



## OPEN ACCESS

## EDITED BY

Giulio Aniello Santoro,  
Ospedale di Treviso, Italy

## REVIEWED BY

ALESSANDRO MANNUCCI,  
San Raffaele Hospital (IRCCS), Italy

## \*CORRESPONDENCE

Mu Zhang

✉ 1069667039@qq.com

Wei Xu

✉ weixumedic@163.com

<sup>†</sup>These authors have contributed equally to this work and share first authorship

RECEIVED 12 October 2025

REVISED 04 November 2025

ACCEPTED 14 November 2025

PUBLISHED 28 November 2025

## CITATION

Tang L, Zhao X, Wang G, Huang J, Zhang M and Xu W (2025) Advances in colorectal cancer screening: technological innovations, guideline discrepancies, and individualized strategies.  
*Front. Oncol.* 15:1723546.  
doi: 10.3389/fonc.2025.1723546

## COPYRIGHT

© 2025 Tang, Zhao, Wang, Huang, Zhang and Xu. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

# Advances in colorectal cancer screening: technological innovations, guideline discrepancies, and individualized strategies

Li Tang<sup>1†</sup>, Xiaoyong Zhao<sup>1†</sup>, Guohong Wang<sup>1</sup>, Jiehao Huang<sup>2</sup>, Mu Zhang<sup>1\*</sup> and Wei Xu<sup>1\*</sup>

<sup>1</sup>Department of Anesthesiology, the First Affiliated Hospital, Yangtze University, Jingzhou, Hubei, China, <sup>2</sup>Department of Ultrasound, the First Affiliated Hospital, Yangtze University, Jingzhou, Hubei, China

Colorectal cancer (CRC) is the second leading cause of cancer-related mortality worldwide. Numerous clinical and epidemiological studies have demonstrated that early screening can significantly reduce both the incidence and mortality of CRC. This review systematically summarizes recent advances in CRC screening technologies. It first reviews the current applications of traditional screening tools such as colonoscopy and fecal occult blood tests, then focuses on emerging molecular detection techniques based on DNA, RNA, proteins, and metabolites, as well as representative multi-omics integration approaches. Furthermore, it discusses the innovative use of artificial intelligence (AI) and image recognition technologies in CRC screening. At the guideline level, we compare recent updates and implementation differences among major national screening guidelines, including those of the U.S. Preventive Services Task Force (USPSTF), and analyze key challenges in current screening practices. Finally, we propose directions for future development. By integrating existing evidence, this review aims to provide clinical reference for transforming CRC screening from population-based to precision-based individualized prevention, promoting its wide, efficient, and sustainable implementation.

## KEYWORDS

colorectal cancer, Screening technology, Early detection, guideline discrepancies, Molecular diagnostics, artificial intelligence

# 1 Introduction

Colorectal cancer (CRC) is the third most common malignancy worldwide and the second leading cause of cancer-related death, posing a major public health burden. Epidemiological studies have revealed marked geographic and population-based variations in incidence and mortality, closely associated with genetic susceptibility, lifestyle, and dietary factors (1). In recent years, lifestyle changes have contributed to a continuous rise in CRC incidence, with an increasing trend toward younger onset (2). In China, CRC ranks first globally in both new cases and deaths, representing a particularly heavy disease burden (3).

Early screening is the cornerstone of CRC prevention and control, effectively reducing incidence and mortality. Standardized screening can increase early diagnostic rates by over 40% and markedly improve long-term prognosis (4). Current screening modalities include colonoscopy (the “gold standard”), fecal immunochemical test (FIT), and liquid biopsy based on circulating tumor DNA (ctDNA) (5–7). However, the efficacy and applicability of these methods vary among populations, and the adherence rate for colonoscopy remains below 50%, making optimization of screening strategies essential (8, 9).

With the advancement of artificial intelligence (AI) and genomics, CRC screening is undergoing continuous innovation (10, 11). AI-assisted colonoscopy has been shown to significantly improve adenoma detection rates (ADR). A meta-analysis including 6,800 cases reported an odds ratio of 1.51 in favor of AI-assisted detection (12). These technologies provide new avenues for developing individualized screening strategies and improving early detection efficiency (13). This review systematically summarizes recent advances in CRC screening technologies, integrating epidemiological and public health perspectives to explore future research directions and technological innovations.

# 2 Traditional screening methods

## 2.1 Colonoscopy and sigmoidoscopy

Colonoscopy remains the gold standard for CRC screening, allowing simultaneous detection and removal of polyps, with high diagnostic accuracy (14). However, its complexity, time requirement, and operator dependence limit widespread use (15). Sigmoidoscopy is easier, better tolerated, and requires minimal preparation but only assesses the distal colon, risking missed right-sided lesions (16). These methods are complementary: colonoscopy suits high-risk individuals, while sigmoidoscopy can serve as a primary community screening tool. Table 1 summarizes key features of common CRC screening modalities.

## 2.2 Fecal occult blood test and fecal immunochemical test

FOBT was the earliest non-invasive CRC screening method, including the guaiac-based test (gFOBT) and the immunochemical test (FIT). The gFOBT detects the peroxidase activity of hemoglobin via a guaiac reaction but has low sensitivity and is affected by diet and medications (17–19). FIT employs antibodies against human hemoglobin, offering higher specificity and minimal interference from external factors (20). Studies have shown that FIT significantly outperforms gFOBT in detecting early CRC and advanced adenomas. Adjusting the cut-off value allows for individualized balancing between sensitivity and specificity (21, 22). Owing to its superior accuracy and convenience, FIT has been endorsed by international guidelines as the preferred fecal-based CRC screening method (23).

TABLE 1 Comparison of several common colorectal screening methods.

Dimension	Colonoscopy	Sigmoidoscopy	FOBT/FIT	Multi-target stool DNA test
Screening value for CRC	Gold standard: enables full visualization of the colon, detection and removal of polyps, significantly reducing CRC incidence	Moderate: covers only distal colon; may miss proximal lesions	Non-invasive initial screening method; FIT shows higher sensitivity than gFOBT for early cancer and advanced adenomas	High sensitivity for CRC (93.9%) and advanced precancerous lesions (43.4%); higher than FIT but slightly lower specificity
Diagnostic & therapeutic purpose	Both diagnostic and therapeutic; allows biopsy and polyp removal during the same procedure	Mainly used for distal colorectal lesion evaluation; suitable for preliminary or complementary screening	Detects occult bleeding; suitable for population-based screening	Combines methylated DNA and hemoglobin detection to improve early diagnostic accuracy
Advantages	High diagnostic accuracy; allows immediate intervention	Simple, minimal preparation, and well tolerated	Non-invasive, low cost, easy sampling, widely accepted	High sensitivity; integrates molecular and immunologic biomarkers; quantitative and automated
Limitations	Invasive; requires skilled operators; limited scalability in large populations	Limited detection range; cannot assess proximal colon	gFOBT has low sensitivity and is affected by diet or medication; repeated testing needed	Slightly lower specificity; high cost and complex laboratory workflow
Clinical recommendation	Recommended for high-risk or symptomatic individuals	Suitable for preliminary screening in primary care or low-resource settings	FIT is recommended by international guidelines as the first-line non-invasive CRC screening method	Included in several national guidelines as an alternative to FIT

