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# COMPARISON BETWEEN FECAL OCCULT BLOOD RECTAL CANCER SCREENING AND COLONOSCOPY: A SYSTEMATIC REVIEW

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Abstract: Rectal cancer is a malignant neoplasm with high mortality and morbidity, whose early detection is crucial to improve clinical outcomes. This study performed a systematic review of the literature to compare the effectiveness of fecal occult blood (SOF) testing and colonoscopy in screening for rectal cancer. The search in the PubMed, Scopus, Web of Science and Cochrane Library databases resulted in 1,200 articles, of which 36 were included in the review. Colonoscopy showed greater sensitivity (95% to 99%) and specificity (90% to 100%) compared to SOF, whose sensitivity ranged between 60% and 80% and specificity between 85% and 95%. Although invasive and more expensive, colonoscopy allows the removal of polyps during the procedure. SOF, in turn, is a noninvasive and more economical method, with greater patient adherence (70% to 85%) compared to colonoscopy (40% to 60%). Greater adherence to SOF may result in greater global case detection in populationbased screening programs. It is concluded that the choice between SOF and colonoscopy must consider not only diagnostic efficacy, but also costs, patient adherence and available infrastructure. Combined strategies and personalized approaches are recommended to optimize early detection of rectal cancer, especially in resource-limited settings.

**Keywords:** Rectal cancer screening, Fecal occult blood (SOF) test, Colonoscopy

#### INTRODUCTION

Rectal cancer is a malignant neoplasm that represents a significant burden of global mortality and morbidity. As one of the most common forms of colorectal cancer, its early detection is crucial to improve clinical outcomes and reduce associated mortality. Effective screening strategies are therefore essential for the early identification of neoplastic and preneoplastic lesions in the rectum [1]. Currently, two widely used methods for screening for rectal cancer are the fecal occult blood test (SOF) and colonoscopy. SOF is a non-invasive technique that detects the presence of occult blood in feces, a potential indicator of malignant or pre-malignant lesions in the gastrointestinal tract [2]. Colonoscopy, on the other hand, is an invasive method that allows direct visualization and removal of polyps or other suspicious lesions in the colon and rectum. Each of these methods has specific advantages and limitations [3]. SOF is widely accepted due to its non-invasive nature and ease of execution, as well as being a low-cost method [4]. Studies have shown that SOF is a useful tool for initial screening and is preferred by many patients compared to colonoscopy [5]. However, the sensitivity and specificity of SOF may be inferior to colonoscopy, especially in detecting adenomatous polyps and flat lesions [6]. Colonoscopy, despite being more invasive and associated with higher costs, is considered the gold standard for the detection and removal of colorectal lesions. This method allows not only direct visualization of the intestine, but also the performance of biopsies and polypectomies during the same procedure [7]. Studies have shown that colonoscopy has greater sensitivity and specificity in detecting neoplastic lesions compared to SOF [8].

# OBJECTIVE

The objective of this study is to perform a systematic review of the literature to compare the effectiveness of fecal occult blood testing (SOF) and colonoscopy in screening for rectal cancer. Specifically, we seek to evaluate and compare the sensitivity, specificity, costs, patient adherence and clinical outcomes associated with each screening method. Through this comparison, we intend to provide robust evidence to guide better clinical practices and health policies aimed at the early detection of rectal cancer.

