A Systematic Review Comparing Screening Modalities for Colorectal Cancer: Diagnostic Accuracy, Patient Compliance, and Cost-effectiveness

Carrine Kogulan, BS
Kansas City University

Abstract

Colorectal cancer (CRC) is the fourth most common cancer among men and women in the United States, affecting around 200,000 people annually. CRC is a highly preventable disease, with extensive screening methods and lifestyle changes being among the most effective preventive measures. Current screening methods range from stool or blood-based tests to endoscopic and imaging techniques.

The objective of this review is to compare the accessibility and effectiveness of current CRC screening modalities to combat the rise of CRC in the United States. Studies published between 2015-2025 were searched across various databases including Google Scholar, PubMed and Cochrane library. These studies were then reviewed for specificity, sensitivity, patient adherence, and cost. Additionally, using the GRADE framework, we evaluated the quality of evidence among the screening tests.

Overall, colonoscopy continues to be the gold standard for screening, due to its high sensitivity and therapeutic capabilities. However, due to its increased invasiveness compared to screening modalities, there is less patient adherence to regular screening. Comparatively, FIT and gFOBT demonstrate high specificity and better compliance, especially in widespread preventative screening programs. Cologuard exhibits better sensitivity than FIT, though its cost and lower specificity limit widespread adoption. Conversely, Shield tests offer increased convenience and adherence, yet studies suggest reduced sensitivity for early-stage CRC with a rating of low certainty of evidence based on the GRADE criteria.

Although non-invasive screening tools enhance patient adherence, they are often associated with limitations in diagnostic performance. Blood-based tests such as Shield are gaining attention as potential alternatives in CRC screening, though current evidence is limited, and further research is needed to optimize their screening efficacy. The optimal screening modality must consider patient preferences, testing accuracy, and cost-effectiveness to enhance patient adherence to screening for one of the deadliest yet preventable cancers. Extensive research has not been conducted on the implementation of osteopathic medicine in colorectal cancer. Additional studies are needed to explore and refine current osteopathic techniques and how they can be implemented for high-risk patients. Soft tissue and muscle energy techniques could be beneficial for changes in bowel movements and abdominal pain that is associated with CRC.

Introduction

• Background

Colorectal cancer (CRC) is the fourth most common cancer in the U.S., with ~154,000 new cases projected in 2025. While incidence has declined since 1999 due to screening, rates are rising by 2.4% annually in individuals under 50. Early detection significantly improves outcomes, with a 5-year survival of 88.5% for localized versus 16.3% for metastatic disease.

• Screening

Current guidelines recommend starting CRC screening at age 45 (colonoscopy every 10 years, FIT or gFOBT annually, sigmoidoscopy every 5 years). Those with a first-degree relative diagnosed before 60 should begin earlier. Screening methods include colonoscopy, FIT, gFOBT, multitarget stool DNA (Cologuard), and blood-based tests. Serum tumor markers (CEA, CA 19-9) lack sufficient sensitivity and specificity for screening but are useful in monitoring.

• Challenges

Despite multiple modalities, 60–70% of CRC cases are detected at Stage II or later, and only 59% of eligible adults undergo screening. Most CRC deaths are linked to missed or delayed screening.

• Objective

This review evaluates the accuracy, compliance, cost-effectiveness, and limitations of current CRC screening methods to guide improvements in patient adherence and early detection.

Methodology

- **Design**: Systematic literature review (2015–2025)
- **Databases**: PubMed, Cochrane Library, Google Scholar
- **Inclusion**: Studies evaluating ≥2 CRC screening modalities, clinical trials, systematic reviews, and peer-reviewed original research
- **Exclusion**: Case reports and non–peer-reviewed articles
- **Data Extraction**: Diagnostic accuracy (sensitivity/specificity), cost-effectiveness, adherence rates, and clinical outcomes
- **Analysis**: Narrative synthesis organized by key themes; GRADE Criteria

Outcome	Screening Modality	No. of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Certainty of Evidence
Sensitivity for CRC detection	Colonoscopy	6	Serious	Not serious	Not serious	Not serious	Unlikely	●●●○ (Moderate)
	FIT	10	Not serious	Serious	Not serious	Not serious	Possible	●●○○ (Low)
	gFOBT	7	Not serious	Serious	Not serious	Serious	Possible	●●○○ (Low)
	mt-sDNA (Cologuard)	4	Not serious	Not serious	Not serious	Serious	Possible	●●●○ (Moderate)
	SEPT9 (blood-based)	5	Serious	Serious	Serious	Serious	Likely	●○○○ (Very Low)
Patient adherence/ compliance	Colonoscopy	8	Not serious	Not serious	Not serious	Not serious	Unlikely	●●●● (High)
	FIT	6	Not serious	Not serious	Not serious	Not serious	Unlikely	●●●● (High)
	mt-sDNA	4	Not serious	Not serious	Not serious	Serious	Possible	●●●○ (Moderate)
	Shield (cfDNA blood test)	2	Serious	Serious	Serious	Serious	Likely	●○○○ (Very Low)
Risk of complications	Colonoscopy	7	Not serious	Not serious	Not serious	Not serious	Unlikely	●●●● (High)
	Non-invasive (FIT, mt-sDNA, SEPT9)	10	Not serious	Not serious	Not serious	Not serious	Unlikely	●●●● (High)