### 3 DNA-based and biomarker detection

#### 3.1 DNA methylation testing

With the progress of molecular diagnostics, DNA methylation testing has shown great promise in CRC screening. This technique identifies methylation signatures in tumor-derived DNA from stool or blood samples, enabling the detection of early cancer and precancerous lesions (24, 25). Common biomarkers include mSEPT9, mNDRG4, and SFRP2, all of which demonstrate strong diagnostic performance (26, 27). mSEPT9, one of the most extensively validated markers, captures cancer signals through methylation of the SEPT9

promoter region in ctDNA (28). It exhibits high sensitivity for detecting CRC and advanced adenomas, particularly useful for individuals unable or unwilling to undergo colonoscopy (29). Methylated mNDRG4 is strongly associated with CRC development; compared with FIT, it significantly improves early cancer and advanced adenoma detection rates while reducing false positives (30, 31). SFRP2, a regulator in the Wnt signaling pathway, is frequently silenced by promoter methylation, contributing to tumorigenesis (32–34). Combined detection of multiple methylation markers yields synergistic effects, substantially improving both sensitivity and specificity (35, 36). Table 2 summarizes biomarker-based colorectal cancer screening methods.

TABLE 2 Summary of biomarker-based colorectal cancer screening methods.

Biomarker type	Detection technique	Advantages	Limitations	Representative studies/products	Overall evaluation
Stool DNA Methylation (mNDRG4, SFRP2)	Methylation PCR, NGS	Clear tissue origin; high cancer specificity; sensitive for early detection	Weak signal in some cancers (sarcoma); sample quality affected by stool preservation	Cologuard, ColoClear	Widely studied and clinically applied; methylation-based NGS is a core technology in MCED
Blood DNA Methylation (mSEPT9, SDC2)	Methylation-specific PCR (MSP), bisulfite sequencing, targeted NGS	Minimally invasive; suitable for early detection; high CRC-specific methylation signature specificity.	Low cfDNA concentration in early-stage CRC; possible interference from non-tumor cfDNA; requires high analytical sensitivity	ColonAiQ, Shield, Epi proColon, ColoVantage	Clinically validated and increasingly adopted; promising for population-level CRC screening and MRD monitoring
ctDNA Mutation	dPCR, NGS	Directly reflects driver gene alterations; valuable for targeted therapy guidance	Low abundance in early stages; affected by clonal hematopoiesis; difficult to trace origin	ColoScape, CancerGuard	Requires combination with other biomarkers to improve sensitivity; limited value when used alone
Circulating Tumor DNA (ctDNA)	dPCR, NGS	Enables dynamic monitoring of recurrence risk; noninvasive evaluation of treatment response; prognostic prediction	Low ctDNA levels in early tumors; high testing cost	Guardant360	Expanding clinical applications; combination with CEA improves recurrence risk stratification
Multitarget stool-RNA (mt-sRNA)	qRT-PCR or ddPCR	Reflects gene-expression changes in exfoliated intestinal cells; suitable for early CRC screening	RNA instability; high sample processing requirements; limited sensitivity for advanced adenomas	ColoSense	First RNA-based noninvasive CRC screening test FDA-approved (PMA P230001, 2024); clinically promising but requires further real-world validation
Circulating cell-free RNA (cfRNA)	RNA-seq, qRT-PCR	Higher sensitivity than cfDNA; extracellular vesicle RNA is more stable	Risk of sample degradation; complex analytical procedures	ThromboSeq(TEP RNA, blood-based liquid biopsy)	Emerging liquid biopsy approach; strong potential for multi-omics integration
Protein Biomarkers (CEA, CRP, GZMB, MMP12)	Mass spectrometry, Olink platform	Mature technology; rapid detection;several proteins show clinical relevance	Limited sensitivity and specificity; single protein cannot reflect overall changes	OncoSeek	Traditional and novel combined strategies in use; facilitates multi-omics diagnostic approaches
Metabolites & Microbiota-Derived Metabolites	Mass spectrometry, 16S rRNA sequencing	Reflects metabolic state; reveals CRC-related microbiota and immune pathways	Complex metabolic flux; easily affected by diet	MNALCI	High interpretability; promising for CRC progression monitoring and immune response evaluation
Multi-omics Integration	Combined NGS, proteomics, metabolomics and AI analytics	Enhanced overall performance; complementary signal coverage across omics layers	High cost; complex data processing; difficult biological interpretation	AlphaLiquid, Freenome	Offers comprehensive detection and systemic insights; cost-benefit balance required; suitable as a complementary approach

## 3.2 Next-generation multi-target fecal DNA testing

Next-generation multi-target fecal DNA testing integrates methylation biomarkers with hemoglobin detection (37). In a prospective study involving 20,176 asymptomatic individuals aged  $\geq 40$  years, the test achieved a sensitivity of 93.9% for CRC, 43.4% for advanced precancerous lesions, and a specificity of 90.6% for advanced neoplasia. Compared with FIT, it demonstrated significantly higher sensitivity for CRC and advanced precancerous lesions ( $P < 0.001$ ), with a slight decrease in specificity ( $P < 0.001$ ) but no major adverse events (38). This method has already been included in screening guidelines in several countries.

## 3.3 Circulating tumor DNA testing

Cell-free DNA (cfDNA) refers to double-stranded DNA fragments released from apoptotic or necrotic cells into the bloodstream. Tumor cells also release cfDNA carrying tumor-specific genetic information, known as ctDNA (39). As an emerging liquid biopsy approach, ctDNA testing can identify tumor-related genetic alterations in blood, making it suitable for recurrence monitoring and therapeutic response evaluation (40, 41).

Mo S et al. (25) analyzed six methylation markers in ctDNA from pre- and postoperative samples of 299 patients with stage I–III CRC. Preoperatively, 78.4% of patients were ctDNA-positive; one month post-surgery, ctDNA positivity was associated with a 17.5-fold higher risk of recurrence. Combining ctDNA with CEA further optimized risk stratification. Dynamic postoperative monitoring revealed that ctDNA-positive patients relapsed earlier, with ctDNA detection preceding radiologic evidence by approximately 3.3 months, suggesting strong potential for early recurrence prediction and individualized management.