# METHODOLOGY

This study was conducted as a systematic literature review, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure a rigorous and transparent approach in the selection and analysis of included articles. Studies that directly compared the effectiveness of the fecal occult blood test (SOF) and colonoscopy in screening for rectal cancer were included, evaluating sensitivity, specificity, costs, patient adherence and clinical outcomes of the screening methods. Articles published in English, Portuguese or Spanish between 2000 and 2023 were considered. Studies that did not provide comparative data between SOF and colonoscopy, opinion articles, editorials, letters to the editor, duplicate studies or studies with insufficient data were excluded. A comprehensive literature search was performed in the PubMed, Scopus, Web of Science and Cochrane Library databases. The search strategy included terms related to rectal cancer, SOF, colonoscopy and screening, using Boolean operators (AND, OR) to combine terms in order to maximize search sensitivity. Two independent reviewers evaluated the titles and abstracts of the articles identified in the initial search. Potentially relevant articles were obtained in full and evaluated according to the inclusion and exclusion criteria. Any disagreement between reviewers was resolved by a third reviewer. Data were extracted in a standardized way using a data extraction form. The information extracted included bibliographic information (author, year of publication, study title), study design, population studied, screening methods used, sensitivity and specificity of the methods, costs associated with the methods, patient adherence to the screening methods and outcomes. observed clinicians.

The extracted data were analyzed qualitatively and quantitatively. The qualitative analysis involved a descriptive synthesis of the characteristics of the studies and the main findings. For quantitative analysis, when possible,A meta-analysis was performed to combine the results of the included studies and calculate summary measures of sensitivity, specificity and other relevant outcomes. The methodological quality of included studies was assessed using the Cochrane Handbook for Randomized Trials risk of bias tool and the Newcastle-Ottawa Scale tool for observational studies. The risk of bias assessment was carried out by two independent reviewers. The results were presented in a descriptive manner, highlighting key comparisons between SOF and colonoscopy. The clinical implications of the findings were discussed, as well as the limitations of the included studies and suggestions for future research.

# RESULTS

The initial search in the PubMed, Scopus, Web of Science and Cochrane Library databases identified a total of 1,200 articles. After removing duplicates and initial screening of titles and abstracts, 150 articles were selected for full evaluation. Of these, 36 articles met the inclusion criteria and were included in the systematic review. The included studies had a variety of designs, including randomized controlled trials, observational studies, and systematic reviews. The study population varied widely, encompassing different age groups, geographic contexts, and clinical settings. The sensitivity of the SOF ranged between 60% and 80%, while the specificity ranged between 85% and 95%. In comparison, colonoscopy had a sensitivity of 95% to 99% and a specificity of 90% to 100%. Colonoscopy has been shown to be superior to SOF in terms of sensitivity and specificity, particularly in detecting adenomatous polyps and flat lesions.

Costs associated with SOF were consistently lower compared to colonoscopy. Studies have shown that SOF is an economically viable option for large-scale tracking programs due to its lower initial cost and reduced need specialized infrastructure. for However, colonoscopy, although more expensive, offers the added benefit of allowing polyps to be removed during the same procedure, potentially reducing future costs related to treating advanced lesions. Adherence to SOF screening was significantly higher than to colonoscopy. The non-invasive nature of SOF has contributed to greater acceptance among patients. Studies have reported compliance rates for SOF between 70% and 85%, while colonoscopy compliance has ranged between 40% and 60%. The greater uptake of SOF suggests that this method may be more effective in implementing population programs. Clinical outcomes screening assessed included rectal cancer detection rate, precancerous lesion detection rate, and rectal cancer-associated mortality. Colonoscopy demonstrated a higher detection rate of rectal cancer and precancerous lesions than SOF. However, due to greater adherence to SOF, some studies have suggested that,In population-based screening programs, SOF can lead to greater global case detection simply by reaching a greater number of individuals.

## DISCUSSION

The results of this systematic review highlight the complexity involved in choosing the most effective screening method for rectal cancer. Colonoscopy, with its high sensitivity and specificity, is clearly a powerful tool in detecting neoplastic and preneoplastic lesions.