Results

Test	Sensitivity	Specificity	Cost (out-of-pocket after insurance coverage)	Patient Adherence Rate
Shield Blood Test	83%	90%	$0	>90%
SEPT9 Methylation Assay	76.6%	95.9%	$1170-192	85%
Cologuard (FIT-DNA Test)	92.3%	87%	$0	67%
gFOBT Test	33-79%	87-98%	$280	33.4%
FIT Test	73.8%	94%	$24-55	42.6%
Colonoscopy	95%	87%	$79	38%
SEPT9 + FIT	75%	94%	$10-50	65%

Shield Blood Test & SEPT9 Methylation

Shield is a newly FDA-approved (July 2024) cell-free DNA (cfDNA) blood test developed by Guardant Health for colorectal cancer (CRC) screening. This non-invasive test detects cfDNA alterations linked to precancerous polyps and tumors. In clinical studies, Shield demonstrated 83% sensitivity for CRC, 13% for advanced precancerous lesions, and 90% specificity. Sensitivity is highest in stage II–IV CRC but limited for stage I and precursor lesions. It is indicated for patients ≥45 years and is covered by Medicare at no cost (market price: $1495).

Shield targets gene alterations including methylation of SEPT9, a tumor suppressor gene essential in regulating cell division. Hypermethylation of the SEPT9 promoter region leads to circulating tumor DNA (ctDNA) release, serving as a biomarker for CRC detection, prognosis, and treatment response. SEPT9 methylation testing achieves ~77% sensitivity and 96% specificity but is costly ($1170–192) and influenced by comorbidities.

While colonoscopy remains the gold standard, blood-based tests like Shield offer improved accessibility and higher patient adherence (>90%), compared to stool-based tests (33–68%). However, lower sensitivity for early-stage disease underscores the need for complementary use with established modalities.

Conclusions

Colorectal Cancer (CRC) Screening Overview

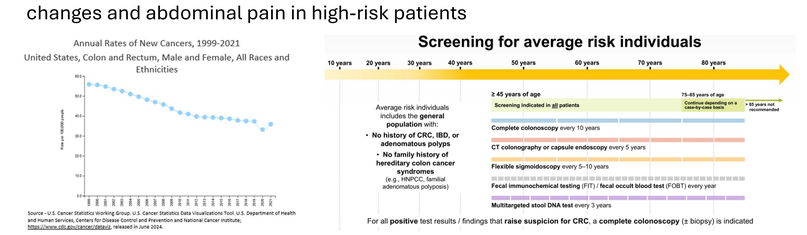
- **Colonoscopy** remains the gold standard due to high sensitivity and therapeutic capabilities but has lower adherence because of invasiveness
- **FIT & gFOBT**: high specificity, lower cost, better compliance in population screening
- **Cologuard**: higher sensitivity than FIT but limited by cost and lower specificity
- **Shield Test**: FDA-approved cfDNA blood test; highly sensitive for high-grade lesions, but reduced performance for adenomas/early CRC. Provides greater convenience and compliance, yet not a replacement for colonoscopy
- **Cost & Evidence**: Blood and fecal DNA tests improve early detection but are costly. Shield is rated “low certainty of evidence” (GRADE)

Barriers to Screening

- Positive predictive value, side effects, preparation burden, cost, and convenience affect patient adherence

Osteopathic Medicine & CRC

- Limited research on osteopathic approaches
- Potential role for soft tissue and muscle energy techniques in managing bowel changes and abdominal pain in high-risk patients