## 4 Detection of RNA and its biomarkers

### 4.1 miRNA and gut microbiota detection

MicroRNAs (miRNAs) are a class of non-coding RNAs that regulate gene expression by binding to target mRNAs, thereby influencing cell proliferation, differentiation, and apoptosis. Studies have shown that miRNAs play critical roles in CRC initiation, progression, metastasis, and treatment response (42, 43). Analysis of fecal miRNA expression profiles indicates that specific miRNA signatures are closely associated with CRC occurrence and can serve as potential biomarkers for early screening and prognosis evaluation (44).

Meanwhile, gut microbiota profiling based on 16S rRNA sequencing has revealed distinct microbial signatures in CRC patients (45), which show potential for clinical staging and KRAS

mutation prediction. Liu J et al. (46) analyzed preoperative fecal samples from 192 CRC patients and found that Simpson diversity indices were lower in stage III–IV cases, with enrichment of Proteobacteria. O-glycan biosynthesis pathways were strongly associated with tumor progression. Microbiota-based models effectively distinguished cancer stages, suggesting that specific bacterial taxa may contribute to tumor progression through immune modulation or endoplasmic reticulum stress mechanisms.

### 4.2 Circulating cell-free RNA detection

Circulating cell-free RNA (cfRNA) is an emerging non-invasive biomarker for CRC detection. Plasma cfRNA sequencing identifies CRC-specific transcriptomic signatures, achieving high sensitivity and specificity in distinguishing early-stage CRC from healthy individuals (47). Analysis of microbe-derived cfRNA modifications further improves discrimination between CRC and non-CRC samples (48). Compared with cfDNA, cfRNA provides higher detection sensitivity and richer pathway information, highlighting its advantages in multi-omics blood-based surveillance (49, 50).

Advancements in low-input methylation sequencing and optimized library construction enhance cfRNA detection efficiency and coverage (51, 52). Using DETECTOR-seq, Wang H et al. systematically analyzed cfRNA profiles from plasma and extracellular vesicles (EVs) (53). Plasma was enriched in circular RNAs, tRNAs, Y RNAs, and viral RNAs, whereas EVs contained more mRNAs and srpRNAs. Both sources effectively distinguished cancer patients from healthy controls, and microbial RNA signatures in plasma showed strong potential for cancer-type classification.

## 5 Protein and metabolite biomarkers

### 5.1 Blood protein biomarkers

Blood protein biomarkers, such as carcinoembryonic antigen (CEA) and C-reactive protein (CRP), have been widely employed in colorectal cancer (CRC) research. Using Olink proteomics technology, researchers have identified numerous protein biomarkers with potential diagnostic value. For instance, in saliva samples, the expression levels of GZMB (granzyme B) and MMP12 (matrix metalloproteinase 12) are significantly altered in CRC patients, demonstrating high diagnostic sensitivity and specificity (54). Furthermore, serum proteomics analyses have revealed abnormal expression of coagulation factor XIII A chain (F13A1) and plasma kallikrein (KLKB1) in CRC patients, which are closely associated with tumour progression (55). Studies have also reported that plasma concentrations of several amino acids (including L-valine, L-threonine, L-methionine, and glycine) are abnormal in CRC patients, reflecting dysregulated energy metabolism and tumour cell proliferation (56, 57).

## 5.2 Microbiota-derived metabolites

Extensive evidence indicates that the gut microbiota and their metabolites play key regulatory roles in CRC initiation and progression. These metabolites, derived from microbial catabolism of dietary nutrients and host components, can influence tumorigenesis and microenvironment remodeling through multiple pathways. Short-chain fatty acids, bile acids, tryptophan metabolites, and polyamines produced by gut microbes can promote CRC by modulating inflammation, immune responses, and cellular metabolism (58, 59). Emerging metabolites, such as hydrogen sulfide (H<sub>2</sub>S) and formate, have recently drawn attention for their roles in CRC pathogenesis (60, 61). Yue T et al. (62) demonstrated that H<sub>2</sub>S is a critical factor affecting CRC immunotherapy efficacy; high expression in tumour tissue interferes with immune balance via protein persulfidation, promoting Treg activation and inhibiting CD8<sup>+</sup> T-cell migration. Reduction of H<sub>2</sub>S levels can reverse these effects, improving the tumour immune microenvironment and enhancing checkpoint inhibitor efficacy. Ternes D et al. (63) further confirmed that formate produced by nucleated Clostridia can reprogramme CRC cell metabolism, activate pro-invasion signaling pathways, and enhance tumour invasiveness and inflammatory infiltration, accelerating CRC progression.

## 6 Several representative screening techniques and detection platforms

### 6.1 CancerGuard technology

CancerGuard (previously known as CancerSEEK) is a representative multi-cancer early detection (MCED) approach, integrating liquid biopsy analysis of circulating tumour DNA (ctDNA) mutations with plasma protein biomarkers to achieve multi-cancer screening, including CRC (64). CancerGuard uses a multi-analyte approach, combining genomic alterations and protein biomarker quantification. By analyzing around 2000 unique genomic loci, it identifies mutations, deletions, amplifications, and other alterations specific to cancer cells. Alongside this, it quantifies eight key protein biomarkers linked to cancer progression and metastasis. The integration of genomic and proteomic data provides a comprehensive view of the tumor's molecular landscape. This approach helps in early cancer detection, personalized treatment strategies, and monitoring therapy response or recurrence. The assay was originally developed by the Johns Hopkins University team and was rebranded as CancerGuard following its commercial advancement in recent years to reflect updated analytical and clinical validation progress. Cohen JD et al. (65) applied **CancerGuard** to 1,005 early-stage cancer patients across eight tumour types, reporting an overall median positive rate of 70%. Sensitivity for five cancers lacking routine screening ranged from 69% to 98%, specificity in healthy controls exceeded 99%, and 83% of positive cases could be localised to the potential tumour site. These findings confirm **CancerGuard** potential for

non-invasive CRC screening, although independent validation remains necessary.

### 6.2 DELFI method

DELFI (DNA Evaluation of Fragments for Early Interception) is a liquid biopsy technology based on cell-free DNA (cfDNA) fragmentomics. It employs low-pass whole-genome sequencing (WGS) to comprehensively analyse cfDNA fragment features, including size distribution, end motifs, and nucleosome positioning, combined with machine learning algorithms to identify tumour-associated DNA fragment abnormalities. Its advantage lies in tumour detection without reliance on specific gene mutation analysis (66).

Studies show that DELFI-TF (Tumour Fraction) scores are highly correlated with ctDNA levels ( $r=0.90$ ), effectively estimating tumour burden even when mutations are undetected, enabling monitoring of tumour dynamics (67).

