

Advances in Colorectal Cancer Detection: A Review of Biomarkers, Imaging and Prevention

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ABSTRACT

Background: Colorectal cancer (CRC) continues to be a primary cause of cancer-related morbidity and mortality globally, with an increasing incidence in both developed and developing areas. Early detection greatly enhances prognosis; nevertheless, traditional screening techniques, including colonoscopy and faecal occult blood tests, possess drawbacks such as invasiveness, accessibility, and inconsistent sensitivity. Recent progress in biomarkers, imaging technology, and preventive methods presents prospects to improve CRC identification and monitoring.

Objective: This review seeks to furnish a thorough examination of contemporary and novel methodologies for colorectal cancer (CRC) detection, with a focus on stool- and blood-based biomarkers, imaging techniques, and preventive measures. It emphasises their clinical value, constraints, and prospective incorporation into multi-modal detection frameworks.

Methods: A narrative assessment of contemporary literature (2014–2025) was performed utilising PubMed, Scopus, and Web of Science, concentrating on studies assessing CRC biomarkers, imaging technology, and preventative measures. The focus was on translational research, clinical usefulness, and innovations having the potential for deployment at the population level.

Results: Stool- and blood-based biomarkers, such as faecal immunochemical tests, multi-target stool DNA assays, circulating tumour DNA, and circulating tumour cells, show good specificity and are becoming useful for early diagnosis and monitoring of minimal residual disease. Imaging technologies, including high-definition colonoscopy, chromoendoscopy, CT colonography, and MRI, are being enhanced by artificial intelligence to facilitate superior polyp diagnosis and risk classification. Preventive methods, including lifestyle change, chemoprevention, and risk-adapted screening, are essential for alleviating the burden of colorectal cancer (CRC). Integrated strategies that use both biomarkers and imaging could lead to personalised, non-invasive ways to find things. Challenges remain, especially with cost, accessibility, standardization, and population-specific variability in test performance.

Conclusion: Recent advancements in biomarkers, imaging, and preventive measures have significantly enhanced colorectal cancer (CRC) detection, with multimodal techniques presenting the most promising guarantee for improving early diagnosis and clinical outcomes. Future research should concentrate on validation across varied populations, cost-effectiveness, and incorporation into national screening initiatives to optimize public health outcomes.

Keywords: Artificial intelligence, Biomarkers; Circulating tumour DNA; Colorectal cancer, Colonoscopy; Early detection; Imaging modalities; Minimal residual disease; Prevention strategies; Screening.

Introduction

Colorectal cancer (CRC) ranks among the primary causes of cancer-related morbidity and mortality worldwide, accounting for an estimated 1.9 million new cases and 900,000 deaths annually {1}. Historically, its incidence has been greater in developed nations; however, recent epidemiological trends reveal an increasing prevalence in low- and middle-income areas, particularly in Sub-Saharan Africa and Asia, mostly attributable to westernised foods, sedentary lifestyles, and rising life expectancy {2,3}. Early diagnosis is still very important for improving survival rates. When CRC is found at a localized stage, the 5-year survival rate is over 90%, but when it is found at a metastatic stage, the rate is less than 15% {4}. In high-resource areas, traditional screening methods, including colonoscopy, flexible sigmoidoscopy, and faecal occult blood testing (FOBT), have greatly lowered the number of deaths from CRC {5}.

However, these procedures have some built-in problems: colonoscopy is intrusive, takes a lot of resources, and can vary from operator to operator; FOBT is not very sensitive, especially for advanced adenomas; and many people do not follow screening programs as well as they should {6,7}. These problems show how important it is to come up with new, non-invasive, and very delicate ways to find things.

Recent advancements in molecular biomarkers and imaging technologies have revolutionised the field of colorectal cancer detection. Stool- and blood-based biomarkers, such as faecal immunochemical tests (FIT), multi-target stool DNA assays, circulating tumour DNA (ctDNA), and circulating tumour cells (CTCs), present potential opportunities for early diagnosis, risk classification, and monitoring of minimal residual illness {8,9}. Simultaneous advancements in imaging, including high-definition colonoscopy, chromoendoscopy, computed tomography colonography, and magnetic resonance imaging,

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are progressively integrating artificial intelligence (AI) to improve polyp identification and diagnostic precision {10,11}. Combining these methods with preventive measures, from changing one's way of life to chemoprevention, could enhance results for the whole population and help precision screening programs.