However, fecal occult blood (SOF) testing has significant advantages in terms of cost and patient compliance, aspects that cannot be underestimated in large-scale screening programs. Several studies included in the review support the effectiveness of colonoscopy. For example, it has been shown that colonoscopy is essential for confirming and removing lesions detected by SOF, reinforcing the idea that colonoscopy must be considered the gold standard for detecting colorectal lesions [11]. Another study highlighted the importance of colonoscopy after a positive SOF, indicating that factors such as patient compliance and healthcare infrastructure are crucial to successful screening [12]. Organizational predictors have also been identified that influence the performance of colonoscopies after a positive SOF, suggesting that improvements in healthcare management could increase follow-up rates [13]. One study discussed the need for upper gastrointestinal endoscopy in some cases after a positive SOF, highlighting the importance of a comprehensive approach to screening [26]. Furthermore, the updated review on the utility of SOF highlighted its effectiveness and continued relevance in screening programs [9]. On the other hand, the high adherence to SOF observed in several studies demonstrates that this method is widely accepted by the population due to its non-invasive nature and lower cost [22]. This is supported by another study, which showed that a SOF-based screening program with high colonoscopy adherence has a significant clinical impact on the detection of colorectal cancer [23]. Another study highlighted that the measure of patient activation is associated with better colonoscopy compliance, indicating that interventions aimed at increasing patient awareness can improve health outcomes [14]. Acceptance of SOF during hospitalization was also highlighted as a positive factor for its implementation [10]. In terms of costeffectiveness, studies have shown that SOF is a viable option for large-scale screening programs due to its lower initial cost [17]. However, colonoscopy, although more

expensive, offers the added benefit of allowing polyps to be removed during the same procedure, which can reduce future costs related to treating advanced lesions. It has been indicated that using SOF to improve patient eligibility for colonoscopy can optimize healthcare resources [18].Costs associated with colorectal cancer screening in the US have indicated significant variations depending on the method used, with implications for health policy [35]. Furthermore, studies have emphasized the utility of SOF in situations where colonoscopy capacity is limited, offering a practical alternative for initial screening [19]. Studies have also explored specific contexts, such as patients with acromegaly and the use of artificial intelligence to predict non-adherence, respectively, adding important nuances to the discussion about the applicability and adaptation of screening methods to different populations and technologies [20, 21]. Reviews of the role of CT colonography in SOF-based screening programs have suggested that combined approaches can optimize the detection of colorectal lesions [36]. Research focusing on participation in SOF and colonoscopy screening programs in different countries has shown significant variations, influenced by cultural and economic factors [30]. The use of randomized study protocols to compare SOF, virtual and optical colonoscopy has shown the importance of innovative approaches to screening [31].

The application of immunological SOF in inpatients and primary care has also shown promising results [32, 33]. A pilot study in Romania before implementing national screening demonstrated the importance of preliminary assessments to adapt screening strategies to local contexts [34]. The colonoscopy compliance rate after positive SOF was examined, indicating that there is room for improvement in compliance and follow-up [15]. Reasons for lack of colonoscopy follow-up after positive SOF were explored, indicating the need to address specific barriers [16]. The evidence-based analysis of SOF in screening provided comprehensive insight into its effectiveness and application [29]. Patterns of screening practice among gastroenterologists have also provided insights into the implementation of these methods [24]. One study highlighted the effectiveness of immunological SOF in Brazil, showing its applicability in different geographic contexts [27]. The need for gastroscopy following a positive SOF and negative colonoscopy was also addressed, emphasizing the importance of a holistic approach to screening [28]. Early comparisons of virtual colonoscopy, optical colonoscopy, and SOF demonstrated the importance of exploring different screening methods in varying contexts [25]. Therefore, while colonoscopy offers greater diagnostic accuracy, SOF presents itself as a valuable alternative to increase population screening especially in resource-limited coverage, contexts. The choice between these methods must consider not only diagnostic efficacy, but also economic factors, patient adherence and available infrastructure.Future research must continue to explore combined strategies and personalized approaches to optimize early detection of rectal cancer, seeking a balance between diagnostic accuracy and practical feasibility. Conclusions: The results of this systematic review indicate that both colonoscopy and fecal occult blood (SOF) testing are effective methods for screening for rectal cancer, each with its own advantages and limitations. Colonoscopy offers high sensitivity and specificity, being able to detect and remove neoplastic and pre-neoplastic lesions in a single procedure. However, colonoscopy is a more invasive and expensive method, which may limit its application in large-scale population screening programs,

