



Colorectal cancer worldwide: epidemiological trends, economic burden, and the promise of AI-driven solutions

Dinh T. P. Le^{1*} , Tuan D. Pham^{2*} 

¹Managed Care Department, New York Health and Hospitals Corporation, New York, NY 10041, USA

²Barts and The London School of Medicine and Dentistry, Queen Mary University of London, E1 2AD London, UK

***Correspondence:** Dinh T. P. Le, Managed Care Department, New York Health and Hospitals Corporation, New York, NY 10041, USA. led1@nychhc.org; Tuan D. Pham, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, E1 2AD London, UK. tuan.pham@qmul.ac.uk

Academic Editor: Amedeo Lonardo, Retired, Azienda Ospedaliero-Universitaria di Modena (–2023), Italy

Received: August 5, 2025 **Accepted:** October 19, 2025 **Published:** November 19, 2025

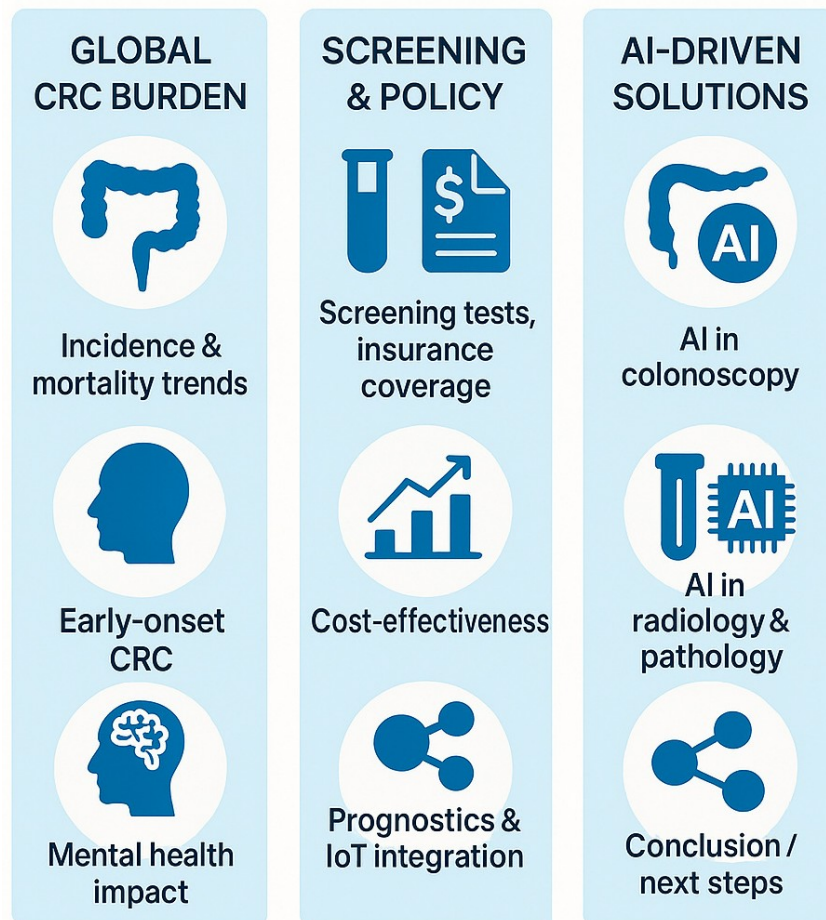
Cite this article: Le DTP, Pham TD. Colorectal cancer worldwide: epidemiological trends, economic burden, and the promise of AI-driven solutions. *Explor Med.* 2025;6:1001371. <https://doi.org/10.37349/emed.2025.1001371>

Abstract

Colorectal cancer (CRC) remains a significant global health challenge due to its high incidence and mortality, underscoring the need for early detection and precise diagnosis to improve survival outcomes. Recent advances in artificial intelligence (AI), particularly deep learning and machine learning (ML), have revolutionized medical imaging and reshaped CRC screening, diagnosis, and prognosis. AI algorithms demonstrate strong performance in analyzing computed tomography, magnetic resonance imaging, and endoscopic images, achieving superior sensitivity, specificity, and efficiency in detecting and characterizing colorectal lesions. These developments enhance lesion identification, risk stratification, and treatment planning, advancing the broader goal of precision medicine. Importantly, AI has the potential to reduce health disparities by extending access to high-quality diagnostic capabilities in low-resource regions where shortages of expert radiologists delay detection. Despite these advantages, implementation in clinical practice remains limited by several challenges, including data bias, lack of population diversity in training datasets, limited generalizability, operator dependency, and integration difficulties within existing workflows. Moreover, ethical and economic considerations—such as algorithm transparency, data privacy, and cost-effectiveness—continue to shape adoption. This review synthesizes current evidence on AI applications in CRC imaging, emphasizing methodological progress, clinical performance, and translational challenges. It also evaluates the readiness of AI systems for real-world use, highlighting ongoing needs for validation, regulatory oversight, and interdisciplinary collaboration. Ultimately, AI holds transformative potential to enhance CRC detection and management, improve diagnostic accuracy, and promote equitable access to advanced screening worldwide, provided that technological, ethical, and implementation barriers are effectively addressed.



Colorectal Cancer Worldwide: Epidemiological Trends, Economic Burden, and the Promise of AI-Driven Solutions



Graphical abstract. Colorectal cancer worldwide: burden, policy, and AI-enabled progress.

Keywords

colorectal cancer, cancer screening, precision medicine, personalized treatment, epidemiological trends, microbiome alterations, liquid biopsies, AI-driven tools

Introduction

Cancer is the second leading cause of death in the United States after heart disease, responsible for one in five deaths nationwide. In 2025, approximately 2,041,910 new cancer cases and 618,120 cancer-related deaths are projected, corresponding to an incidence rate of 445.8 per 100,000 and a mortality rate of 145.4 per 100,000 individuals [1, 2]. These figures underscore the ongoing need for effective prevention, early detection, and treatment strategies. Colorectal cancer (CRC), in particular, imposes a significant burden, with U.S. healthcare costs reaching \$24.3 billion in 2022—second only to breast cancer [3, 4]. More broadly, cancer-related expenditures in the U.S. were projected to rise to \$208.9 billion by 2020, largely due to population aging and expanding care needs [5–7].

Globally, CRC incidence is expected to rise sharply. By 2030, new cases are projected to exceed 2.2 million, with over 1.1 million annual deaths. By 2040, these numbers may climb to 3.2 million new cases

and 1.6 million deaths. Most of this increase will occur in countries with high or very high Human Development Index (HDI) rankings, reflecting aging populations and lifestyle-related risk factors such as diet and sedentary behavior [8]. Significant variation exists in CRC incidence and mortality worldwide, strongly influenced by healthcare access and development level [9]. Global analyses reveal a tenfold disparity in CRC rates, with low- and middle-income countries (LMICs) experiencing accelerating incidence compared to high-income nations, where rates have plateaued or declined due to widespread screening and advanced therapies [9, 10]. In LMICs, limited access to timely diagnosis and care results in later-stage presentation, higher mortality, and substantial out-of-pocket costs that often drive families into poverty. For instance, CRC ranked as the second leading cause of cancer-related death in Europe in 2015, with annual costs estimated at €19.1 billion, including indirect costs from lost productivity [11]. These financial burdens are even more acute in LMICs due to systemic infrastructure limitations.

Understanding CRC's global impact requires comparative insights into its epidemiology and economic consequences, particularly in LMICs where incidence is rising due to urbanization, aging populations, and shifting lifestyles [8]. These trends highlight the urgent need for accessible, cost-effective interventions. Innovations such as artificial intelligence (AI) offer potential solutions, enabling scalable diagnostic tools that could improve timely CRC detection in low-resource settings. This review presents a synthesis of recent CRC incidence and mortality data, with a focus on AI-driven strategies that may reduce disparities through enhanced prevention, early detection, and treatment. Special attention is given to the implications for LMICs, where novel approaches are essential to improve equity and advance sustainable global cancer care.

Colorectal cancer incidence, mortality, and the impact of screening

CRC is the third most commonly diagnosed cancer worldwide and the second leading cause of cancer death in the United States [12–17]. In 2025, an estimated 107,320 colon and 46,950 rectal cancer cases will occur in the U.S. [17]. Globally, 20 million new cancer cases and 9.7 million deaths were reported in 2022, with projections reaching 35 million cases by 2050 due to population growth alone [13, 14].

In the U.S., CRC accounted for 51,869 deaths in 2020, with an age-adjusted mortality rate of 12.6 per 100,000 [18]. Lifetime risk is 4.4% in men and 3.9% in women, with respective mortality risks of 1.6% and 1.5% [18, 19]. SEER data show that incidence peaked in the 1980s, while mortality has declined steadily since 1984, accelerating post-2000 [20, 21]. From 2011–2019, incidence declined about 1% annually in individuals ≥ 65 but increased 1–2% per year in those < 55 , representing a 51% rise in early-onset CRC (EOCRC) since 1994 [22, 23]. Adults aged 50–54 now have rates comparable to those aged 55–59, and underserved groups—including Alaska Native, American Indian, and Black populations—bear disproportionate burdens [24, 25].