This narrative review offers a thorough examination of current and developing methodologies for colorectal cancer detection. It looks at the clinical usefulness, strengths, and weaknesses of biomarkers and imaging techniques, assesses preventive methods, and emphasises integrative multi-modal approaches. Lastly, it points out problems, areas of research that need more work, and potential paths to help these improvements become part of everyday medical practice.

Risk Factors and Preventive Strategies

Risk Factors: Colorectal cancer (CRC) develops from a multifaceted interaction of genetic, environmental, and lifestyle influences. Non-modifiable risk variables encompass age, particularly with a large rise in occurrence post-50 years; sex; and a familial history of colorectal cancer or adenomatous polyps {9,10}. Hereditary disorders, including Lynch syndrome and familial adenomatous polyposis (FAP), account for around 5–10% of cases and are linked to early-onset colorectal cancer (CRC) {11,12}

Modifiable risk factors significantly contribute to sporadic CRC. Consistently, eating a lot of red and processed meats, not enough fibres, and too much alcohol is connected to a higher risk {13,14}. Obesity, physical inactivity, and smoking exacerbate carcinogenesis via chronic inflammation, insulin resistance, and epigenetic modifications {15,16}. New evidence suggests that the gut microbiome may also play a role in the development of CRC, with dysbiosis encouraging tumorigenesis through inflammatory and metabolic pathways {17}. (Figure 1)

Ways to Prevent: Primary prevention is all about lowering risks that can be changed. Lifestyle therapies, encompassing augmented physical activity, weight regulation, and the adoption of a fibre-rich diet with restricted red and processed meat intake, have evidenced substantial decreases in colorectal cancer incidence {18,19}. Chemoprevention utilising agents such as aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) has demonstrated effectiveness in high-risk populations, especially those with hereditary syndromes, although the risk of bleeding requires meticulous patient selection {20,21}. Secondary prevention via population-based screening continues to be essential. Evidence-based methodologies, such as faecal immunochemical testing (FIT), colonoscopy, and sigmoidoscopy, facilitate the early identification of precancerous lesions and nascent tumours, therefore decreasing mortality rates {22,23}. Risk-adapted screening techniques, informed by family history, genetic markers, and lifestyle factors, provide more tailored therapies. To effectively prevent CRC, we need to make changes to our daily lives, give some groups of people chemoprevention, and set up organised screening programs. The combination of new biomarkers and risk stratification technologies can make preventative efforts even better by improving early diagnosis and lowering the global burden of disease.

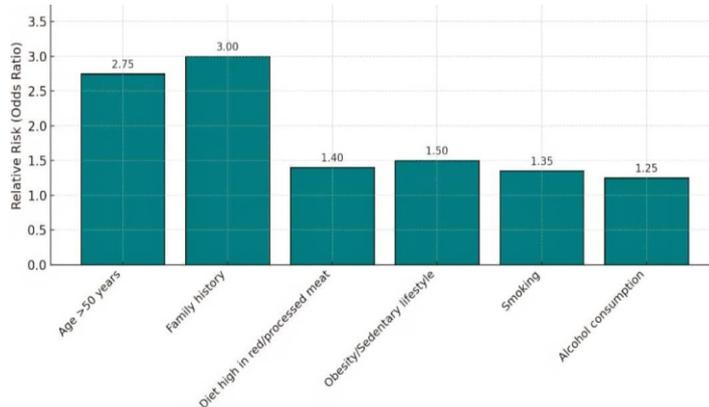


Figure 1: Relative risk of major CRC risk factors

Relative risk values are approximate averages from multiple epidemiological studies

Biomarkers for Detection and Monitoring:

Biomarkers have become essential instruments for the early identification, risk assessment, and surveillance of colorectal cancer (CRC). They provide the possibility for non-invasive screening, enhance traditional imaging, and provide minimal residual disease (MRD) monitoring. There are three main types of biomarkers: stool-based, blood-based, and genomic/epigenomic.

