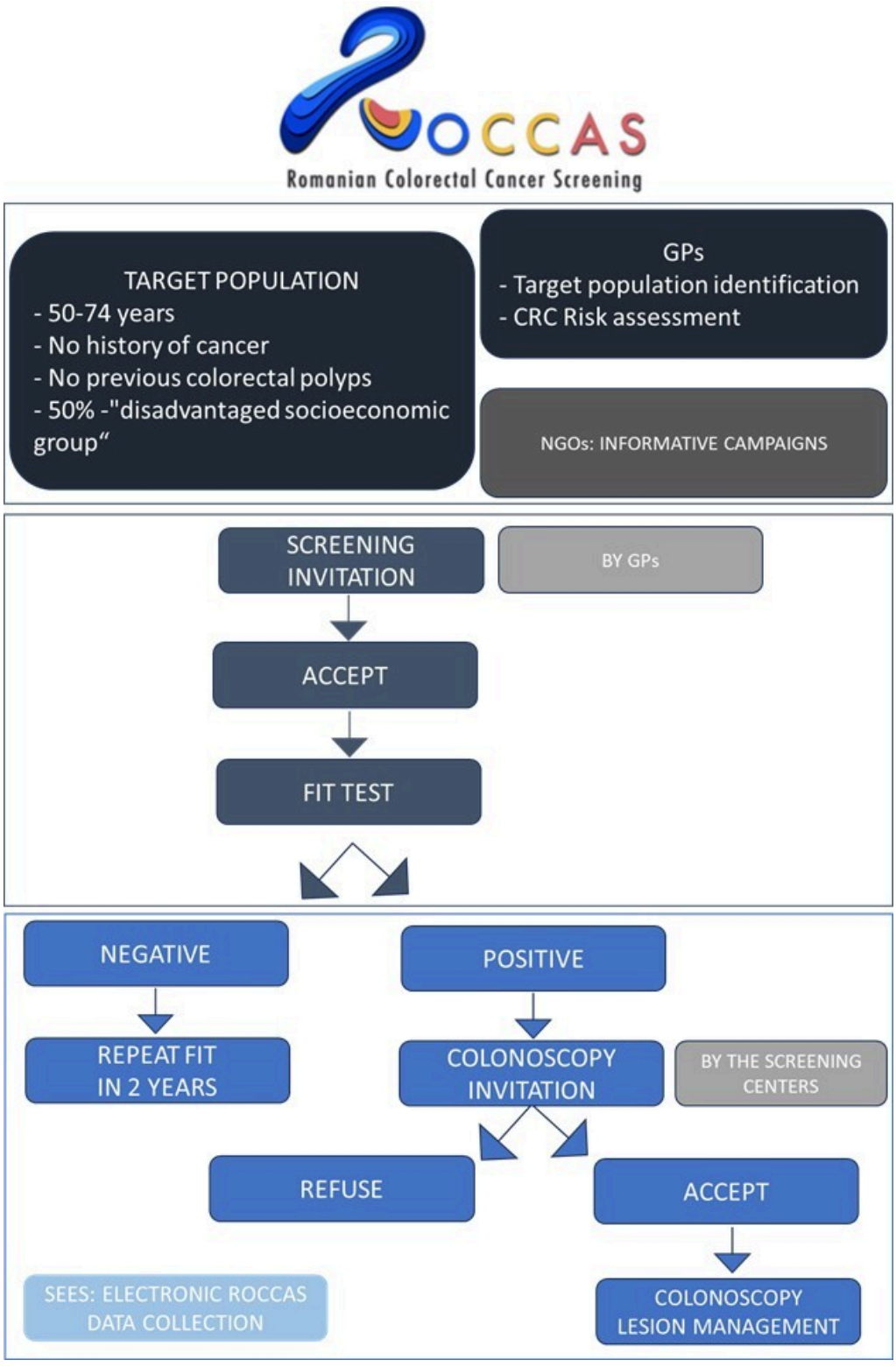


Figure 1

Study framework of the ROCCAS population-based pilot colorectal cancer screening program

Figure legend: The program targeted average-risk individuals aged 50–74 years and was designed as a biennial, FIT-based screening initiative. Target population identification, screening invitation, and FIT distribution and recovery were performed by general practitioners (GPs) using a standardized risk

assessment questionnaire. Non-governmental organizations (NGOs) supported identification and engagement of individuals from disadvantaged socioeconomic groups, predefined to represent approximately 50% of the target population, particularly among persons living in remote areas or not registered with a GP. Participants performed a home-based fecal immunochemical test (FIT). Individuals with a negative FIT were advised to repeat screening after two years, whereas those with a positive FIT result were invited to undergo diagnostic colonoscopy at the designated regional screening center. Colonoscopy invitations and scheduling were coordinated by the screening center, with NGOs providing transportation when needed. Colonoscopies were performed in an ambulatory setting by experienced endoscopists, with lesion management according to standard clinical practice. Individuals identified as high CRC risk at initial GP assessment were directly referred for colonoscopy. Quality monitoring and outcome assessment were ensured through prospective data collection in a standardized Electronic Screening Record System. The registry captured participant demographics and socioeconomic status, comorbidities and antithrombotic therapy, FIT values, sedation details and related adverse events, colonoscopy quality indicators and histopathology results.

Supplementary Files

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