Men consistently exhibit higher CRC incidence and mortality than women (35.3–52.3 vs. 25.0–45.1 per 100,000) across all racial groups [19]. While most cases occur in individuals ≥ 55 , approximately 15% affect those aged 45–54, with incidence peaking between 65–74 years [19, 23, 26]. Rising incidence in adults 40–54 has been linked to poor diet, obesity, inactivity, inflammation, microbiome changes, and possible environmental or epigenetic factors [27, 28].

Early-onset colorectal cancer: an emerging global challenge

The global incidence of EOCRC—defined as CRC diagnosed before age 50—is rising sharply, particularly among women and racial/ethnic minorities, driven by strong birth cohort effects projected to persist through 2040 [29–32]. From 1990 to 2021, incidence increased from 5.4 to 6.1 per 100,000 (AAPC = 0.39), with the steepest annual rises in individuals aged 20–29 (7.9%), 30–39 (4.9%), and 40–49 (1.6%) [30, 32]. In Norway, EOCRC rose by 66% from 1993 to 2022, and global projections estimate an increase of roughly 5.4% by 2030 [30, 32].

EOCRC is frequently diagnosed at advanced stages due to delayed symptom recognition. Common symptoms—rectal bleeding, anemia, weight loss, and abdominal pain—are often overlooked, leading to diagnostic delays of 4–6 months [33]. These delays are more pronounced in high-risk populations,

including Native Hawaiian, Pacific Islander, Black, and Hispanic individuals, who face elevated incidence and mortality due to systemic inequities [29].

Studying EOCRC on a global scale remains difficult due to inconsistent disease classification, fragmented data systems, limited international collaboration, and disparities in healthcare access. Cultural and structural barriers—including poverty, stigma, fatalism, and uneven screening availability—further impede prevention and timely diagnosis [34–36].

Despite ongoing challenges, growing awareness, international collaboration, and advances in data science are enabling global progress in EOCRC prevention. Recent initiatives support risk prediction modeling, early detection, and public health campaigns via traditional and digital platforms. The 2025 Global Early-Onset Colorectal Cancer Think Tank (GEOCRCTT) convened stakeholders from 23 countries to establish coordinated strategies, following a 2024 workshop series by Fight CRC aimed at advancing risk stratification and international research efforts (Fight CRC 2024; GEOCRCTT 2025). ML models using real-world electronic health record data show promise for EOCRC risk prediction, even among individuals below traditional screening age [37].

The rising burden of EOCRC—marked by increasing incidence, delayed diagnosis, and distinct molecular features—underscores the urgency of implementing equitable, risk-adapted screening and prevention strategies for CRCs. Established screening modalities have significantly reduced CRC incidence and mortality: sigmoidoscopy lowers distal CRC mortality [38], colonoscopic polypectomy removes precancerous lesions [39], and annual fecal occult blood testing (FOBT) reduces mortality by approximately 33% [40]. Randomized and observational studies confirm the benefit of flexible sigmoidoscopy [41, 42], and although its effect on all-cause mortality is debated, the impact on CRC-specific outcomes is clear [43, 44]. Early detection improves outcomes through the identification and removal of precursor lesions [45, 46].

CRC trends in the U.S. from 1975 to 2022 reveal substantial improvements in prevention, treatment, and outcomes. Long-term trends in CRC incidence, mortality, and 5-year relative survival in the United States from 1975 to 2022 are illustrated in Figure 1, based on SEER and national mortality data [47]. The incidence rate, based on SEER 8 data, peaked in the mid-1980s at approximately 66.6 per 100,000 and declined steadily to about 35.8 per 100,000 by 2022—a 46% reduction—reflecting the impact of widespread screening, removal of precancerous polyps, and modifiable risk factor control. Mortality rates also fell markedly, from roughly 28 per 100,000 in 1975 to 12.8 per 100,000 in 2022 (a 54% decline), with acceleration after the mid-1990s likely due to earlier detection, advances in treatment, and coordinated care. Concurrently, 5-year relative survival improved from 49% in 1975 to over 69% by 2016, largely attributable to earlier-stage diagnoses and enhanced therapeutic strategies. While the incidence and mortality trends continue to improve, the recent plateau in survival gains highlights the need for novel approaches, including personalized treatments, targeted efforts for EOCRC, and focused interventions in high-risk populations.

Trends in CRC incidence by age group are presented in Figure 2, though some subgroup data for 2007–2008 were not available [1, 48].

Mental health disorders in colorectal cancer patients after postoperative complications

CRC patients face substantial psychological challenges after surgery, especially when postoperative complications occur [49, 50]. Complications such as infections, anastomotic leaks, prolonged recovery, and stoma formation increase the risk of depression, anxiety, and adjustment disorders, compounding physical discomfort, body-image disturbance, and social functioning difficulties. Psychiatric comorbidities in CRC patients are linked to poorer adherence to treatment, longer hospital stays, higher healthcare costs, and worse survival, underscoring the importance of early psychological screening, timely psychiatric intervention, and integration of mental health care into multidisciplinary practice [50].

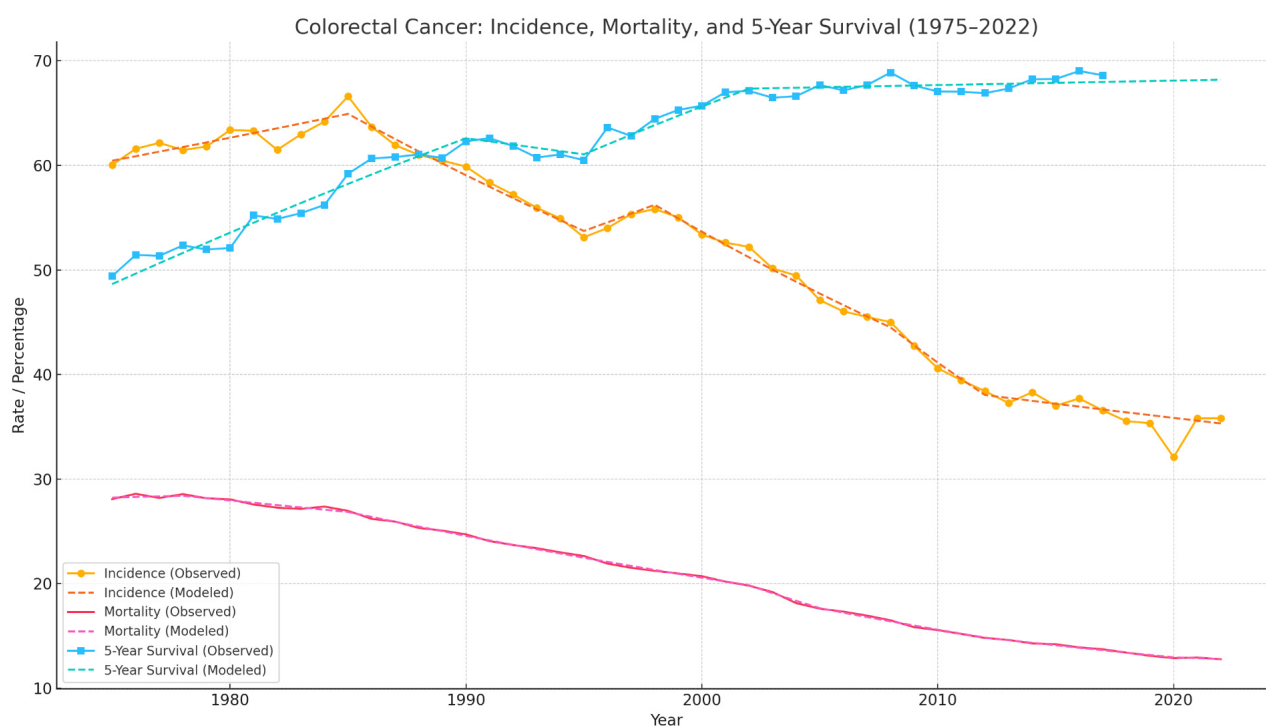


Figure 1. Colorectal cancer mortality over years in the U.S.