Biomarkers Found in Stool: Faecal immunochemical assays (FIT) identify occult blood with enhanced sensitivity compared to conventional guaiac-based faecal occult blood tests (gFOBT) and are extensively utilised for population screening {24,25}. Multi-target stool DNA (mt-sDNA) tests integrate molecular indicators, such as aberrant DNA methylation and KRAS mutations, with haemoglobin detection, resulting in enhanced sensitivity for both advanced adenomas and early-stage colorectal cancer (CRC) {26,27}. These tests are easy on patients and don't require any intrusive procedures, but the expense and lack of laboratory infrastructure can make it hard to use them widely.

Blood-Based Biomarkers: Circulating tumour DNA (ctDNA) has become significant for early identification of colorectal cancer (CRC) and monitoring minimal residual disease (MRD). Circulating tumour DNA indicates tumour-specific genomic modifications, encompassing point mutations, copy number variations, and methylation abnormalities {28,29}. Circulating tumour cells (CTCs) offer further insights into cancer burden and metastatic capability. Protein-based indicators, such as carcinoembryonic antigen (CEA) and CA19-9, have been previously utilised for monitoring but exhibit limited sensitivity for early detection {30}. The integration of ctDNA with conventional markers may improve diagnostic accuracy.

Genomic and Epigenomic Biomarkers: Tumour tissue and liquid biopsy analyses facilitate the discovery of microsatellite instability (MSI), KRAS, BRAF, APC, and TP53 mutations, which are essential for prognostication and treatment decision-making. Epigenetic biomarkers, such as methylation of SEPT9 and NDRG4, exhibit potential for non-invasive screening; however, confirmation at the population level is still in progress {34}. Multi-omics methodologies that amalgamate genomic, epigenomic, and transcriptomic data are becoming recognised as potent instruments for individualised detection and surveillance techniques. (Figure 2)

Usefulness and Limitations in the Clinic: Biomarkers are better since they are easier to get, can be used again and again, and can be used for risk-adapted screening. But their sensitivity and specificity differ among populations and tumour stages, and cost-effectiveness is still an issue, especially in areas with limited resources. To get more people to use them, tests need to be standardised, get regulatory approval, and be added to clinical workflows.

Stool- and blood-based biomarkers, along with genomic and epigenomic analysis, are changing how we detect and monitor CRC. Combining these biomarkers with imaging and preventive measures could lead to more accurate screenings and better outcomes for patients.

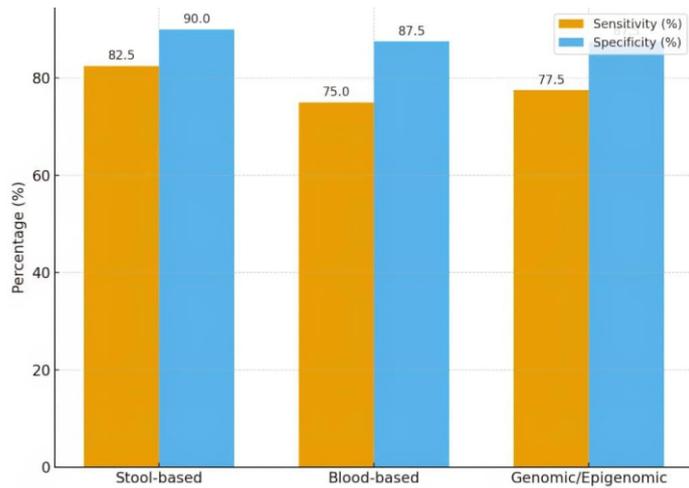


Figure 2: Diagnostic Performance of Biomarker Modalities in Colorectal Cancer

Sensitivity and specificity values represent approximate averages from reported ranges; clinical applications and limitations vary by biomarker type.