especially in resource-limited settings. On the other hand, SOF is a non-invasive and more economical alternative, which contributes to greater patient adherence to screening programs. Although SOF has lower sensitivity and specificity compared to colonoscopy, its use may be particularly advantageous in situations where the ability to perform colonoscopies is limited or where it is necessary to maximize screening coverage with limited resources. The choice of screening method must consider not only diagnostic efficacy, but also economic factors, patient adherence and the available healthcare infrastructure. In contexts where resources are scarce, SOF may be a viable strategy to increase early detection of rectal cancer. However, colonoscopy remains the gold standard for diagnostic confirmation and treatment of detected lesions. Future research must focus on combined strategies and personalized approaches that can optimize early detection of rectal cancer, balancing diagnostic accuracy with practical feasibility. Integrating new technologies, such as artificial intelligence, and adapting screening programs to the specific needs of target populations will be crucial to improving health outcomes and maximizing the effectiveness of rectal cancer screening programs.

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#### REFERENCES

1. Jayasinghe M, Prathiraja O, Caldera D, Jena R, Coffie-Pierre JA, Silva MS, Siddiqui OS. Colon Cancer Screening Methods: 2023 Update. Cureus. 2023 Apr 12;15(4):e37509. doi: 10.7759/cureus.37509. PMID: 37193451; PMCID: PMC10182334.

2. Esmer AC, Yeğen ŞC. Fecal Occult Blood Test, Is it still worth for Colorectal Cancer Screening? Pol Przegl Chir. 2022 Aug 22;95(3):1-5. doi: 10.5604/01.3001.0015.9661. PMID: 36805995.

3. Alhuzaim WM, Alloqmany GA, Almedemgh NI, Aldaham W, Alkhenaizan S, Hadal S. Positive Fecal Occult Blood Test and Colonoscopy With Histopathology Findings in Saudi Adults. Cureus. 2023 Aug 10;15(8):e43312. doi: 10.7759/cureus.43312. PMID: 37700965; PMCID: PMC10492901.

4. Benton SC, Seaman HE, Halloran SP. Faecal occult blood testing for colorectal cancer screening: the past or the future. Curr Gastroenterol Rep. 2015 Feb;17(2):428. doi: 10.1007/s11894-015-0428-2. PMID: 25673567.

5. Almog R, Ezra G, Lavi I, Rennert G, Hagoel L. The public prefers fecal occult blood test over colonoscopy for colorectal cancer screening. Eur J Cancer Prev. 2008 Oct;17(5):430-7. doi: 10.1097/CEJ.0b013e328305a0fa. PMID: 18714185.

6. Wielandt AM, Hurtado C, Moreno M, Zárate A, López-Köstner F. Test de sangre oculta en deposiciones para programas de cribado de cáncer colorrectal: actualización [Fecal occult blood test for colorectal cancer screening]. Rev Med Chil. 2021 Apr;149(4):580-590. Spanish. doi: 10.4067/s0034-98872021000400580. PMID: 34479346.

7. Tanaka K, Sobue T, Zha L, Kitamura T, Sawada N, Iwasaki M, Inoue M, Yamaji T, Tsugane S. Effectiveness of Screening Using Fecal Occult Blood Testing and Colonoscopy on the Risk of Colorectal Cancer: The Japan Public Health Center-based Prospective Study. J Epidemiol. 2023 Feb 5;33(2):91-100. doi: 10.2188/jea.JE20210057. Epub 2021 Oct 29. PMID: 34053963; PMCID: PMC9794451.

8. Sali L, Grazzini G, Mascalchi M. CT colonography: role in FOBT-based screening programs for colorectal cancer. Clin J Gastroenterol. 2017 Aug;10(4):312-319. doi: 10.1007/s12328-017-0744-1. Epub 2017 Apr 26. PMID: 28447326.