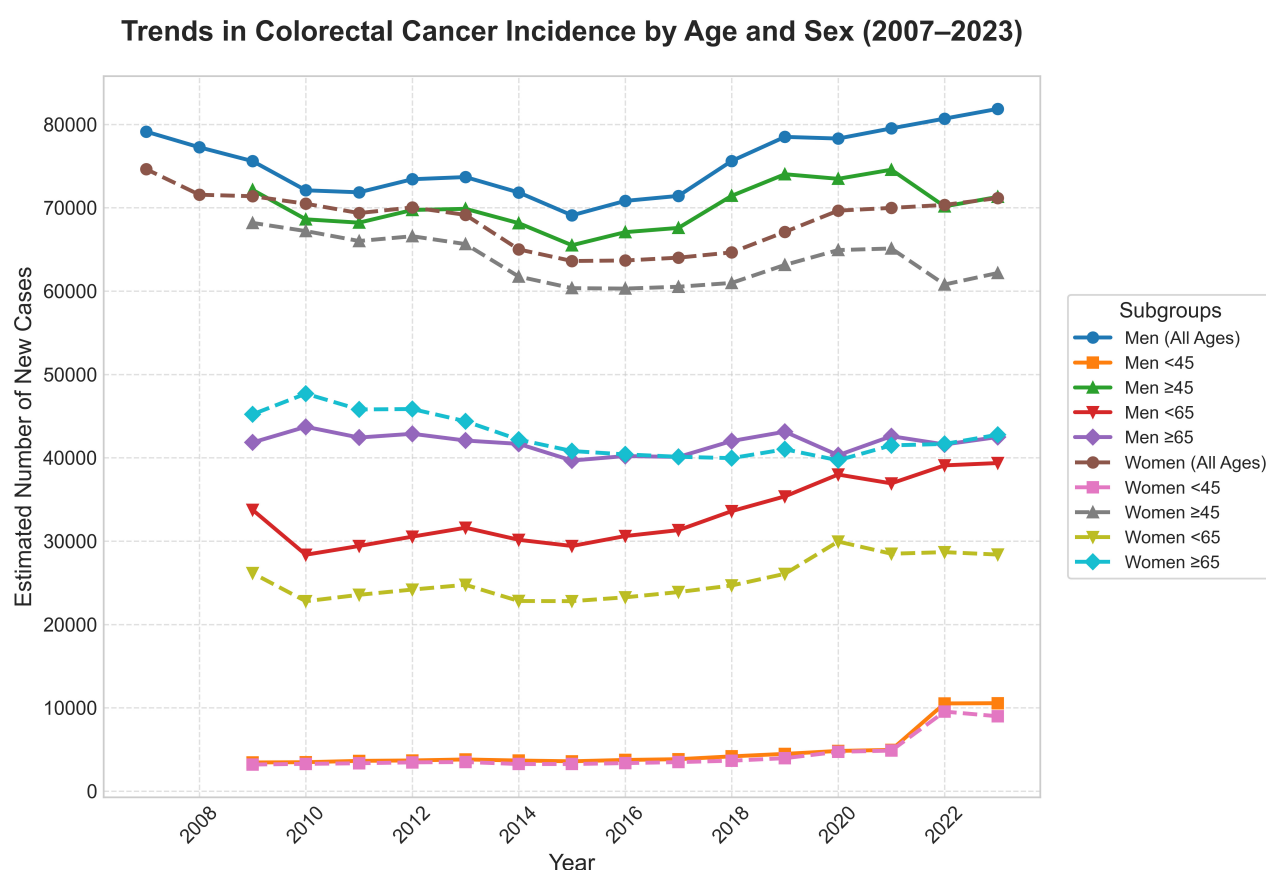


Figure 2. Colorectal cancer incidence over years in the U.S.

Evidence supports the prognostic impact of these disorders. A three-year follow-up study of gastrointestinal cancer patients ($n = 320$; 210 CRC) reported baseline rates of anxiety ($\sim 40\%$) and depression ($\sim 33\%$), both of which worsened over time, with depression independently associated with reduced survival [51]. Prospective cohort studies confirm that complications and stoma creation predict poorer emotional outcomes and lower health-related quality of life, while higher anxiety and depression

scores correlate with increased mortality. Predictive tools, such as risk nomograms incorporating postoperative complications, stoma creation, comorbidities, and adjuvant therapy, demonstrate good accuracy (AUC $\approx$ 0.79–0.81) in identifying high-risk patients [52]. Furthermore, a meta-analysis showed that anxiety modestly increases mortality risk (OR $\approx$ 1.07), while depression more than doubles it (OR $\approx$ 2.76) [53].

Taken together, these findings demonstrate that postoperative complications not only worsen psychological outcomes but may also directly influence long-term survival. Addressing mental health proactively is therefore critical for optimizing recovery, quality of life, and prognosis in CRC patients. Common disorders are summarized in Table 1.

Table 1. Mental health disorders in CRC patients following postoperative complications.

Disorder	Triggers/Associations	Impact on patients
Depression	Prolonged recovery, infections, stoma formation, loss of independence	Reduced quality of life, poor adherence to therapy, higher risk of mortality
Anxiety	Fear of recurrence, uncertainty after complications, changes in body image	Sleep disturbances, impaired coping, increased healthcare utilization
Adjustment disorder	Difficulty adapting to stoma, functional limitations, lifestyle disruption	Social withdrawal, reduced occupational functioning, prolonged psychological distress
Post-traumatic stress disorder (PTSD)	Severe or unexpected surgical complications (e.g., anastomotic leak, ICU stay)	Flashbacks, hypervigilance, avoidance behaviors, impaired daily functioning
Body image disturbance	Stoma placement, surgical scarring, altered bowel function	Low self-esteem, social anxiety, sexual dysfunction

CRC: colorectal cancer.

Integrated analysis of colorectal cancer diagnosis, prognosis, and modifiable determinants

CRC prognosis is influenced by tumor stage, histologic grade, molecular features, and host factors. Early detection through screening and molecular diagnostics has contributed to improvements in 5-year survival—from $\sim$ 50% in the 1970s to 65% between 2012 and 2018—though disparities remain across age and racial groups [25, 54]. CRC development involves a complex interplay between genetic predisposition, epigenetic regulation, environmental exposures, and modifiable lifestyle factors [21, 55, 56].

Inherited syndromes (e.g., Lynch syndrome, FAP) and somatic mutations in genes such as *APC*, *KRAS*, *BRAF*, and *TP53* underlie many CRC cases [57–59]. Epigenetic mechanisms, including *MLH1* and *MGMT* promoter methylation, influence prognosis and therapy response. Biomarkers such as methylated *NDRG4*, *BMP3*, *SEPT9*, and specific miRNAs, detectable via liquid biopsy, are increasingly used for diagnosis and surveillance [60]. Polygenic risk scores enable stratified risk prediction [61], and targeted epigenetic therapies, such as DNMT and HDAC inhibitors, are under investigation [62, 63].

Modifiable risk factors include family CRC history, high-risk adenomas, IBD, diabetes, radiation exposure, and dietary habits [64, 65]. CRC often arises from adenomatous or serrated polyps, especially in the proximal colon [66, 67]. A 2025 UK cohort of over 540,000 women linked high-fiber, plant-based diets and low red/processed meat intake with lower CRC incidence, while higher fecal bile acid levels were associated with increased risk [68, 69]. Physical activity, healthy weight, and avoidance of alcohol and tobacco remain key preventive strategies [70, 71].

Environmental factors such as green space access and lower socioeconomic disadvantage are also protective [72]. The gut microbiome serves as a mediator, with *Fusobacterium nucleatum* promoting immune evasion and CRC progression, while beneficial microbial metabolites influence therapeutic response [73, 74]. Dietary interventions post-diagnosis—emphasizing whole grains, calcium, and coffee—improve survival, whereas high sugar and alcohol intake worsen outcomes. Obesity, especially in youth, elevates CRC risk through inflammatory and metabolic pathways, contributing to EOCRC with a 1.54-fold increased risk [32, 75]. A murine RCT showed that ketogenic diets reduced tumor burden by modulating microbiota [76], and probiotic or fiber-rich interventions are gaining clinical interest [77, 78].

Immunologically, mismatch repair-deficient (dMMR)/high microsatellite instability (MSI-H) tumors respond well to immune checkpoint inhibitors, while microsatellite stable (MSS) CRCs (~85%) remain resistant due to poor antigenicity and suppressive microenvironments [79–91]. Novel strategies such as tumor mutational burden (TMB)-based stratification, CAR-T cells, vaccines, and oncolytic viruses are being explored to overcome immune resistance [92–100].

Advanced molecular diagnostics, including next-generation sequencing (NGS), identify actionable mutations for targeted therapy and resistance prediction (e.g., *KRAS*, *NRAS*, *BRAF*, *PIK3CA*) [101–104]. Liquid biopsies enable real-time monitoring of circulating tumor DNA (ctDNA), improving surveillance for minimal residual disease and enabling adaptive treatment strategies [105–108].

Molecular pathological epidemiology (MPE) provides a transdisciplinary framework for integrating these factors [109]. MPE links exposures—such as diet, BMI, and aspirin use—with tumor-specific molecular alterations, including MSI, CIMP, and LINE-1 methylation, offering insights into etiologic heterogeneity and clinical stratification [110–116]. Gestational and early-life exposures may shape CRC phenotypes, and MPE-based pregnancy cohort studies could further elucidate these connections [117–119]. AI enhances MPE by predicting molecular subtypes from histology (e.g., Swin Transformers) and identifying prognostic multi-omics signatures, improving the integration of exposomic, imaging, and biomarker data into personalized oncology [114, 119–121].

Colorectal cancer screening and costs

CRC screening options vary in sensitivity, specificity, cost, and accessibility, with test selection influenced by age, risk, and patient preference. Positive results typically require diagnostic follow-up via colonoscopy. The U.S. Preventive Services Task Force (USPSTF) recommends several screening methods, including HSgFOBT, fecal immunochemical test (FIT), FIT-DNA (Cologuard), computed tomography (CT) colonography, flexible sigmoidoscopy, and colonoscopy, each with different costs and effectiveness profiles (Table 2).

Table 2. USPSTF recommended colorectal cancer screening tests.