Imaging Modalities in Colorectal Cancer Diagnosis

Imaging is essential for the diagnosis, characterisation, and staging of colorectal cancer (CRC). Colonoscopy is still the best way to diagnose, although improvements in both endoscopic and cross-sectional imaging have made it easier to find lesions early and better describe them.

Endoscopy methods: Colonoscopy enables direct visualisation, biopsy, and excision of precancerous polyps. High-definition colonoscopy, together with chromoendoscopy and narrow-band imaging, makes it easier to find adenomas by showing small changes in the mucosa {35,36}.

Table 3: Comparison of Imaging Modalities for Colorectal Cancer Detection

Imaging Modality	Sensitivity (%)	Specificity (%)	Key Advantages	Limitations	Clinical Use
Colonoscopy (HD)	85–95	90–95	Direct visualisation, polyp removal	Invasive, operator-dependent	Gold-standard screening
Flexible Sigmoidoscopy	70–85	85–90	Less invasive, lower prep	Misses proximal lesions	Screening (distal colon)
CT Colonography	80–90	85–90	Minimally invasive, full colon visualisation	Radiation, bowel prep	Alternative for incomplete colonoscopy
MRI	75–85	85–90	Excellent soft tissue contrast	Expensive, limited availability	Rectal cancer staging
PET-CT	60–80	85–95	Detects metastases	High cost, low polyp sensitivity	Recurrent/metastatic disease

Rationale: This table provides a direct comparison of imaging modalities, highlighting sensitivity, specificity, advantages, limitations, and clinical applications

Combining biomarkers and imaging:

The integration of biomarker analysis and advanced imaging techniques signifies a transformative advancement in the detection and surveillance of colorectal cancer (CRC). Biomarkers and imaging provide complementary insights; when combined, they provide personalised, risk-adapted screening, early detection, and minimal residual disease (MRD) monitoring.

The recent incorporation of artificial intelligence (AI) methods, such as computer-aided detection (CADe), has shown enhanced sensitivity for polyp identification, especially in high-risk and average-risk groups {37,38}. Flexible sigmoidoscopy is still an option for screening the distal colon, although it misses lesions in the proximal colon and isn't used as much in some areas.

Cross-Sectional Imaging: Computed tomography colonography (CTC) and magnetic resonance colonography (MRC) offer minimally invasive methods for comprehensive visualisation of the colon. CTC shows a high level of sensitivity for finding lesions that are 6 mm or larger. It is especially helpful for people who can't have a regular colonoscopy {39}. MRI is not often used for primary screening, although it is useful for staging rectal malignancies and checking for local tumour invasion and mesorectal lymph nodes [40]. Positron emission tomography-computed tomography (PET-CT) is utilised exclusively for identifying recurring or metastatic disease, due to its elevated cost and lower sensitivity for tiny polyps.

Comparative Effectiveness: Endoscopic and cross-sectional imaging techniques are mutually beneficial. Colonoscopy is still the best way to see directly and remove polyps, although CTC and MRI are better for people who are at higher risk of complications or who have had a partial colonoscopy. Combining biomarker-based risk stratification with imaging selection can help choose the right tests, set the right screening intervals, and find problems earlier {41,42}. (Table1)

Clinical Utility and Limitations: Imaging modalities still have problems, even if technology has improved. These problems include differences in operator expertise, cost, accessibility, and patient adherence. Radiation exposure from CTC, the necessity for bowel preparation, and the restricted access to high-definition scopes or AI-assisted instruments in resource-constrained environments are significant obstacles {43}. To get the most out of imaging in CRC detection, it is important to standardise techniques and training and combine them with biomarker-guided screening.

Recent advancements in endoscopic and cross-sectional imaging, notably high-definition visualisation and AI-assisted detection, enhance conventional colonoscopy in colorectal cancer screening. When used with biomarker-based methods, these tools make it possible to create personalised, risk-adjusted detection tactics that lead to better early diagnosis and clinical results.