### 6.3 Cologuard

Cologuard is primarily designed for colorectal cancer (CRC) screening, analyzing stool samples for human hemoglobin and methylated DNA biomarkers, while its reliance on early mutation-based targets has been reduced in the current version (68). The updated multitarget stool DNA test (Cologuard Plus) demonstrated a sensitivity of 93.9% (95% CI, 87.1–97.7) for CRC and 43.4% (95% CI, 41.3–45.6) for advanced precancerous lesions, with a specificity of 90.6% (95% CI, 90.1–91.0) in asymptomatic adults (69).

### 6.4 Shield test

The **Shield Test** is a blood-based colorectal cancer (CRC) screening assay developed by Guardant Health, employing cell-free DNA (cfDNA) methylation analysis combined with machine learning for non-invasive detection of CRC and advanced precancerous lesions (70). In a large prospective study (10,258 participants), the Shield test achieved **sensitivity of 83% for CRC** and **specificity of 90%** for advanced neoplasia detection, demonstrating clinical performance comparable to FIT but with greater patient compliance due to its blood-based nature. It represents an emerging non-invasive alternative to stool-based tests such as Cologuard and ColoSense, marking a significant step toward precision CRC screening through epigenomic profiling (71).

### 6.5 Multi-cancer early detection platform

Galleri is a blood-based **multi-cancer early detection (MCED) platform** that analyses cfDNA methylation patterns using machine learning to detect signals from multiple cancer types and predict



tissue of origin (72, 73). It can detect over 50 tumour types with specificity exceeding 99%, a false-positive rate below 1%, overall sensitivity of 54.9%, early-stage (I–III) sensitivity of 43.9%, and 93% accuracy for tissue-of-origin prediction (74). As an MCED platform, Galleri is distinct from CRC-specific assays, such as Cologuard or ColoSense, which focus solely on colorectal cancer and advanced precancerous lesions. Galleri embodies a “breadth-first” strategy for multi-cancer detection, complementary to the “depth-first” approach of CRC-targeted assays.

## 6.6 Freenome multi-omics platform

Freenome is a blood-based multi-omics screening platform that integrates cell-free DNA (cfDNA) methylation, fragmentomics features, and plasma proteomics data, combined with machine learning algorithms to identify early cancer signals.

In a recent large-scale study, the Freenome colorectal cancer (CRC) screening test demonstrated a **sensitivity of 79.2%** for CRC detection and a **specificity of 91.5%** for advanced tumors. The **negative predictive value (NPV)** for advanced CRC was **90.8%**, and the **positive predictive value (PPV)** was **15.5%** (75). These findings indicate that multi-omics integration models outperform single-omics approaches in early cancer detection.

## 7 Artificial intelligence and imaging recognition in CRC screening

### 7.1 AI-Assisted colonoscopy systems

AI-based imaging recognition has been widely applied in CRC screening, particularly in colonoscopy, significantly reducing missed lesions. Multicentre RCTs have demonstrated that AI-assisted colonoscopy systems (e.g., the “Eagle-Eye” system) can increase adenoma detection rates (ADR) from 32.4% to 39.9%, and improve detection of advanced adenomas (76). A multicentre trial in China also showed that CAdE systems significantly increased the number of adenomas detected per procedure (APC) and polyp detection rate (PDR) (77). A 2024 RCT using RetinaNet-based AI further confirmed superior PDR and ADR outcomes compared with conventional methods (78). Beyond detection, AI shows potential in polyp characterisation and optical biopsy, enabling differentiation of benign and malignant lesions and prediction of invasion (79).

### 7.2 AI-Assisted computed tomography colonography and 3D reconstruction

CT colonography (CTC) is a non-invasive low-dose spiral CT method that provides “virtual endoscopy” through 2D and 3D reconstructions, enabling detection of polyps, strictures, and tumours (80). Studies indicate that CTC sensitivity for  $\geq 10$  mm adenomas or cancers is comparable to conventional colonoscopy, with detection of 6–9 mm lesions continuously improving (81).

Modern Deep-Learning Reconstruction (DLR) technology significantly enhances image signal-to-noise ratio and reduces artefacts at low radiation doses, providing high-quality inputs for 3D surface reconstruction, thereby improving lesion visualisation and detection accuracy (82). Importantly, as a non-invasive and sedation-free technique, CTC reduces the need for anesthesia-assisted procedures, improving patient comfort and compliance while maintaining diagnostic accuracy.

## 7.3 Deep learning and multimodal data integration

AI and multimodal data fusion have demonstrated notable potential in CRC screening and precision treatment. Deep learning models can extract complex imaging features to predict prognosis and treatment response. Multi-stain deep learning models (MSDLM) analysing tumour immune microenvironments outperform traditional indices in survival prediction (83); models based on H&E images can identify consensus molecular subtypes (CMS), informing personalised therapy (84). Multimodal models integrating MRI, pathology, and clinical data offer comprehensive disease characterisation, with multicentre studies showing improved survival prediction accuracy (C-index=0.86) (85). Multi-task deep learning excels in tumour segmentation and treatment response prediction, with pCR identification AUC reaching 0.95 (86). Weakly supervised models combining MRI and pathology have achieved lymph node diagnostic accuracy approaching expert levels (87).

## 8 Key updates and implementation differences in international screening guidelines

The latest USPSTF update highlights the increasing incidence of early-onset colorectal cancer (EOCRC) and recommends lowering the screening initiation age from 50 to 45 years, while maintaining FIT and colonoscopy as core modalities. In contrast, several European countries (e.g., Germany) continue to start at 50 years, emphasizing early intervention in genetically high-risk groups (88). Implementation varies globally due to differences in cost-effectiveness, coverage, and healthcare resources. In low-resource regions, FIT is preferred for its affordability and non-invasiveness, though colonoscopy adherence remains low (30%–60%). Despite public awareness efforts, screening coverage in some areas remains below 40%, reflecting inequitable resource allocation (89).

## 9 Current challenges in colorectal cancer screening

Despite proven mortality reduction, global CRC screening participation remains suboptimal, influenced by inadequate public

awareness, lack of physician recommendation, and fear of colonoscopy. Novel biomarkers such as circulating tumour DNA (ctDNA) exhibit high sensitivity but limited capacity for detecting precancerous lesions; for example, the PREEMPT CRC study reported a sensitivity of only 12.5%, indicating the need for further clinical validation (90). Additionally, AI applications in screening face challenges related to algorithm interpretability, data privacy and security, and population generalisability, raising ethical and regulatory concerns (91). Improving public adherence, optimising biomarker technologies, and establishing robust AI regulatory frameworks are pivotal to advancing CRC screening.

## 10 Limitations

This review has several limitations. Rapid technological advances mean some recent data may be excluded. Study heterogeneity also restricts direct comparison across platforms. Moreover, no quantitative meta-analysis was performed. Future research should update datasets and use standardized evaluation methods to enhance comparability.