Test	USPSTF recommended frequency	Sensitivity	Specificity	Cost	CDPHP coverage
High-sensitivity guaiac fecal occult blood test (HSgFOBT)	Every year	Low (33%)	Moderate	\$22	Yes
Fecal immunochemical test (FIT-iFOBT)	Every year	Moderate (75%)	Moderate	\$22	Yes
FIT-DNA (Cologuard)	Every 3 years	High (92%)	High	\$502	Yes
Computed tomography colonography	Every 5 years	High (89%)	High (75%)	\$315	Prior authorization required
Flexible sigmoidoscopy	Every 5 years	Moderate to high (> 95% in distal colon)	High	\$520	Yes
Colonoscopy	Every 10 years	High (93%)	High (73%)	\$950	Yes

USPSTF: U.S. Preventive Services Task Force.

Cologuard, despite its \$502 price, offers high sensitivity, non-invasiveness, and at-home convenience, enhancing compliance and early detection. Colonoscopy remains the gold standard with high accuracy but is more costly and invasive. Prices vary significantly by provider type: surgery centers offer 29% lower costs than outpatient hospitals—for example, \$1,136 vs. \$1,608 for standard colonoscopy [122].

A detailed breakdown shows facility fees make up nearly 64% of total colonoscopy costs, with anesthesia and provider fees comprising the remainder [123]. Costs also vary by state: Alaska has the highest average at \$2,033, while Iowa has the lowest at \$1,430 [123].

Understanding the financial aspects of CRC screening is vital for improving access, especially among uninsured populations. Transparent pricing, insurance coverage, and cost-effective options are essential to reducing disparities and enhancing preventive care.

Insurance coverage for colorectal cancer screening

The Affordable Care Act (ACA) mandates that private health plans initiated on or after September 23, 2010, cover USPSTF-recommended CRC screening tests with no out-of-pocket costs for eligible individuals [124]. Medicare and most Medicaid programs also cover CRC screening—including colonoscopy, sigmoidoscopy, fecal occult blood tests, and stool DNA tests—though Medicaid eligibility and guidelines vary by state [22, 125, 126]. A summary of coverage across insurance types is presented in Table 3.

Table 3. Insurance coverage for colorectal cancer screening tests.

Insurance type	Screening tests covered	Out-of-pocket costs	Guidelines and eligibility
Medicare	Colonoscopy, Sigmoidoscopy, Fecal Occult Blood Test, Stool DNA Test	No out-of-pocket costs for most services	Coverage for eligible beneficiaries as per CMS guidelines
Medicaid	Colonoscopy, Sigmoidoscopy, Fecal Occult Blood Test, Stool DNA Test	Varies by state	Coverage and eligibility criteria differ by state; states follow CMS and USPSTF recommendations
Private insurance	Colonoscopy, Sigmoidoscopy, Fecal Occult Blood Test, Stool DNA Test	No out-of-pocket costs for most services	Coverage mandated by ACA for plans starting on or after September 23, 2010; adheres to USPSTF recommendations

CMS: Centers for Medicare and Medicaid Services; USPSTF: U.S. Preventive Services Task Force; ACA: Affordable Care Act.

Despite these provisions, disparities persist. National Health Interview Survey (NHIS) and Behavioral Risk Factor Surveillance System (BRFSS) data show lower CRC screening rates among uninsured individuals compared to those with Medicaid or private insurance [24, 127]. In adults aged 50–64, the 2005 NHIS data found screening rates of 48.5% [private Health Maintenance Organization (HMO)], 45.2% (private non-HMO), 42.1% (medicaid/other public), and only 17.2% (uninsured) [127].

Insurance coverage is critical to expanding access to preventive care. By removing financial barriers, Medicare, Medicaid, and ACA-aligned private plans improve screening uptake and early CRC detection, especially in underserved populations [128–130].

Colorectal cancer screening tests

CRC screening includes stool-based, blood-based, and visual/structural exams, each with distinct sensitivity, specificity, and frequency considerations.

Stool-based tests

- gFOBT detects hidden blood via a chemical reaction but requires dietary restrictions and has low specificity [131, 132].
- FIT uses antibodies to detect human hemoglobin without dietary restrictions; annual use is recommended with 79% sensitivity and 94% specificity [133–135].
- FIT-DNA (Cologuard®) combines FIT with DNA testing (e.g., *KRAS*, *BMP3*), offering 92% sensitivity for CRC and a 3-year interval [136–138].

See Table 4 for test comparisons.

Table 4. Fecal occult blood tests (FOBT) for colorectal cancer screening.

Test type	Example brand	Detection method	Dietary restrictions	Sensitivity to human hemoglobin
gFOBT	Hemocult®	Chemical reaction	Yes	Less specific
FIT	InSure®	Immunological reaction	No	More specific and sensitive
FIT-DNA	ColoGuard®	DNA and immunological test	No	More specific and sensitive

FIT: fecal immunochemical test.

Blood-based tests

- Blood-based screening detects CRC-related cell-free DNA (cfDNA) and methylation markers like methylated SEPT9 (mSEPT9). Tests include Epi proColon[®], Guardant, Freenome, Grail, and others [139, 140].
- Epi proColon[®] is an FDA-approved blood-based screening test for CRC that detects mSEPT9 DNA in plasma. However, its sensitivity (approximately 48–73%) and specificity (around 80%) do not meet the Centers for Medicare and Medicaid Services (CMS) minimum thresholds for coverage ($\geq 74\%$ sensitivity and $\geq 90\%$ specificity), and thus it is not currently covered by Medicare [139, 141–145].
- Guardant Shield, validated by Chung et al. [146], showed 83.1% sensitivity and 89.6% specificity in average-risk adults.
- Compared to FIT, mSEPT9 has lower specificity (82% vs. 97%) [147].

See Table 5 for details.

Table 5. CRC screening tests using blood-based markers with AI integration and cited performance.

Blood test name or vendor	Analytes	Target	AI algorithm + input Data	Performance metrics	References
mSEPT9	ctDNA	CRC specific	Random forest (cfDNA methylation data)	AUC 0.82–0.89; Sens 69–77%; Spec 88–92%	[148, 149]
Freenome	ctDNA + protein	CRC specific	Ensemble deep learning (multi-omics: cfDNA, protein)	AUC 0.94; Sens 79–91%; Spec 91–96%	[150, 151]
CancerSEEK	ctDNA + protein	Multi-cancer	Random forest + logistic regression (multi-analyte)	AUC 0.94; Sens 69% (CRC); Spec 99%	[152, 153]
Guardant	ctDNA	CRC specific	Targeted NGS + ML classifier (proprietary)	Sens ~91%; Spec ~94%	[154, 155]
Grail (Galleri)	ctDNA	Multi-cancer	Deep neural networks (cfDNA methylation)	Sens 67% (CRC); Spec 99.5%; PPV 88.7%; early-stage sens ~27.5%	[156–165]
Clinical Genomics	ctDNA	CRC specific	Likely logistic regression/SVM on methylation	Sens 81%; Spec 91% (early trials)	[166–169]

CRC: colorectal cancer; AI: artificial intelligence; mSEPT9: methylated SEPT9; ctDNA: circulating tumor DNA; cfDNA: cell-free DNA; Sens: sensitivity; Spec: specificity; ML: machine learning.

Visual or structural exams

- Capsule endoscopy captures images via a swallowed camera capsule; sensitivity is 88% for polyps ≥ 6 mm, but may miss sessile/flat lesions [170, 171].
- CT colonography is noninvasive, with 67–98% sensitivity for adenomas ≥ 6 –10 mm but less effective for flat polyps; recommended every 5 years [172, 173].
- Sigmoidoscopy visualizes the distal colon; less favored in the U.S. due to its limited reach (only 60% of CRCs occur distally) [131].
- Colonoscopy is the gold standard, enabling full visualization and polyp removal, with a 10-year screening interval and rare complications [131].

Each test offers trade-offs in accuracy, invasiveness, and cost. Selection should consider patient risk, preference, and access. Combining emerging technologies (e.g., liquid biopsy) with traditional screening methods may enhance early detection and population coverage.

Effectiveness, strategies, and innovations in colorectal cancer screening

CRC screening has substantially reduced incidence and mortality, accounting for 53% of a 26% decline in U.S. CRC mortality between 1975 and 2000 [174]. Screening effectiveness depends on test sensitivity, specificity, and evidence quality. The CMS recommends triennial blood-based screening for adults aged 50–85 only if sensitivity is $\geq 74\%$ and specificity $\geq 90\%$ [175, 176].

Historically, FOBT was supported by randomized trials, but it is no longer recommended due to limited accuracy. The FIT is now preferred for annual screening because of superior sensitivity and specificity, while stool DNA-FIT tests (e.g., Cologuard), though more costly and prone to false positives, are suggested every 1–3 years [177–179]. Colonoscopy remains the gold standard, offering the greatest reduction in CRC risk and mortality; for example, a large cohort study showed that a normal colonoscopy reduced CRC risk by 46% and mortality by 88% over 12 years [180]. Comparative modeling supports lowering the screening initiation age to 45, given the rise in EOCRC [181]. Colonoscopy prevents the most CRC cases and deaths but requires more procedures and carries higher complication risks, while FIT and stool DNA-FIT result in fewer colonoscopies per 1,000 individuals screened [182].