Reason for Integration:

Biomarkers, including stool-based DNA assays and circulating tumour DNA (ctDNA), are non-invasive and can identify patients at increased risk or detect early neoplastic changes prior to their visibility on imaging {44,45}. High-definition colonoscopy, CT colonography, and MRI are examples of imaging techniques that give structural and spatial information. This makes it possible to find and describe lesions exactly {46,47}. Combining molecular and structural data makes diagnoses more accurate, lowers the number of false negatives, and helps plan tailored treatments.

Clinical uses:

Screening: Using biomarker panels to sort people by risk can help you choose which imaging tests to do and how often to do them. For instance, people with positive multi-target stool DNA results or high ctDNA may have a colonoscopy or CT colonography sooner than people who are not at risk {48}.
Surveillance and MRD Monitoring: ctDNA can be used to keep an eye on patients after surgery to see if they still have cancer or if it comes back early. Imaging is only done on people who have positive molecular signals {49}.

Treatment Planning: Combining genomic biomarker data with imaging helps in staging, planning surgery, and choosing additional medications {50}.

Pros and Cons

Integrated techniques provide enhanced sensitivity and specificity, customised screening paths, and possible cost reductions by minimising superfluous operations. But there are certain problems, such as differences in how well assays work in different groups of people, the need for biomarker tests to be standardised, the fact that AI-assisted imaging is not widely available, and the high costs in places where resources are restricted {51,52}. For successful deployment, it is also important to get regulatory approval, make sure that data can be shared between systems, and train clinicians (Figure 4).

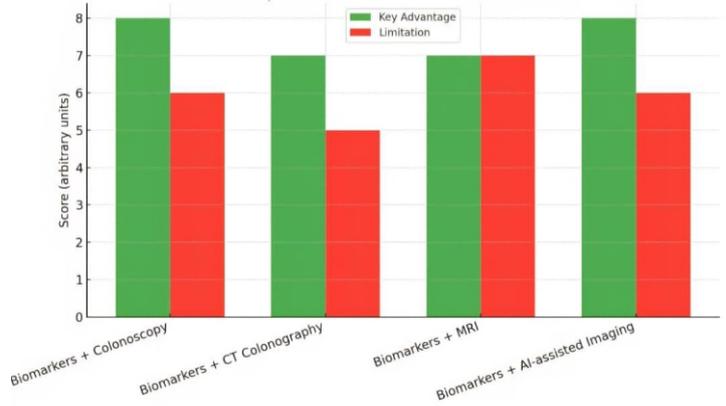
Future Outlooks

New multi-omics and radiogenomic methods offer better integration, where imaging features are linked to molecular profiles for predictive modelling. AI-powered platforms could automate risk assessment, lesion diagnosis, and long-term monitoring, making it possible to create completely personalised CRC care paths {53}.

The integration of biomarkers and imaging offers a powerful, complementary strategy for CRC detection, surveillance, and management. Multi-modal approaches enhance sensitivity, allow tailored interventions, and support early detection of minimal residual disease, with the potential to transform population-level screening and clinical outcomes. (Figures 3 and 4)A

1. Risk assessment → 2. Biomarker testing (stool/blood) → 3. Imaging (colonoscopy/CT/MRI) → 4. Personalized follow-up (treatment or surveillance).

Figure 3: A schematic showing a multi-modal CRC detection workflow



Scores are illustrative of the advantages vs. limitations of each multimodal detection strategy.

Figure 4: Clinical utility vs limitations of multimodal CRC detection

Challenges, Constraints, and Prospective Pathways:

Even while biomarkers and imaging have made it much easier to find colorectal cancer (CRC), there are still several problems that make it hard to use them widely and in the clinic. To make screening programs better and plan future research, it's important to know what these barriers are.

Differences in Sensitivity and Specificity: The efficacy of biomarkers and imaging modalities can differ markedly among populations, tumour stages, and lesion kinds. For instance, stool-based DNA testing and circulating tumour DNA (ctDNA) assays may demonstrate diminished sensitivity for tiny adenomas or early-stage malignancies, but imaging techniques like CT colonography may overlook flat or serrated lesions {54,55}. The inconsistency in endoscopic detection outcomes is also due to operator dependency and differences in equipment {56}.