## 11 Summary and perspectives

CRC screening is moving towards personalized, precision strategies integrating genetics, lifestyle, and environment. In parallel, the principles of individualized management in anesthesiology offer valuable insights for personalized CRC screening and perioperative strategies. In anesthetic practice, patient-specific physiological variability, genetic differences in drug metabolism, and comorbidity profiles are increasingly integrated into precision anesthesia protocols. Similarly, individualized CRC screening should account for genetic susceptibility, metabolic status, and systemic inflammatory responses that may influence both cancer risk and perioperative outcomes. The convergence of precision anesthesiology and precision oncology underscores a broader trend toward data-driven, individualized medicine, highlighting the importance of integrating multidisciplinary insights into CRC prevention and management.

Early genetic testing (e.g., APC, MLH1) in high-risk groups improves early detection (92). Multi-omics approaches combining plasma proteomics, ctDNA, and machine learning enhance early lesion prediction (93, 94). AI-driven multimodal integration further supports dynamic, individualized management, while real-time imaging with deep learning optimizes detection and treatment response (95). Future research should prioritize validating

emerging multi-omics assays, developing interpretable and generalizable AI models, and exploring the integration of CRC screening with perioperative and anesthetic management to advance personalized cancer care.

## Author contributions

LT: Writing – review & editing, Formal analysis, Conceptualization, Writing – original draft. XZ: Writing – review & editing, Investigation, Data curation. GW: Writing – review & editing, Resources, Validation. JH: Project administration, Writing – original draft. MZ: Validation, Writing – review & editing. WX: Writing – review & editing.

## Funding

The author(s) declare that financial support was received for the research and/or publication of this article.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

## Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

## References

1. Song M. Global epidemiology and prevention of colorectal cancer. *Lancet Gastroenterol Hepatol.* (2022) 7:588–90. doi: 10.1016/S2468-1253(22)00089-9
2. Venugopal A, Carethers JM. Epidemiology and biology of early onset colorectal cancer. *EXCLI J.* (2022) 21:162–82. doi: 10.17179/excli2021-4456
3. Yang Y, Han Z, Li X, Huang A, Shi J, Gu J. Epidemiology and risk factors of colorectal cancer in China. *Chin J Cancer Res.* (2020) 32:729–41. doi: 10.21147/j.issn.1000-9604.2020.06.06
4. Zhou YY, Li N, Lu B, Luo CY, Zhang YH, Luo JH, et al. Value of fecal immunochemical test in colorectal cancer screening. *Zhonghua Zhong Liu Za Zhi.* (2023) 45:911–8. doi: 10.3760/cma.j.cn112152-20230418-00176