Despite strong evidence, screening efficacy is limited by test performance and implementation challenges. FIT may miss serrated lesions, stool DNA-FIT has higher false-positive rates, and nearly 23% of CRC deaths are linked to missed or incomplete screening [183]. Colonoscopy outcomes depend on bowel preparation quality, endoscopist skill, sedation practices, and completeness of lesion removal. Higher adenoma detection rates (ADR) are directly protective; a 1% increase in ADR reduces interval CRC risk by 3% [184, 185]. To optimize outcomes, some institutions restrict procedures to gastroenterologists, and regional differences in sedation practices affect exam completeness and patient tolerance [186]. Expanded colonoscopy uptake, as seen in Korea, has improved early detection rates [187].

Emerging innovations are reshaping CRC screening. Liquid biopsy enables early detection and recurrence monitoring through ctDNA [188], while AI-assisted tools improve polyp detection and risk stratification [189–191]. However, AI adoption faces barriers including algorithmic bias from non-representative datasets, limited annotated samples, inconsistent data quality, and ethical issues related to privacy, consent, and the opacity of “black-box” algorithms. These challenges limit clinical trust and regulatory approval, particularly in low-resource settings with constrained infrastructure and expertise.

Persistent disparities in screening uptake across income, race, gender, and geography remain a critical concern [192, 193]. Targeted strategies—such as mailed FIT kits, telehealth, mobile clinics, and culturally tailored outreach—have been effective in improving access [194–198]. Policy initiatives, including expanded insurance coverage and preventive care subsidies, have also helped reduce racial disparities in CRC outcomes by nearly 50% over the past decade [199, 200].

A combined approach—anchored in evidence-based guidelines, optimized procedural quality, technological innovation, and equitable access—is essential to maximize CRC screening effectiveness and reduce disease burden across diverse populations.

Colorectal cancer screening rates, public health goals, and quality metrics

CRC screening remains a cornerstone of early detection and prevention efforts in the U.S. [201–203]. National campaigns—such as the National Colorectal Cancer Roundtable’s “80% by 2018” and Healthy People 2020—have aimed to boost uptake [204, 205]. Surveillance tools like BRFSS, NHIS, and the NCI State Cancer Profiles track national and subnational progress and disparities [203].

Screening rates for adults aged ≥ 45 rose from 52% in 2002 to 68% in 2020 but remain suboptimal, with state-level rates ranging from 50–70% [206, 207]. Disparities persist among younger adults, Asian Americans, women, and the uninsured due to lower referral rates, provider preferences, or structural barriers [25, 208, 209]. Notably, 83% of unscreened individuals had never undergone testing [208]. In light of rising EOCRC, likely due to birth-cohort effects, guidelines now recommend beginning screening at age 45 [210].

While modeling suggests that lowering the screening age to 45 could prevent 29,400 CRC cases and 11,100 deaths over five years, raising screening rates to 80% among those aged 50–75 could avert nearly three times as many deaths at a lower cost [211, 212].

Quality measurement frameworks such as the Healthcare Effectiveness Data and Information Set (HEDIS) further support screening improvements. Used by over 90% of U.S. health plans and integrated

into Medicare Advantage Star Ratings, HEDIS identifies care gaps and supports performance benchmarking [213, 214]. CRC screening rates derived from HEDIS data guide incentive programs like Pay for Performance and Quality Bonus Funds [215, 216], relying on accurate billing and documentation to ensure quality assessment [217–219].

The CRC screening measure assesses adults ages 50–75 who received appropriate screening using any of the following modalities: annual fecal occult blood test, flexible sigmoidoscopy every 5 years, colonoscopy every 10 years, CT colonography every 5 years, or stool DNA test every 3 years. In alignment with the USPSTF recommendations, the HEDIS Measurement Year 2022 update expanded the eligible age range to 45–75 years [220].

Longitudinal data from 2004 to 2023 indicate evolving colorectal cancer (CRC) screening rates across four major insurance categories [220]. Commercial HMO and Medicare HMO plans consistently achieved higher screening rates compared to their Preferred Provider Organization (PPO) counterparts. Medicare HMO showed a substantial increase beginning around 2010, peaking above 70% in 2018 and 2020, while Commercial HMO maintained relatively stable rates in the low-to-mid 60% range. Medicare PPO exhibited a similar upward trend, albeit with greater variability, and Commercial PPO—though improving—persistently trailed behind HMO plans throughout the period.

Data for 2019 were unavailable for both Medicare HMO and Medicare PPO due to the CMS suspension of reporting during the COVID-19 pandemic, underscoring broader disruptions to healthcare quality measurement. These long-term trends highlight the effectiveness of managed care models, particularly HMOs, in promoting preventive screening. Ongoing investment in public health initiatives and standardized quality metrics remains essential to increasing CRC screening uptake and reducing disparities across insured populations.

AI in colorectal cancer screening: from potential to practical impact

AI, particularly deep learning, is rapidly transforming modern medicine, and CRC diagnosis is no exception. Built on neural network architectures, deep learning has shown strong performance in analyzing medical images, pathology slides, and genomic data with high accuracy [221–223].

CRC remains a major global health burden, where early detection is essential to improving survival. Advances in AI and ML are reshaping care through imaging, risk stratification, and precision treatment. AI enhances diagnostic accuracy via automated detection, biomarker discovery, and convolutional neural networks for image analysis, reducing variability in histopathological interpretation and supporting treatment planning [224]. For example, Case Western investigators demonstrated that AI applied to routine magnetic resonance imaging (MRI) could predict rectal cancer outcomes, offering a non-invasive strategy to avoid overtreatment [225]. At the same time, concerns remain that unequal access to quality imaging may exacerbate existing disparities [226].

AI is also transforming traditional CRC screening and diagnostics. Computer-aided detection (CAD) systems in colonoscopy improve adenoma and polyp detection [227, 228], while deep learning applied to CT and MRI enhances staging and localization [229, 230]. In pathology, AI enables automated tumor classification and prediction of MSI, informing immunotherapy decisions [231, 232]. Beyond imaging, AI augments liquid biopsy by interpreting ctDNA signals to detect minimal residual disease and recurrence risk [233]. Innovative platforms such as Zeng et al.'s real-time optical coherence tomography system [234] may improve endoscopic sensitivity, while Bilal et al. [235] and Yu et al. [236] highlight applications in immunotherapy prediction and digital epidemiology, including GeoAI.

Despite this progress, challenges remain, including dataset variability, limited generalizability, and the need for pragmatic, large-scale validation to demonstrate real-world effectiveness [237, 238]. As Wang et al. [239] emphasize, transparent validation, equitable implementation, and integration into clinical workflows are essential for AI to meaningfully advance CRC care. With deep learning and related approaches continuing to evolve, AI is emerging as a transformative tool for screening, diagnosis, and management, moving toward more precise, data-driven, and patient-centered care.

Diagnostic imaging modalities: enhancing colorectal cancer detection with AI

The foundation of accurate CRC diagnosis rests on imaging modalities such as CT, MRI, and 18F-FDG positron emission tomography (PET). CT and MRI offer structural detail for staging, while PET identifies metastatic spread and treatment response. Integration with AI has the potential to elevate these modalities beyond human capabilities.

Several studies have shown how imaging innovations shape CRC management. Taylor et al. [240] found whole-body MRI to be an effective, low-radiation alternative for staging, while Maas et al. [241] demonstrated its accuracy in detecting recurrent disease. García-Figueiras et al. [242, 243] highlight the diagnostic advantage of combining anatomical and molecular data.

AI-augmented radiomics, diffusion-weighted MRI, and contrast-enhanced protocols further refine these modalities. Liu et al. [244] and Serinsöz et al. [245] advocate for a tailored, multimodal imaging approach guided by clinical context. While Dobos et al. [246] and Kekelidze et al. [247] established the groundwork, newer AI-supported tools provide actionable insights that may support earlier detection, more accurate staging, and personalized surveillance.

AI-enhanced endoscopy: improving lesion detection and risk stratification

AI-assisted endoscopy presents a practical avenue for reducing missed lesions and improving ADR. Kudo et al. [248] and Lui et al. [249] demonstrate how real-time AI integration enhances lesion detection, while Sinagra et al. [250] confirm increased adenoma recognition.

Beyond accuracy, AI supports procedural standardization and workflow efficiency. Zhou et al. [251] and Barua et al. [252] showed high diagnostic accuracy with AI models in neoplastic polyp identification. Broader applications are noted by Hsiao et al. [253], who validated AI for gastric cancer diagnosis, hinting at cross-cancer utility.

Despite the enthusiasm, reviews by Messmann et al. [254] and Wallace et al. [255] underscore implementation barriers, such as over-reliance, alert fatigue, and ethical oversight. Koh et al. [256] and Spadaccini et al. [257, 258] propose real-time image analysis and AI-driven classification as the next steps toward precision endoscopy.

Radiology and infrared imaging: expanding non-invasive diagnostics

Advanced imaging, when paired with AI, broadens diagnostic capability beyond conventional tools. Ferrari et al. [259] and Wang et al. [260] illustrate how AI enhances MRI-based assessment of treatment response in rectal cancer. Taylor et al. [240] further validated whole-body MRI as an efficient staging tool.