Cost-Effectiveness and Availability: High expenses and insufficient infrastructure are problems, especially in countries with low or middling incomes. Advanced stool-based tests, ctDNA analysis, and AI-assisted imaging necessitate specialised laboratories, sophisticated equipment, and skilled workers, hence restricting equal access {57,58}. Economic evaluations are essential for ascertaining cost-benefit ratios and establishing priorities for resource allocation.

Problems with standardisation and regulation

Different test procedures, interpretation criteria, and reporting standards make it hard to reproduce results and use them in clinical workflows. Regulatory approvals differ by region, and clinical guidelines frequently trail behind new findings, hindering implementation {59,60}. Setting standard thresholds, doing validation studies, and doing quality control amongst labs are all very important. 7.4 Patient Compliance and Ethical Considerations. Patients' willingness to follow screening schedules is affected by how intrusive the tests are, how much preparation is needed, and cultural considerations. Ethical considerations, such as informed consent, data protection, and equitable access, are especially pertinent for genomic and AI-driven platforms {61}. (Table 4)

Table 4: Challenges and Potential Solutions in Biomarker-Based Colorectal Cancer Screening

Challenge	Description	Potential Solutions	References
Sensitivity variability	Early-stage lesions may be missed	Multi-modal approaches, improved assays	{54,55}
Cost and infrastructure	High cost limits access in LMICs	Affordable assays, regional centers	{57,58}
Standardization	Assay protocols vary	International guidelines, quality control	{59,60}
Patient compliance	Invasive tests reduce adherence	Non-invasive tests, patient education	{61}
Regulatory & ethical	Delayed approvals, privacy concerns	Streamlined approval, data governance	{58,60}

Future Directions

Future research should concentrate on:

- Formulating multi-modal risk-adapted techniques that amalgamate biomarkers, imaging, and clinical data for individualised screening.
- Enhancing the sensitivity and specificity of assays, especially for early-stage and precancerous lesions.
- Using AI and radiogenomics more widely to automate finding, predicting, and long-term monitoring.
- Setting international standards for clinical integration, reporting, and assay validation.
- Improving access in places with few resources by using low-cost platforms and public-private partnerships.

New biomarkers and imaging technologies have the potential to improve CRC outcomes, but they can't be used by everyone since they aren't sensitive enough, easy to get, standardised, or easy for patients to follow. To turn scientific progress into advantages for the whole population, we need to remove these barriers through technological, regulatory, and policy changes.

Conclusion:

Recent advances in colorectal cancer (CRC) detection—particularly stool- and blood-based biomarkers and advanced imaging—are enabling more accurate, non-invasive, and personalised screening approaches. These strategies enhance sensitivity, support minimal residual disease monitoring, and allow risk-adapted care. However, key barriers remain, including inconsistent assay performance, high costs, limited infrastructure, lack of standardisation, and poor patient compliance. Progress will require protocol harmonization, wider access, AI integration, and robust multi-centre research. A multimodal, patient-centred approach holds promise for earlier detection, reduced morbidity, and improved CRC outcomes at both individual and population levels.

Recommendations:

- **Risk-adapted screening:** Combine stool DNA, ctDNA, and CTCs with imaging to tailor screening frequency and methods.
- **Multi-modal integration:** Use biomarkers with colonoscopy, CT colonography, and MRI to improve accuracy, especially for early-stage and MRD detection.
- **AI and multi-omics:** Apply AI, genomic, and epigenomic data to enhance polyp detection, lesion characterisation, and treatment planning.
- **Standardisation:** Develop global standards for biomarker assays, imaging, and reporting to ensure reproducibility and clinical utility.
- **Affordability and access:** Establish regional centres, public-private partnerships, and technology transfer to expand cost-effective screening, especially in LMICs.
- **Patient education and adherence:** Improve awareness, address cultural/behavioural barriers, and promote non-invasive, user-friendly tests.

- **Research support:** Conduct large, longitudinal trials to validate biomarkers, AI tools, and integrated screening strategies across populations.

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