5. Robertson DJ, Rex DK, Ciani O, Drummond MF. Colonoscopy vs the fecal immunochemical test: which is best? *Gastroenterology*. (2024) 166:758–71. doi: 10.1053/j.gastro.2023.12.027
6. Castells A, Quintero E, Bujanda L, Castán-Cameo S, Cubiella J, Díaz-Tasende J, et al. Effect of invitation to colonoscopy versus faecal immunochemical test screening on colorectal cancer mortality (COLONPREV): a pragmatic, randomised, controlled, non-inferiority trial. *Lancet*. (2025) 405:1231–9. doi: 10.1016/S0140-6736(25)00145-X
7. Jain S, Maque J, Galoosian A, Osuna-García A, May FP. Optimal strategies for colorectal cancer screening. *Curr Treat Options Oncol*. (2022) 23:474–93. doi: 10.1007/s11864-022-00962-4
8. VandenHeuvel SN, Nash LL, Raghavan SA. Dormancy in metastatic colorectal cancer: tissue engineering opportunities for *in vitro* modeling. *Tissue Eng Part B Rev*. (2025) 21:1–10. doi: 10.1089/ten.teb.2025.0009
9. Stracci F, Zorzi M, Grazzini G. Colorectal cancer screening: tests, strategies, and perspectives. *Front Public Health*. (2014) 2:210. doi: 10.3389/fpubh.2014.00210
10. Alvarez-Torres MDM, Fu X, Rabadan R. Illuminating the noncoding genome in cancer using artificial intelligence. *Cancer Res*. (2025) 85:2368–75. doi: 10.1158/0008-5472.CAN-25-0482
11. Lou Y, Deng Z, Gao J. Genomics refined: AI-powered perspectives on structural analysis. *Trends Plant Sci*. (2024) 29:123–5. doi: 10.1016/j.tplants.2023.10.005
12. Young E, Edwards L, Singh R. The role of artificial intelligence in colorectal cancer screening: lesion detection and lesion characterization. *Cancers (Basel)*. (2023) 15:5126. doi: 10.3390/cancers15125126
13. Kim H, Melio A, Simianu V, Mankaney G. Challenges and opportunities for colorectal cancer prevention in young patients. *Cancers (Basel)*. (2025) 17:2043. doi: 10.3390/cancers17122043
14. Perrod G, Rahmi G, Cellier C. Colorectal cancer screening in Lynch syndrome: indication, techniques and future perspectives. *Dig Endosc*. (2021) 33:520–8. doi: 10.1111/den.13702
15. Leung WC, Foo DC, Chan TT, Chiang MF, Lam AH, Chan HH, et al. Alternatives to colonoscopy for population-wide colorectal cancer screening. *Hong Kong Med J*. (2016) 22:70–7. doi: 10.12809/hkmj154685
16. Jodal HC, Helsingen LM, Anderson JC, Lytvyn L, Vandvik PO, Emilsson L. Colorectal cancer screening with faecal testing, sigmoidoscopy or colonoscopy: a systematic review and network meta-analysis. *BMJ Open*. (2019) 9:e032773. doi: 10.1136/bmjopen-2019-032773
17. Lin JS, Perdue LA, Henrikson NB, Bean SI, Blasi PR. Screening for colorectal cancer: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. (2021) 325:1978–98. doi: 10.1001/jama.2021.4417
18. Tinmouth J, Patel J, Austin PC, Baxter NN, Brouwers MC, Earle C, et al. Increasing participation in colorectal cancer screening: results from a cluster randomized trial of directly mailed gFOBT kits to previous nonresponders. *Int J Cancer*. (2015) 136:E697–703. doi: 10.1002/ijc.29191
19. Lu J, Xu B, Xu Y, Wu Y, Xie J, Wang J, et al. A novel insight into fecal occult blood test for the management of gastric cancer: complication, survival, and chemotherapy benefit after R0 resection. *Front Oncol*. (2021) 10:526746. doi: 10.3389/fonc.2020.526746
20. Tinmouth J, Lansdorp-Vogelaar I, Allison JE. Faecal immunochemical tests versus guaiac faecal occult blood tests: what clinicians and colorectal cancer screening programme organisers need to know. *Gut*. (2015) 64:1327–37. doi: 10.1136/gutjnl-2014-308074
21. Goede SL, Rabeneck L, van Ballegooijen M, Zauber AG, Paszat LF, Hoch JS, et al. Harms, benefits and costs of fecal immunochemical testing versus guaiac fecal occult blood testing for colorectal cancer screening. *PLoS One*. (2017) 12:e0172864. doi: 10.1371/journal.pone.0172864
22. Meklin J, Syrjänen K, Eskelinen M. Colorectal cancer screening with traditional and new-generation fecal immunochemical tests: a critical review of fecal occult blood tests. *Anticancer Res*. (2020) 40:575–81. doi: 10.21873/anticancer.13987
23. Dimopoulos MP, Verrass GI, Mulita F. Editorial: Newest challenges and advances in the treatment of colorectal disorders; from predictive biomarkers to minimally invasive techniques. *Front Surg*. (2024) 11:1487878. doi: 10.3389/fsurg.2024.1487878
24. Raut JR, Guan Z, Schrotz-King P, Brenner H. Fecal DNA methylation markers for detecting stages of colorectal cancer and its precursors: a systematic review. *Clin Epigenet*. (2020) 12:122. doi: 10.1186/s13148-020-00904-7
25. Mo S, Ye L, Wang D, Han L, Zhou S, Wang H, et al. Early detection of molecular residual disease and risk stratification for stage I to III colorectal cancer via circulating tumor DNA methylation. *JAMA Oncol*. (2023) 9:770–8. doi: 10.1001/jamaoncol.2023.0425
26. Sun Q, Long L. Diagnostic performances of methylated septin9 gene, CEA, CA19-9 and platelet-to-lymphocyte ratio in colorectal cancer. *BMC Cancer*. (2024) 24:906. doi: 10.1186/s12885-024-12670-3
27. Long L, Sun Q, Yang F, Zhou H, Wang Y, Xiao C, et al. Significance of SDC2 and NDRG4 methylation in stool for colorectal cancer diagnosis. *Clin Biochem*. (2024) 124:110717. doi: 10.1016/j.clinbiochem.2024.110717
28. Payne SR. From discovery to the clinic: the novel DNA methylation biomarker (m)SEPT9 for the detection of colorectal cancer in blood. *Epigenomics*. (2010) 2:575–85. doi: 10.2217/epi.10.35