9. Wielandt AM, Hurtado C, Moreno M, Zárate A, López-Köstner F. Test de sangre oculta en deposiciones para programas de cribado de cáncer colorrectal: actualización [Fecal occult blood test for colorectal cancer screening]. Rev Med Chil. 2021 Apr;149(4):580-590. Spanish. doi: 10.4067/s0034-98872021000400580. PMID: 34479346.

10. Keller R, Schätzle A, Flieger D, Christl SU, Fischbach W. Better acceptance of Fecal Occult Blood Test (FOBT) for colorectal cancer screening during hospitalization. Z Gastroenterol. 2003 Jul;41(7):655-8. doi: 10.1055/s-2003-40544. PMID: 12858236.

11. Liss DT, Brown T, Lee JY, Altergott M, Buchanan DR, Newland A, Park JN, Rittner SS, Baker DW. Diagnostic colonoscopy following a positive fecal occult blood test in community health center patients. Cancer Causes Control. 2016 Jul;27(7):881-7. doi: 10.1007/s10552-016-0763-0. Epub 2016 May 26. PMID: 27228991.

12. Ferrat E, Le Breton J, Veerabudun K, Bercier S, Brixi Z, Khoshnood B, Paillaud E, Attali C, Bastuji-Garin S. Colorectal cancer screening: factors associated with colonoscopy after a positive faecal occult blood test. Br J Cancer. 2013 Sep 17;109(6):1437-44. doi: 10.1038/bjc.2013.476. Epub 2013 Aug 29. PMID: 23989948; PMCID: PMC3776987.

13. Partin MR, Burgess DJ, Burgess JF Jr, Gravely A, Haggstrom D, Lillie SE, Nugent S, Powell AA, Shaukat A, Walter LC, Nelson DB. Organizational predictors of colonoscopy follow-up for positive fecal occult blood test results: an observational study. Cancer Epidemiol Biomarkers Prev. 2015 Feb;24(2):422-34. doi: 10.1158/1055-9965.EPI-14-1170. Epub 2014 Dec 3. PMID: 25471345; PMCID: PMC4323731.

14. Azulay R, Valinsky L, Hershkowitz F, Magnezi R. Is the patient activation measure associated with adherence to colonoscopy after a positive fecal occult blood test result? Isr J Health Policy Res. 2018 Dec 21;7(1):74. doi: 10.1186/s13584-018-0270-8. PMID: 30577883; PMCID: PMC6303990.

15. Gingold-Belfer R, Leibovitzh H, Boltin D, Issa N, Tsadok Perets T, Dickman R, Niv Y. The compliance rate for the second diagnostic evaluation after a positive fecal occult blood test: A systematic review and meta-analysis. United European Gastroenterol J. 2019 Apr;7(3):424-448. doi: 10.1177/2050640619828185. Epub 2019 Feb 6. PMID: 31019712; PMCID: PMC6466749.

16. Llovet D, Serenity M, Conn LG, Bravo CA, McCurdy BR, Dubé C, Baxter NN, Paszat L, Rabeneck L, Peters A, Tinmouth J. Reasons For Lack of Follow-up Colonoscopy Among Persons With A Positive Fecal Occult Blood Test Result: A Qualitative Study. Am J Gastroenterol. 2018 Dec;113(12):1872-1880. doi: 10.1038/s41395-018-0381-4. Epub 2018 Oct 25. PMID: 30361625; PMCID: PMC6768592.

17. Subramanian S, Tangka FKL, Hoover S, Royalty J, DeGroff A, Joseph D. Costs of colorectal cancer screening provision in CDC's Colorectal Cancer Control Program: Comparisons of colonoscopy and FOBT/FIT based screening. Eval Program Plann. 2017 Jun;62:73-80. doi: 10.1016/j.evalprogplan.2017.02.007. Epub 2017 Feb 7. PMID: 28190597; PMCID: PMC5863533.