Emerging technologies, such as Fourier transform infrared (FTIR) imaging, benefit from AI's pattern recognition capabilities. Villamanca et al. [261] and Gerwert et al. [262] demonstrated early detection of CRC and MSI, respectively. These technologies could inform treatment pathways without invasive biopsy.

Notably, AI expands accessibility. Waljee et al. [263] applied AI in sub-Saharan Africa, while Ziegelmayr et al. [264] used AI to differentiate CRC from diverticulitis on CT. Peng et al. [265] advanced image fusion methods, optimizing diagnostic efficiency. Together, these studies underscore AI's role in scalable, context-sensitive diagnostics.

AI in pathology imaging: enhancing accuracy and interpretability

AI's application in pathology imaging redefines tissue analysis by enabling automated classification, subtype identification, and biomarker detection. Sirinukunwattana et al. [266] and Wang et al. [267] demonstrated molecular subtype classification using deep learning, which supports tailored treatment planning.

Innovations such as Yu’s semi-supervised learning model [268] allow efficient use of limited labeled data, while Ho et al. [269] and Ju et al. [270] validated AI for tumor staging and survival estimation. Interpretability and transparency remain central concerns; Neto et al. [271] advocate for explainable models suitable for clinical adoption.

Saillard et al. [272] validated MSIntuit for MSI detection, and studies by Bilal [273], Griem [274], and Prezja [275] confirm AI’s effectiveness in prescreening and tissue classification. These tools collectively enable more efficient workflows and potentially reduce diagnostic delays.

Image-based prognostics: toward dynamic, personalized risk models

AI’s ability to extract prognostic features from histopathology and imaging has advanced survival prediction in CRC. Kather et al. [276] demonstrated survival estimation using digitized slides, while Pai et al. [277] and Pham et al. [278, 279] built hybrid models incorporating imaging, gene expression, and deep learning for recurrence-free survival predictions.

Jiang et al. [280] validated MRI-based AI prognostics for rectal cancer, and L’Imperio et al. [281] used ML for colon cancer risk stratification. Wagner et al. [120] advanced biomarker prediction with transformer-based models, while Yin et al. [191] introduced a generalized transfer learning method for broader applicability.

Together, these findings suggest that AI-driven prognostics may surpass traditional staging in predicting outcomes and guiding treatment. Still, challenges remain in achieving cross-population generalizability and clinical integration.

Chronological overview of AI applications in colorectal cancer diagnosis, prognosis, and treatment

The integration of AI in medicine has been transformative, especially for complex diseases like CRC. AI technologies, from deep learning to advanced imaging, have significantly improved the accuracy, efficiency, and personalization of cancer diagnostics and treatments. This table (Table 6) provides a chronological summary of key studies on AI in CRC, detailing each AI model, its benefits, and limitations. This organization illustrates both the technological advancements and the ongoing challenges in adopting AI tools in oncology, reflecting nearly two decades of progressive impact in the field.

Table 6. A chronological overview of AI applications in colorectal cancer diagnosis, prognosis, and treatment.

Citation	Authors (year)	AI model	Advantages	Disadvantages
[259]	Ferrari et al. (2019)	MR-based AI model	Predicts therapy response, non-invasive	Requires high-quality MRI, expensive technology
[282]	Yang et al. (2019)	Deep learning for imaging	High accuracy, non-invasive diagnosis	Requires large datasets, high computational resources
[283]	Mao et al. (2020)	MRI	High specificity for liver metastasis, non-invasive	High costs, availability limitations
[234]	Zeng et al. (2020)	PR-OCT with deep learning	Rapid diagnosis, high sensitivity	Expensive technology, requires specialized equipment
[239]	Wang et al. (2020)	AI for diagnosis and therapy	Improves diagnostic accuracy, potential for therapy optimization	High initial costs, need for integration into clinical practice
[248]	Kudo et al. (2020)	AI-assisted endoscopy	Improves adenoma detection rates, real-time analysis	Potential over-reliance on AI, need for high-quality images
[249]	Lui et al. (2020)	AI in colonoscopy	Reduces missed polyps, enhances detection rates	False positives, potential for over-screening
[250]	Sinagra et al. (2020)	AI for adenoma detection	Enhances detection rates, supports endoscopists	Requires large datasets for training, potential biases in AI models
[251]	Zhou et al. (2020)	Deep learning for optical diagnosis	High accuracy in optical diagnosis, non-invasive	Requires large datasets, expensive to implement

Table 6. A chronological overview of AI applications in colorectal cancer diagnosis, prognosis, and treatment.
(continued)

Citation	Authors (year)	AI model	Advantages	Disadvantages
[225]	News-Medical.Net (2021)	AI-driven imaging	Real-time analysis, improved detection rates	Limited by data quality, potential biases
[253]	Hsiao et al. (2021)	AI in endoscopic screening	Early detection, high sensitivity	Expensive technology, requires specialized equipment
[284]	Parsa et al. (2021)	AI for polyp characterization	Reduces human error, enhances polyp characterization	Potential for over-reliance on AI, requires continuous updates
[285]	Wang et al. (2021)	AI for polyp detection	Improves detection rates, real-time classification	Requires large datasets, potential for false positives
[260]	Wang et al. (2021)	MRI-based AI model	High specificity for rectal cancer, non-invasive	High costs, limited availability
[266]	Sirinukunwattana et al. (2021)	Deep learning for subtyping	High accuracy in molecular subtyping, aids in personalized treatment	Requires large datasets, expensive to implement
[267]	Wang et al. (2021)	AI for histopathology	High accuracy in diagnosis, supports pathologists	Requires large annotated datasets, potential biases in AI models
[268]	Yu et al. (2021)	Semi-supervised deep learning	Reduces need for labeled data, high accuracy	Computationally intensive, requires continuous updates
[235]	Bilal et al. (2023)	Digital pathology with AI	Facilitates large-scale analysis, enhances pathology workflow	Potential for over-reliance on AI, data security concerns
[236]	Yu et al. (2022)	ML	Predictive capabilities, personalized treatment plans	Algorithm complexity, requires ongoing updates
[252]	Barua et al. (2022)	AI-based optical diagnosis	Real-time analysis, high accuracy in polyp detection	Potential for false positives, requires high-quality images
[254]	Messmann et al. (2022)	AI in gastrointestinal endoscopy	Standardizes detection, improves consistency	High costs, requires extensive training
[255]	Wallace et al. (2022)	AI in neoplasia detection	Reduces miss rates, enhances detection accuracy	Potential over-reliance on AI, needs constant updates
[261]	Villamanca et al. (2022)	AI with Fourier transform infrared	Non-invasive, high sensitivity	Requires specialized equipment, limited clinical application
[263]	Waljee et al. (2022)	AI/ML for early detection	Early detection in low-resource settings, scalable	Requires data and infrastructure, potential biases in training data
[269]	Ho et al. (2022)	Deep learning for histopathology	High accuracy, supports pathologists	Requires high-quality images, potential for false positives
[270]	Ju et al. (2022)	AI for pathological staging	High accuracy, non-invasive staging	Requires large datasets, expensive to implement
[256]	Koh et al. (2023)	AI-aided endoscopy	Enhances detection rates, supports experienced endoscopists	Expensive, requires integration into clinical practice
[257]	Spadaccini et al. (2023)	AI-aided endoscopy	Improves screening accuracy, real-time feedback	Potential for false positives, requires large training datasets
[262]	Gerwert et al. (2023)	AI-integrated infrared imaging	Label-free detection, fast results	Expensive technology, requires specialized training
[264]	Ziegelmayr et al. (2023)	Deep learning for CT imaging	Differentiates conditions accurately, non-invasive	Requires high-quality CT images, potential for misclassification
[273]	Bilal et al. (2023)	AI-based prescreening	Reduces workload for pathologists, improves efficiency	Potential for over-reliance on AI, data security concerns
[274]	Griem et al. (2023)	AI for tumor detection	Enhances detection accuracy, supports tissue analysis	Requires high-quality images, potential for false positives
[275]	Prezja et al. (2023)	Refined deep learning	High accuracy, supports tissue decomposition analysis	Requires large datasets, high computational resources
[272]	Saillard et al. (2023)	AI for MSI detection	High accuracy, supports pre-screening	Expensive to implement, requires specialized training
[120]	Wagner et al. (2023)	Transformer-based AI	High accuracy, supports biomarker prediction	Requires large datasets, computationally intensive
[191]	Yin et al. (2023)	Deep learning	High accuracy in diagnosis, early detection	Requires large datasets for training, high computational resources
[286]	Yin et al. (2023)	Generalized AI with	High flexibility, supports multiple	Requires large datasets,

Table 6. A chronological overview of AI applications in colorectal cancer diagnosis, prognosis, and treatment.
(continued)

Citation	Authors (year)	AI model	Advantages	Disadvantages
		transfer learning	tasks	potential for overfitting
[279]	Pham et al. (2023)	AI fusion	Combines multiple data sources, high accuracy	Requires high-quality data, expensive to implement
[280]	Jiang et al. (2023)	Deep learning for MRI	Predicts outcomes, supports clinical decisions	Requires high-quality MRI, computationally expensive
[281]	L'Imperio et al. (2023)	ML for risk stratification	High accuracy, supports clinical risk assessment	Requires validation, potential for misclassification
[287]	Pham et al. (2023)	Markov models with AI	Predicts survival outcomes, supports clinical decision-making	Requires large datasets, computationally intensive
[288]	Tsai et al. (2023)	AI for multi-omics prediction	High accuracy, supports personalized medicine	Requires high-quality data, expensive to implement
[258]	Spadaccini et al. (2024)	AI-assisted colonoscopy	Enhances screening, reduces miss rates	Expensive, requires integration into existing systems
[265]	Peng et al. (2024)	ML for image fusion	Combines multiple imaging modalities, improves accuracy	Computationally expensive, requires large datasets
[271]	Neto et al. (2024)	Interpretable ML system	High interpretability, supports diagnosis	Requires high-quality images, potential for misclassification

AI: artificial intelligence; MRI: magnetic resonance imaging; CT: computed tomography; ML: machine learning.