29. Imperiale TF, Ransohoff DF, Itzkowitz SH, Levin TR, Lavin P, Lidgard GP, et al. Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med*. (2014) 370:1287–97. doi: 10.1056/NEJMoa1311194
30. Kadiyska T, Nossikoff A. Stool DNA methylation assays in colorectal cancer screening. *World J Gastroenterol*. (2015) 21:10057–61. doi: 10.3748/wjg.v21.i35.10057
31. Melotte V, Lentjes MH, van den Bosch SM, Hellebrekers DM, de Hoon JP, Wouters KA, et al. N-Myc downstream-regulated gene 4 (NDRG4): a candidate tumor suppressor gene and potential biomarker for colorectal cancer. *J Natl Cancer Inst*. (2009) 101:916–27. doi: 10.1093/jnci/djp131
32. Boughanem H, Pilo J, García-Flores LA, Arranz I, Ramos-Fernandez M, Ortega-Castan M, et al. Identification of epigenetic silencing of the SFRP2 gene in colorectal cancer as a clinical biomarker and molecular significance. *J Transl Med*. (2024) 22:509. doi: 10.1186/s12967-024-05329-x
33. Cohen ML, Brumwell AN, Ho TC, Garakani K, Montas G, Leong D, et al. A fibroblast-dependent TGF- $\beta$ 1/sFRP2 noncanonical Wnt signaling axis promotes epithelial metaplasia in idiopathic pulmonary fibrosis. *J Clin Invest*. (2024) 134:e174598. doi: 10.1172/JCI174598
34. Park SK, Baek HL, Yu J, Kim JY, Yang HJ, Jung YS, et al. Is methylation analysis of SFRP2, TFIPI2, NDRG4, and BMP3 promoters suitable for colorectal cancer screening in the Korean population? *Intest Res*. (2017) 15:495–501. doi: 10.5217/ir.2017.15.4.495
35. Anghel SA, Ioniță-Mândrican CB, Luca I, Pop AL. Promising epigenetic biomarkers for the early detection of colorectal cancer: a systematic review. *Cancers (Basel)*. (2021) 13:4965. doi: 10.3390/cancers13194965
36. Liu R, Su X, Long Y, Zhou D, Zhang X, Ye Z, et al. A systematic review and quantitative assessment of methylation biomarkers in fecal DNA and colorectal cancer and its precursor, colorectal adenoma. *Mutat Res Rev Mutat Res*. (2019) 779:45–57. doi: 10.1016/j.mrrrev.2019.01.003
37. Toes-Zoutendijk E, Kooyker AI, Elferink MA, Spaander MCW, Dekker E, Koning HJ. Stage distribution of screen-detected colorectal cancers in the Netherlands. *Gut*. (2018) 9:1745–6. doi: 10.1136/gutjnl-2017-315111
38. Imperiale TF, Porter K, Zella J, Gagrut ZD, Olson MC, Statz S, et al. Next-generation multitarget stool DNA test for colorectal cancer screening. *N Engl J Med*. (2024) 390:984–93. doi: 10.1056/NEJMoa2310336
39. Alix-Panabières C, Pantel K. Clinical applications of circulating tumor cells and circulating tumor DNA as liquid biopsy. *Cancer Discov*. (2016) 6:479–91. doi: 10.1158/2159-8290.CD-15-1483
40. Malla M, Loree JM, Kasi PM, Parikh AR. Using circulating tumor DNA in colorectal cancer: current and evolving practices. *J Clin Oncol*. (2022) 40:2846–57. doi: 10.1200/JCO.21.02615
41. Zhou H, Zhu L, Song J, Wang G, Li P, Li W, et al. Liquid biopsy at the frontier of detection, prognosis and progression monitoring in colorectal cancer. *Mol Cancer*. (2022) 21:86. doi: 10.1186/s12943-022-01556-2
42. Huang X, Zhu X, Yu Y, Zhu W, Jin L, Zhang X, et al. Dissecting miRNA signature in colorectal cancer progression and metastasis. *Cancer Lett*. (2021) 501:66–82. doi: 10.1016/j.canlet.2020.12.025
43. Dong J, Tai JW, Lu LF. miRNA-microbiota interaction in gut homeostasis and colorectal cancer. *Trends Cancer*. (2019) 5:666–9. doi: 10.1016/j.trecan.2019.08.003
44. Balacescu O, Sur D, Cainap C, Visan S, Cruceriu D, Manzat-Saplaçan R, et al. The impact of miRNA in colorectal cancer progression and its liver metastases. *Int J Mol Sci*. (2018) 19:3711. doi: 10.3390/ijms19123711
45. Huang Z, Huang X, Huang Y, Liang K, Chen L, Zhong C, et al. Identification of KRAS mutation-associated gut microbiota in colorectal cancer and construction of predictive machine learning model. *Microbiol Spectr*. (2024) 12:e0272023. doi: 10.1128/spectrum.02720-23
46. Liu J, Huang X, Chen C, Wang Z, Huang Z, Qin M, et al. Identification of colorectal cancer progression-associated intestinal microbiome and predictive signature construction. *J Transl Med*. (2023) 21:373. doi: 10.1186/s12967-023-04119-1
47. Kandimalla R, Gao F, Matsuyama T, Ishikawa T, Uetake H, Takahashi N. Genome-wide discovery and identification of a novel miRNA signature for recurrence prediction in stage II and III colorectal cancer. *Clin Cancer Res*. (2018) 16:3867–77. doi: 10.1158/1078-0432.CCR-17-3236
48. Yang Y, Misra BB, Liang L, Bi D, Weng W, Wu W. Integrated microbiome and metabolome analysis reveals a novel interplay between commensal bacteria and metabolites in colorectal cancer. *Theranostics*. (2019) 14:4101–14. doi: 10.7150/thno.35186
49. Chen S, Jin Y, Wang S, Xing S, Wu Y, Tao Y, et al. Cancer type classification using plasma cell-free RNAs derived from human and microbes. *Elife*. (2022) 11:e75181. doi: 10.7554/eLife.75181
50. Tao Y, Xing S, Zuo S, Bao P, Jin Y, Li Y, et al. Cell-free multi-omics analysis reveals potential biomarkers in gastrointestinal cancer patients' blood. *Cell Rep Med*. (2023) 4:101281. doi: 10.1016/j.xcrm.2023.101281
51. Ju CW, Lyu R, Li H, Wei J, Parra Vitela AJ, Dougherty U, et al. Modifications of microbiome-derived cell-free RNA in plasma discriminates colorectal cancer samples. *Nat Biotechnol*. (2025) 23:1–10. doi: 10.1038/s41587-025-02731-8
52. Wang J, Huang J, Hu Y, Guo Q, Zhang S, Tian J, et al. Terminal modifications independent cell-free RNA sequencing enables sensitive early cancer detection and classification. *Nat Commun*. (2024) 15:156. doi: 10.1038/s41467-023-44461-y