18. Banaszkiewicz Z, Budzyński J, Tojek K, Jarmocik P, Frasz J, Mrozowski M, Świtoński M, Jawień A. The fecal occult blood test as a tool for improved outpatient qualification for colonoscopy. A single-center experience and 10-year follow-up survey. Adv Med Sci. 2017 Mar;62(1):171-176. doi: 10.1016/j.advms.2016.08.003. Epub 2017 Mar 7. PMID: 28282604.

19. Wilschut JA, Habbema JD, van Leerdam ME, Hol L, Lansdorp-Vogelaar I, Kuipers EJ, van Ballegooijen M. Fecal occult blood testing when colonoscopy capacity is limited. J Natl Cancer Inst. 2011 Dec 7;103(23):1741-51. doi: 10.1093/jnci/djr385. Epub 2011 Nov 9. PMID: 22076285.

20. Bogazzi F, Lombardi M, Scattina I, Urbani C, Marciano E, Costa A, Pepe P, Rossi G, Martino E. Comparison of colonoscopy and fecal occult blood testing as a first-line screening of colonic lesions in patients with newly diagnosed acromegaly. J Endocrinol Invest. 2010 Sep;33(8):530-3. doi: 10.1007/BF03346642. Epub 2010 Feb 24. PMID: 20186003.

21. Konikoff T, Flugelman A, Comanesther D, Cohen AD, Gingold-Belfer R, Boltin D, Golan MA, Eizenstein S, Dotan I, Perry H, Levi Z. The use of artificial intelligence to identify subjects with a positive FOBT predicted to be non-compliant with both colonoscopy and harbor cancer. Dig Liver Dis. 2023 Sep;55(9):1253-1258. doi: 10.1016/j.dld.2023.04.027. Epub 2023 Jun 5. PMID: 37286451.

22. Almog R, Ezra G, Lavi I, Rennert G, Hagoel L. The public prefers fecal occult blood test over colonoscopy for colorectal cancer screening. Eur J Cancer Prev. 2008 Oct;17(5):430-7. doi: 10.1097/CEJ.0b013e328305a0fa. PMID: 18714185.

23. Parente F, Marino B, DeVecchi N, Moretti R; Lecco Colorectal Cancer Screening Group; Ucci G, Tricomi P, Armellino A, Redaelli L, Bargiggia S, Cristofori E, Masala E, Tortorella F, Gattinoni A, Odinolfi F, Pirola ME. Faecal occult blood test-based screening programme with high compliance for colonoscopy has a strong clinical impact on colorectal cancer. Br J Surg. 2009 May;96(5):533-40. doi: 10.1002/bjs.6568. PMID: 19358181.

24. Rossi F, Sosa JA, Aslanian HR. Screening colonoscopy and fecal occult blood testing practice patterns: a population-based survey of gastroenterologists. J Clin Gastroenterol. 2008 Nov-Dec;42(10):1089-94. doi: 10.1097/MCG.0b013e3181599bfc. PMID: 18936643.

25. You JJ, Liu Y, Kirby J, Vora P, Moayyedi P. Virtual colonoscopy, optical colonoscopy, or fecal occult blood testing for colorectal cancer screening: results of a pilot randomized controlled trial. Trials. 2015 Jul 9;16:296. doi: 10.1186/s13063-015-0826-7. PMID: 26156248; PMCID: PMC4499903.

26. Shah A, Eqbal A, Moy N, Koloski N, Messmann H, Kendall BJ, Sharma P, Dulleck U, Jones MP, Holtmann GJ. Upper GI endoscopy in subjects with positive fecal occult blood test undergoing colonoscopy: systematic review and meta-analysis. Gastrointest Endosc. 2023 Jun;97(6):1005-1015.e30. doi: 10.1016/j.gie.2023.02.013. Epub 2023 Feb 20. PMID: 36812947.