References

- CDC. Colorectal Cancer Statistics. Colorectal Cancer. June 12, 2024. Accessed April 11, 2025. https://www.cdc.gov/colorectal-cancer/statistics/index.html
- American Cancer Society. Colorectal Cancer Statistics | How Common Is Colorectal Cancer? American Cancer Society. Accessed April 11, 2025. https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html
- US Cancer Statistics Work Group. USCS Data Visualizations. US Cancer Statistics Data Visualizations Tool. Accessed April 11, 2025. https://gis.cdc.gov/grasp/USCS/DataViz.html
- Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin. 2018;68(4):250-281. doi:10.3322/caac.21457
- Colorectal Cancer. American College of Gastroenterology. Accessed July 22, 2025. https://gi.org/topics/colorectal-cancer/
- Song L, Li Y. SEPT9: A Specific Circulating Biomarker for Colorectal Cancer. In: Makowski GS, ed. Advances in Clinical Chemistry. Vol 72. Elsevier; 2015:171-204. doi:10.1016/bs.acc.2015.07.004
- Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024;74(1):12-49. doi:10.3322/caac.21820
- Doubeni CA, Fedewa SA, Levin TR, et al. Modifiable Failures in the Colorectal Cancer Screening Process and Their Association With Risk of Death. Gastroenterology. 2019;156(1):63-74.e6. doi:10.1053/j.gastro.2018.09.040
- Guardant Health, Inc. Guardant Health’s Shield(TM) Blood Test Approved by FDA as a Primary Screening Option, Clearing Path for Medicare Reimbursement and a New Era of Colorectal Cancer Screening - News Hub. July 29, 2024. Accessed April 11, 2025. https://newshub.medianet.com.au/2024/07/guardant-healths-shieldtm-blood-test-approved-by-fda-as-a-primary-screening-option-clearing-path-for-medicare-reimbursement-and-a-new-era-of-colorectal-cancer-screening/59389/
- Business Wire. FDA Advisory Committee Panel Strongly Recommends Approval of ShieldTM Blood Test for Colorectal Cancer Screening as a Primary Non-Invasive Screening Option | The AI Journal. May 23, 2024. Accessed April 14, 2025. https://aijourn.com/fda-advisory-committee-panel-strongly-recommends-approval-of-shield-blood-test-for-colorectal-cancer-screening-as-a-primary-non-invasive-screening-option/
- Voss A. Colorectal Cancer Screening: Where Does the Shield Liquid Biopsy Fit In? October 11, 2024. Accessed April 12, 2025. https://www.cancer.gov/news-events/cancer-currents-blog/2024/shield-blood-test-colorectal-cancer-screening
- Chung DC, Grayll DM, Singh H, et al. A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening. N Engl J Med. Published online March 14, 2024. doi:10.1056/NEJMoa2304714
- Tariq M, Ahmed M, Khan M, Khan F. A cell-free DNA colorectal cancer screening test promising enhanced accessibility and early detection. Int J Colorectal Dis. 2024;39(1):162. doi:10.1007/s00384-024-04706-8
- Ladabaum U, Mannalithara A, Schoen RE, Dominitz JA, Lieberman D. Projected Impact and Cost-Effectiveness of Novel Molecular Blood-Based or Stool-Based Screening Tests for Colorectal Cancer. Ann Intern Med. 2024;177(12):1610-1620. doi:10.7326/ANNALS-24-00910
- Liu SC, Zhang H. Early diagnostic strategies for colorectal cancer. World J Gastroenterol. 2024;30(33):3818-3822. doi:10.3748/wjg.v30.i33.3818
- Coverage and support details. ShieldTM by Guardant Health. Accessed July 18, 2025. https://www.shieldcancerscreen.com/hcp/coverage-and-support/
- Poüs C, Klipfel L, Baillet A. Cancer-Related Functions and Subcellular Localizations of Septins. Front Cell Dev Biol. 2016;4. doi:10.3389/fcell.2016.00126
- Wang Y, Chen PM, Liu RB. Advance in plasma SEPT9 gene methylation assay for colorectal cancer early detection. World J Gastrointest Oncol. 2018;10(1):15-22. doi:10.4251/wjgo.v10.i1.15
- Poüs C, Klipfel L, Baillet A. Cancer-Related Functions and Subcellular Localizations of Septins. Front Cell Dev Biol. 2016;4. doi:10.3389/fcell.2016.00126
- Kaur K, Zubair M, Adamski JJ. Fecal Occult Blood Test. In: StatPearls. StatPearls Publishing; 2025. Accessed July 21, 2025. http://www.ncbi.nlm.nih.gov/books/NBK537138/
- Boersma P. Prevalence of Multiple Chronic Conditions Among US Adults, 2018. Prev Chronic Dis. 2020;17. doi:10.5888/pcd17.200130
- Lin JS, Perdue LA, Henrikson NB, Bean SI, Blasi PR. Adherence to Initial CRC Screening. In: Screening for Colorectal Cancer: An Evidence Update for the U.S. Preventive Services Task Force [Internet]. Agency for Healthcare Research and Quality (US); 2021. Accessed July 24, 2025. https://www.ncbi.nlm.nih.gov/books/NBK570918/
- Song LL, Li YM. Current noninvasive tests for colorectal cancer screening: An overview of colorectal cancer screening tests. World J Gastrointest Oncol. 2016;8(11):793. doi:10.4251/wjgo.v8.i11.793