53. Wang H, Zhan Q, Ning M, Guo H, Wang Q, Zhao J, et al. Depletion-assisted multiplexed cell-free RNA sequencing reveals distinct human and microbial signatures in plasma versus extracellular vesicles. *Clin Transl Med.* (2024) 14:e1760. doi: 10.1002/ctm2.1760
54. Su H, Gu X, Zhang W, Lin F, Lu X, Zeng X, et al. Identification of salivary biomarkers in colorectal cancer by integrating Olink proteomics and metabolomics. *J Proteome Res.* (2025) 24:2542–52. doi: 10.1021/acs.jproteome.5c00091
55. Rao J, Wan X, Tou F, He Q, Xiong A, Chen X, et al. Molecular characterization of advanced colorectal cancer using serum proteomics and metabolomics. *Front Mol Biosci.* (2021) 8:687229. doi: 10.3389/fmolb.2021.687229
56. Ma Y, Zhang P, Wang F, Liu W, Yang J, Qin H. An integrated proteomics and metabolomics approach for defining oncofetal biomarkers in the colorectal cancer. *Ann Surg.* (2012) 255:720–30. doi: 10.1097/SLA.0b013e31824a9a8b
57. Santos MD, Barros I, Brandão P, Lacerda L. Amino acid profiles in the biological fluids and tumor tissue of CRC patients. *Cancers (Basel).* (2023) 16:69. doi: 10.3390/cancers16010069
58. Cao Q, Yang M, Chen M. Metabolic interactions: how gut microbial metabolites influence colorectal cancer. *Front Microbiol.* (2025) 16:1611698. doi: 10.3389/fmicb.2025.1611698
59. Cui W, Hao M, Yang X, Yin C, Chu B. Gut microbial metabolism in ferroptosis and colorectal cancer. *Trends Cell Biol.* (2024) 35:341–51. doi: 10.1016/j.tcb.2024.08.006
60. Nguyen LH, Cao Y, Hur J, Mehta RS, Sikavi DR, Wang Y, et al. The sulfur microbial diet is associated with increased risk of early-onset colorectal cancer precursors. *Gastroenterology.* (2021) 161:1423–1432.e4. doi: 10.1053/j.gastro.2021.07.008
61. Yue T, Li J, Zhu J, Zuo S, Wang X, Liu Y, et al. Hydrogen sulfide creates a favorable immune microenvironment for colon cancer. *Cancer Res.* (2023) 83:595–612. doi: 10.1158/0008-5472.CAN-22-1837
62. Lin H, Yu Y, Zhu L, Lai N, Zhang L, Guo Y, et al. Implications of hydrogen sulfide in colorectal cancer: mechanistic insights and diagnostic and therapeutic strategies. *Redox Biol.* (2023) 59:102601. doi: 10.1016/j.redox.2023.102601
63. Ternes D, Tsenkova M, Pozdeev VI, Meyers M, Koncina E, Atatri S, et al. The gut microbial metabolite formate exacerbates colorectal cancer progression. *Nat Metab.* (2022) 4:458–75. doi: 10.1038/s42255-022-00558-0
64. Killock D. Diagnosis: cancerSEEK and destroy-a blood test for early cancer detection. *Nat Rev Clin Oncol.* (2018) 15:133. doi: 10.1038/nrclinonc.2018.21
65. Cohen JD, Li L, Wang Y, Thoburn C, Afsari B, Danilova L, et al. Detection and localization of surgically resectable cancers with a multi-analyte blood test. *Science.* (2018) 359:926–30. doi: 10.1126/science.aar3247
66. Dong W, Hu W, Lu Y, Zheng Q. Cell-free DNA fragmentomics: a universal framework for early cancer detection and monitoring. *Am J Clin Exp Immunol.* (2025) 14:237–40. doi: 10.62347/EBRY4326
67. van 't Erve I, Alipanahi B, Lumbard K, Skidmore ZL, Rinaldi L, Millberg LK, et al. Cancer treatment monitoring using cell-free DNA fragmentomes. *Nat Commun.* (2024) 15:8801. doi: 10.1038/s41467-024-53017-7
68. Ladabaum U, Mannalithara A, Weng Y, Schoen RE, Dominitz JA, Desai M, et al. Comparative effectiveness and cost-effectiveness of colorectal cancer screening with blood-based biomarkers (liquid biopsy) vs fecal tests or colonoscopy. *Gastroenterology.* (2024) 167:378–91. doi: 10.1053/j.gastro.2024.03.011
69. Imperiale TF, Porter K, Zella J, Gagrut ZD, Olson MC, Statz S, et al. BLUE-C study investigators. Next-generation multitarget stool DNA test for colorectal cancer screening. *N Engl J Med.* (2024) 390:984–93. doi: 10.1056/NEJMoa2310336
70. Mannucci A, Goel A. Stool and blood DNA tests for colorectal cancer screening. *N Engl J Med.* (2024) 390:2224. doi: 10.1056/NEJMoa2404924
71. Chung DC, Gray DM2nd, Singh H, Issaka RB, Raymond VM, Eagle C, et al. A cell-free DNA blood-based test for colorectal cancer screening. *N Engl J Med.* (2024) 390:973–83. doi: 10.1056/NEJMoa2304714
72. Pyzocha NJ. Galleri test for the detection of cancer. *Am Fam Physician.* (2022) 106:459–60.
73. Schrag D, Beer TM, McDonnell CH3rd, Nadauld L, Dilaveri CA, Reid R, et al. Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study. *Lancet.* (2023) 402:1251–60. doi: 10.1016/S0140-6736(23)01700-2
74. Klein EA, Richards D, Cohn A, Tummala M, Lapham R, Cosgrove D, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. *Ann Oncol.* (2021) 32:1167–77. doi: 10.1016/j.annonc.2021.05.806
75. Shaukat A, Burke CA, Chan AT, Grady WM, Gupta S, Katona BW, et al. Clinical validation of a circulating tumor DNA-based blood test to screen for colorectal cancer. *JAMA.* (2025) 334:56–63. doi: 10.1001/jama.2025.7515
76. Xu H, Tang RSY, Lam TYT, Zhao G, Lau JYW, Liu Y, et al. Artificial intelligence-assisted colonoscopy for colorectal cancer screening: a multicenter randomized controlled trial. *Clin Gastroenterol Hepatol.* (2023) 21:337–346.e3. doi: 10.1016/j.cgh.2022.07.006
77. Wang P, Liu XG, Kang M, Peng X, Shu ML, Zhou GY, et al. Artificial intelligence empowers the second-observer strategy for colonoscopy: a randomized clinical trial. *Gastroenterol Rep (Oxf).* (2023) 11:goac081. doi: 10.1093/gastro/goac081
78. Park DK, Kim EJ, Im JP, Lim H, Lim YJ, Byeon JS, et al. A prospective multicenter randomized controlled trial on artificial intelligence assisted colonoscopy for enhanced polyp detection. *Sci Rep.* (2024) 14:25453. doi: 10.1038/s41598-024-77079-1
79. Kim ES, Lee KS. Artificial intelligence in colonoscopy: from detection to diagnosis. *Korean J Intern Med.* (2024) 39:555–62. doi: 10.3904/kjim.2023.332
80. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med.* (2003) 349:2191–200. doi: 10.1056/NEJMoa031618
81. Wesp P, Grosu S, Graser A, Maurus S, Schulz C, Knösel T, et al. Deep learning in CT colonography: differentiating premalignant from benign colorectal polyps. *Eur Radiol.* (2022) 32:4749–59. doi: 10.1007/s00330-021-08532-2
82. Szczukutowicz TP, Toia GV, Dhanantwari A, Nett B. A review of deep learning CT reconstruction: concepts, limitations, and promise in clinical practice. *Curr Radiol Rep.* (2022) 10:101–15. doi: 10.1007/s40134-022-00399-5
83. Foersch S, Glasner C, Woerl AC, Eckstein M, Wagner DC, Schulz S, et al. Multistain deep learning for prediction of prognosis and therapy response in colorectal cancer. *Nat Med.* (2023) 29:430–9. doi: 10.1038/s41591-022-02134-1
84. Sirinukunwattana K, Domingo E, Richman SD, Redmond KL, Blake A, Verrill C, et al. Image-based consensus molecular subtype (imCMS) classification of colorectal cancer using deep learning. *Gut.* (2021) 70:544–54. doi: 10.1136/gutjnl-2019-319866
85. Jiang X, Zhao H, Saldanha OL, Nebelung S, Kuhl C, Amygdalos I, et al. An MRI deep learning model predicts outcome in rectal cancer. *Radiology.* (2023) 307:e222223. doi: 10.1148/radiol.222223
86. Jin C, Yu H, Ke J, Ding P, Yi Y, Jiang X, et al. Predicting treatment response from longitudinal images using multi-task deep learning. *Nat Commun.* (2021) 12:1851. doi: 10.1038/s41467-021-22188-y
87. Gupta S. Screening for colorectal cancer. *Hematol Oncol Clin North Am.* (2022) 36:393–414. doi: 10.1016/j.hoc.2022.02.001
88. Waddell O, Keenan J, Frizelle F. Challenges around diagnosis of early onset colorectal cancer, and the case for screening. *ANZ J Surg.* (2024) 94:1687–92. doi: 10.1111/ans.19221
89. Alharbi MB. Colorectal cancer screening modalities among saudi population: significant predictors. *Rev Recent Clin Trials.* (2025) 21. doi: 10.2174/0115748871335743250417103659
90. Mannucci A, Goel A. Circulating tumor DNA-based blood test for colorectal cancer screening. *JAMA.* (2025). doi: 10.1001/jama.2025.14109
91. Tiwari A, Mishra S, Kuo TR. Current AI technologies in cancer diagnostics and treatment. *Mol Cancer.* (2025) 24:159. doi: 10.1186/s12943-025-02369-9
92. Alhassan NS, Beyari MB, Aldeligan SH, Alqusiyyer AA, Almutib SA, Alarfaj MA, et al. Understanding colorectal cancer screening barriers in Saudi Arabia: insights from a cross-sectional study. *J Multidiscip Healthc.* (2025) 18:1335–44. doi: 10.2147/JMDH.S507481
93. Jin H, Deng K, Qi S, Deng Z, Pu L, Xu D, et al. Plasma proteomic high-performance biomarkers for early diagnosis of colorectal cancer. *J Proteome Res.* (2025) 24:5177–89. doi: 10.1021/acs.jproteome.5c00483
94. Alotaibi AG, Alfazan BA, Alotaibi SS, Al Mutairi AS, Al Humoudi AY, Al Jawini NA, et al. CRC management: emerging trends in early detection, diagnosis, biomarkers, treatment, and prevention. *Pathol Res Pract.* (2025) 275:156206. doi: 10.1016/j.prp.2025.156206
95. Biswas S, Chohan DP, Wankhede M, Rodrigues J, Bhat G, Mathew S, et al. Photoacoustic-integrated multimodal approach for colorectal cancer diagnosis. *ACS Biomater Sci Eng.* (2025) 11:4033–49. doi: 10.1021/acsbiomaterials.5c00918