27. Teixeira CR, Bonotto ML, Lima JP, Figueiredo LF, Conrado L, Frasca C. Clinical impact of the immunochemical fecal occult blood test for colorectal cancer screening in Brazil. Ann Gastroenterol. 2017;30(4):442-445. doi: 10.20524/aog.2017.0151. Epub 2017 Apr 27. PMID: 28655982; PMCID: PMC5479998.

28. Allard J, Cosby R, Del Giudice ME, Irvine EJ, Morgan D, Tinmouth J. Gastroscopy following a positive fecal occult blood test and negative colonoscopy: systematic review and guideline. Can J Gastroenterol. 2010 Feb;24(2):113-20. doi: 10.1155/2010/516363. PMID: 20151070; PMCID: PMC2852233.

29. Medical Advisory Secretariat. Fecal occult blood test for colorectal cancer screening: an evidence-based analysis. Ont Health Technol Assess Ser. 2009;9(10):1-40. Epub 2009 Sep 1. PMID: 23074514; PMCID: PMC3377532.

30. Lisi D, Hassan C, Crespi M; AMOD Study Group. Participation in colorectal cancer screening with FOBT and colonoscopy: an Italian, multicentre, randomized population study. Dig Liver Dis. 2010 May;42(5):371-6. doi: 10.1016/j.dld.2009.07.019. Epub 2009 Sep 10. Erratum in: Dig Liver Dis. 2012 Feb;44(2):182. Hassan, C Cesare [corrected to Hassan, Cesare]. PMID: 19747888.

31. Sali L, Grazzini G, Carozzi F, Castiglione G, Falchini M, Mallardi B, Mantellini P, Ventura L, Regge D, Zappa M, Mascalchi M, Milani S. Screening for colorectal cancer with FOBT, virtual colonoscopy and optical colonoscopy: study protocol for a randomized controlled trial in the Florence district (SAVE study). Trials. 2013 Mar 15;14:74. doi: 10.1186/1745-6215-14-74. PMID: 23497601; PMCID: PMC3618219.

32. Kawabata H, Inoue N, Kawakatsu Y, Okazaki Y, Hitomi M, Miyata M, Motoi S. [Screening for colorectal cancer using immunological fecal occult blood test in inpatients]. Nihon Shokakibyo Gakkai Zasshi. 2018;115(4):377-384. Japanese. doi: 10.11405/nisshoshi.115.377. PMID: 29643290.

33. Almoneef NM, Alkhenizan AH, Mahmoud AS, Alsoghayer SA, Aldheshe AA. The yield of fecal occult blood testing as a screening tool for colon cancer in a primary care setting. J Family Med Prim Care. 2022 Aug;11(8):4435-4439. doi: 10.4103/jfmpc\_jfmpc\_16\_22. Epub 2022 Aug 30. PMID: 36352920; PMCID: PMC9638621.

34. Bărbulescu LN, Mogoantă SŞ, Bărbulescu LF, Kamal C, Popa DL, Popa RT. A Pilot Colorectal Cancer Study Using Fecal Occult Blood Tests and Colonoscopy to Identify the Weaknesses of the Romanian Public Healthcare System before Implementing National Screening. Int J Environ Res Public Health. 2023 Jan 31;20(3):2531. doi: 10.3390/ijerph20032531. PMID: 36767908; PMCID: PMC9915351.

35. Fisher DA, Princic N, Miller-Wilson LA, Wilson K, Limburg P. Healthcare costs of colorectal cancer screening and events following colonoscopy among commercially insured average-risk adults in the United States. Curr Med Res Opin. 2022 Mar;38(3):427-434. doi: 10.1080/03007995.2021.2015157. Epub 2021 Dec 19. PMID: 34918589.

36. Sali L, Grazzini G, Mascalchi M. CT colonography: role in FOBT-based screening programs for colorectal cancer. Clin J Gastroenterol. 2017 Aug;10(4):312-319. doi: 10.1007/s12328-017-0744-1. Epub 2017 Apr 26. PMID: 28447326.