Structured evaluation of AI tools in colorectal cancer screening

AI technologies are being applied across multiple domains of CRC screening and diagnosis, with varying levels of maturity, performance, and clinical applicability. CAD for colonoscopy is at an early adoption stage, supported by FDA approval and proven trial benefits, yet real-world outcomes remain inconsistent and operator dependent [176, 289]. Radiology AI (CT/MRI) is still investigational—demonstrating accuracy in staging and localization but hindered by dataset variability and integration challenges [229, 230, 290, 291]. Pathology AI has shown strong accuracy in tumor classification and MSI prediction in pilot studies, but its broader adoption is constrained by the need for large, diverse datasets and costly infrastructure [231, 232]. Infrared imaging with AI (e.g., FTIR spectroscopy) remains in early research, with encouraging sensitivity in distinguishing tumor from normal tissue, though limited by heterogeneity and sparse validation [189–191]. Liquid biopsy with AI (ctDNA) is emerging in clinical trials, offering promise for detecting residual disease and recurrence, but is challenged by low sensitivity in early CRC and assay standardization issues [233]. Collectively, these tools highlight both opportunities and barriers, underscoring the need for pragmatic trials, diverse datasets, transparent validation, and equity-focused implementation.

CAD for colonoscopy readiness: early adoption, with FDA-approved tools in use. Performance: improves adenoma detection in trials. Limitations: mixed results in real-world practice; dependent on visualization quality and bowel preparation. Applicability: useful adjunct for polyp detection but requires skilled operators.

AI in radiology (CT/MRI) readiness: moderate, investigational stage. Performance: accurate for staging and localization. Limitations: dataset variability and challenges with workflow integration. Applicability: potential for preoperative planning and non-invasive staging.

AI in pathology (digital slides) readiness: pilot adoption in select centers. Performance: high accuracy in tumor classification and MSI prediction. Limitations: requires large annotated datasets and costly infrastructure. Applicability: supports diagnostics and reduces workload in high-volume labs.

Infrared imaging + AI (FTIR spectroscopy) readiness: early research stage. Performance: sensitive to tumor-normal tissue distinctions with robust biomarkers. Limitations: experimental heterogeneity and limited clinical validation. Applicability: promising for intraoperative margin assessment but not yet routine.

Liquid biopsy with AI (ctDNA) readiness: emerging, under clinical trial. Performance: detects minimal residual disease and recurrence. Limitations: limited sensitivity in early CRC; assay standardization needed. Applicability: potential for surveillance and therapy guidance once validated.

Role of internet of things (IoT) in colorectal cancer

Recent technological advances in surgical practice have embraced the IoT, which integrates interconnected devices, sensors, and data analytics to optimize patient care. In CRC, IoT applications are emerging across prevention, diagnosis, perioperative care, and long-term follow-up [292–295].

Early detection and screening: IoT-enabled home-based screening devices, such as smart fecal test kits and wearable biosensors, can continuously monitor biomarkers and relay results directly to healthcare providers. This real-time data sharing may enhance adherence to CRC screening programs and facilitate early diagnosis.

Surgical practice and intraoperative monitoring: In minimally invasive colorectal surgery, IoT-based smart instruments and connected laparoscopic systems improve precision, workflow, and safety. Integration with ML further enhances intraoperative decision-making, potentially reducing complications and improving oncological outcomes.

Postoperative care and survivorship: IoT-enabled wearables and mobile health platforms allow remote monitoring of vital signs, bowel function, and quality-of-life indicators after CRC surgery. These tools support early detection of complications, personalized rehabilitation, and continuity of care.

Data-driven personalized medicine: By linking patient-generated health data with electronic health records and AI-driven analytics, IoT provides a foundation for predictive modeling in CRC risk assessment, prognosis, and tailored treatment strategies.

Despite its promise, challenges remain in ensuring data security, interoperability, and equitable access, especially in low-resource settings. Nevertheless, IoT represents a transformative step toward connected, patient-centered CRC care [296].

Discussion

AI has emerged as a transformative force in CRC screening and diagnosis, yet its integration into real-world practice reveals several unresolved challenges. While the USPSTF has established comprehensive CRC screening guidelines emphasizing early detection and test accessibility, a critical but often overlooked barrier involves diagnostic coding. When a colonoscopy is ordered as a “screening colonoscopy,” it is typically covered by insurance at minimal or no cost. Conversely, procedures coded as “diagnostic colonoscopies,” such as those performed for patients presenting with rectal bleeding or after a positive non-invasive test, may not be fully reimbursed, leaving patients responsible for substantial out-of-pocket costs [297]. These discrepancies extend to follow-up procedures after positive FIT or stool DNA assays, where the confirmatory colonoscopy is often reclassified as diagnostic rather than screening. Such financial disincentives may inadvertently discourage patients from participating in non-invasive testing despite its proven effectiveness and convenience.

Beyond systemic coding and reimbursement challenges, AI-driven tools hold great promise for improving CRC screening accuracy, enhancing polyp detection, and enabling more individualized treatment strategies through the integration of radiologic, pathologic, and genomic data. However, AI’s performance remains contingent on the quality of visual information provided during endoscopic procedures. The maxim “AI cannot detect what it cannot see” highlights its dependency on operator technique and visualization quality. Incomplete mucosal inspection due to colonic folds, residual stool, or suboptimal bowel preparation can lead to missed lesions and reduced diagnostic accuracy [176]. As such, technological advances must coincide with rigorous procedural standards and comprehensive operator training.

Evidence from clinical studies underscores the variability of AI performance between controlled and pragmatic environments. Ladabaum et al. (2023) [289] demonstrated that CAD systems did not significantly improve polyp detection rates among colonoscopists in real-world settings, contrasting with earlier randomized trials and meta-analyses showing improved ADR under experimental conditions [227, 228, 298–302]. This discrepancy underscores the persistent gap between experimental efficacy and practical effectiveness. Factors such as operator dependency, variation in bowel preparation, and system

integration influence outcomes. Additional concerns include dataset bias, the generalizability of training populations, and whether excessive reliance on CAD may erode traditional diagnostic competencies among gastroenterology trainees. Several fellowship directors have expressed apprehension that overdependence on AI-assisted devices could impede the development of essential observational and interpretive skills required for independent clinical judgment. These concerns align with broader issues regarding model transparency, accountability, and long-term clinical utility [237, 238, 303].

Collectively, these findings highlight the need for a balanced approach that integrates AI as an adjunct rather than a substitute for human expertise. While AI can augment lesion detection, standardize quality metrics, and provide real-time decision support, its success ultimately depends on maintaining operator proficiency, ensuring rigorous validation, and addressing systemic and ethical constraints.

Next steps

Moving forward, the integration of AI into CRC screening should focus on evidence-based, equitable, and transparent implementation strategies. Large-scale, multicenter pragmatic trials are needed to validate CAD and ML models across diverse patient populations and practice settings, ensuring reproducibility and generalizability beyond controlled environments [238]. Refinement of algorithms to mitigate bias, enhance interpretability, and ensure continuous learning within regulatory frameworks will be essential for clinical trust and adoption [237].

Parallel to technical advancements, structured training programs should educate clinicians on AI-assisted workflows without diminishing traditional diagnostic skill development. AI should serve as a complement to, not a replacement for, the human eye—providing feedback, identifying overlooked regions, and reinforcing procedural completeness. Integration within electronic health record and imaging platforms should prioritize workflow efficiency, data security, and algorithmic transparency [303].

Finally, addressing systemic barriers such as diagnostic coding inconsistencies and financial inequities is essential to ensure that screening innovations translate into real-world health benefits. Policy efforts should advocate for insurance frameworks that classify follow-up colonoscopies after positive non-invasive tests as screening procedures, reducing patient cost burdens and improving adherence. Through interdisciplinary collaboration among gastroenterologists, radiologists, data scientists, ethicists, and policymakers, AI can evolve from an experimental adjunct to a practical, equitable, and ethically grounded instrument in the global effort to reduce CRC mortality.

Conclusions

CRC continues to represent a major public health challenge, demanding innovative yet practical approaches that improve early detection and outcomes. AI has emerged as a pivotal component in this evolution, enhancing diagnostic precision and offering opportunities for individualized, data-driven care. However, its ultimate impact will depend on how effectively technology is aligned with the realities of clinical practice, patient equity, and system-level integration.

As the field advances, emphasis should shift from proof-of-concept demonstrations to measurable improvements in patient outcomes, workflow efficiency, and accessibility. The successful adoption of AI-driven screening requires not only technological refinement but also robust validation, transparent regulation, and sustained clinician engagement. Importantly, ethical stewardship—encompassing data integrity, patient trust, and equitable access—must remain at the forefront of AI implementation.

Looking ahead, a multidisciplinary framework that unites clinicians, data scientists, health economists, and policymakers will be critical to ensure that innovation translates into population-level benefit. By coupling precision technologies with health-system reform and patient-centered delivery models, the integration of AI into CRC screening and diagnosis can meaningfully contribute to reducing disease burden and improving long-term outcomes worldwide.

Abbreviations

ACA: Affordable Care Act
ADR: adenoma detection rates
AI: artificial intelligence
BRFSS: Behavioral Risk Factor Surveillance System
CAD: computer-aided detection
CMS: Centers for Medicare and Medicaid Services
CRC: colorectal cancer
CT: computed tomography
ctDNA: circulating tumor DNA
EOCRC: early-onset colorectal cancer
FIT: fecal immunochemical test
FOBT: fecal occult blood testing
FTIR: Fourier transform infrared
GEOCRCTT: Global Early-Onset Colorectal Cancer Think Tank
HEDIS: Healthcare Effectiveness Data and Information Set
HMO: Health Maintenance Organization
IoT: internet of things
LMICs: low- and middle-income countries
ML: machine learning
MPE: molecular pathological epidemiology
MRI: magnetic resonance imaging
mSEPT9: methylated SEPT9
MSI: microsatellite instability
NHIS: National Health Interview Survey
PET: positron emission tomography
PPO: Preferred Provider Organization
USPSTF: U.S. Preventive Services Task Force

Declarations

Acknowledgments

AI-Assisted Work Statement: During the preparation of this work, the authors used MS PowerPoint and ChatGPT to put together the text and icons to generate the graphical abstract. After using MS PowerPoint and ChatGPT to generate the image, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Author contributions

TDP: Conceptualization. DTPL: Writing—original draft, Conceptualization. Both authors read, edited, and approved the submitted version.

Conflicts of interest

Dr. Tuan D. Pham, who is the Editorial Board Member of Exploration of Medicine, had no involvement in the decision-making or review process of this manuscript. The other author declares that he has no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Copyright

© The Author(s) 2025.

Publisher's note

Open Exploration maintains a neutral stance on jurisdictional claims in published institutional affiliations and maps. All opinions expressed in this article are the personal views of the author(s) and do not represent the stance of the editorial team or the publisher.

References

1. Cancer Stat Facts: Cancer of Any Site [Internet]. National Cancer Institute; [cited 2025 Oct 1]. Available from: <https://seer.cancer.gov/statfacts/html/all.html>
2. United States Cancer Cases and Death Statistics At a Glance [Internet]. Centers for Disease Control and Prevention; [cited 2022 Sep 29]. Available from: https://gis.cdc.gov/Cancer/USCS/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcancer%2Fdataviz%2Findex.htm#/AtAGlance/
3. Financial Burden of Cancer Care [Internet]. National Cancer Institute; [cited 2025 Oct 1]. Available from: https://progressreport.cancer.gov/after/economic_burden
4. Health and Economic Benefits of Colorectal Cancer Interventions [Internet]. Centers for Disease Control and Prevention; [cited 2025 Oct 1]. Available from: https://www.cdc.gov/nccdphp/priorities/colorectal-cancer.html?CDC_AAref_Val=https://www.cdc.gov/chronicdisease/programs-impact/pop/colorectal-cancer.htm
5. Mariotto AB, Yabroff KR, Shao Y, Feuer EJ, Brown ML. Projections of the cost of cancer care in the United States: 2010–2020. *J Natl Cancer Inst*. 2011;103:117–28. [DOI] [PubMed] [PMC]
6. Mariotto AB, Enewold L, Zhao J, Zeruto CA, Yabroff KR. Medical Care Costs Associated with Cancer Survivorship in the United States. *Cancer Epidemiol Biomarkers Prev*. 2020;29:1304–12. [DOI] [PubMed] [PMC]
7. Chen S, Cao Z, Prettner K, Kuhn M, Yang J, Jiao L, et al. Estimates and Projections of the Global Economic Cost of 29 Cancers in 204 Countries and Territories From 2020 to 2050. *JAMA Oncol*. 2023;9:465–72. [DOI] [PubMed] [PMC]

8. Morgan E, Arnold M, Gini A, Lorenzoni V, Cabasag CJ, Laversanne M, et al. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. *Gut*. 2023;72:338–44. [DOI] [PubMed]
9. Global patterns and trends in colorectal cancer incidence and mortality [Internet]. International Agency for Research on Cancer (IARC); c1965–2025 [cited 2025 Oct 1]. Available from: <https://www.iarc.who.int/reference/global-patterns-and-trends-in-colorectal-cancer-incidence-and-mortality/>
10. Schliemann D, Ramanathan K, Matovu N, O'Neill C, Kee F, Su TT, et al. The implementation of colorectal cancer screening interventions in low-and middle-income countries: a scoping review. *BMC Cancer*. 2021;21:1125. [DOI] [PubMed] [PMC]
11. Henderson RH, French D, Maughan T, Adams R, Allemani C, Minicozzi P, et al. The economic burden of colorectal cancer across Europe: a population-based cost-of-illness study. *Lancet Gastroenterol Hepatol*. 2021;6:709–22. [DOI] [PubMed]
12. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74:229–63. [DOI] [PubMed]
13. American Cancer Society. Global cancer facts & figures 5th edition. Atlanta: American Cancer Society; 2024.
14. Global cancer burden growing, amidst mounting need for services [Internet]. WHO; c2025 [cited 2025 Oct 1]. Available from: <https://www.who.int/news/item/01-02-2024-global-cancer-burden-growing--amidst-mounting-need-for-services>
15. Colonoscopy costs at ASCs vs. HOPDs in each state [Internet]. Becker's Healthcare; c2025 [cited 2025 Oct 1]. Available from: <https://www.beckersasc.com/gastroenterology-and-endoscopy/colonoscopy-costs-at-ascs-vs-hopds-in-each-state.html>
16. Cancer cases rising for women and younger adults in US, report finds [Internet]. Guardian News & Media Limited or its affiliated companies; c2025 [cited 2025 Oct 1]. Available from: <https://www.theguardian.com/society/2025/jan/16/cancer-young-women-adults>
17. Key statistics for colorectal (colon & rectal) cancer [Internet]. American Cancer Society, Inc.; c2025 [cited 2025 Oct 1]. Available from: <https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html>
18. Cancer facts & figures 2024 [Internet]. American Cancer Society, Inc.; c2025 [cited 2025 Oct 1]. Available from: <https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2024-cancer-facts-figures.html>
19. All Cancer Sites Combined, Recent Trends in SEER Age-Adjusted Incidence Rates, 2000–2022 [Internet]. National Cancer Institute; [cited 2025 Oct 1]. Available from: <https://seer.cancer.gov/explorer/>
20. Edwards BK, Noone AM, Mariotto AB, Simard EP, Boscoe FP, Henley SJ, et al. Annual Report to the Nation on the status of cancer, 1975–2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. *Cancer*. 2014;120:1290–314. [DOI] [PubMed] [PMC]
21. Colorectal cancer screening (PDQ®)—health professional version [Internet]. National Cancer Institute; [cited 2025 Oct 1]. Available from: https://www.cancer.gov/types/colorectal/hp/colorectal-screening-pdq#section_2.1
22. Wolf AMD, Fontham ETH, Church TR, Flowers CR, Guerra CE, LaMonte SJ, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68:250–81. [DOI] [PubMed]
23. Colorectal cancer statistics [Internet]. Centers for Disease Control and Prevention; [cited 2025 oct 1]. Available from: https://www.cdc.gov/colorectal-cancer/statistics/?CDC_AAref_Val=https://www.cdc.gov/cancer/colorectal/statistics/

24. Cancer facts & figures 2008 [Internet]. American Cancer Society, Inc.; c2025 [cited 2025 Oct 1]. Available from: <https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2008.html>
25. American Cancer Society. Colorectal cancer facts & figures 2023. Atlanta: American Cancer Society; 2023.
26. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Results of screening colonoscopy among persons 40 to 49 years of age. *N Engl J Med*. 2002;346:1781–5. [DOI] [PubMed]
27. Siegel RL, Fedewa SA, Anderson WF, Miller KD, Ma J, Rosenberg PS, et al. Colorectal Cancer Incidence Patterns in the United States, 1974–2013. *J Natl Cancer Inst*. 2017;109:djw322. [DOI] [PubMed] [PMC]
28. Lynch BM. Sedentary behavior and cancer: a systematic review of the literature and proposed biological mechanisms. *Cancer Epidemiol Biomarkers Prev*. 2010;19:2691–709. [DOI] [PubMed]
29. Kehm RD, Terry MB. Early onset cancer trends and the persistently higher burden of cancer in young women. *Oncologist*. 2025;30:oyaf084. [DOI] [PubMed] [PMC]
30. Meng Y, Tan Z, Zhen J, Xiao D, Cai L, Dong W, et al. Global, regional, and national burden of early-onset colorectal cancer from 1990 to 2021: a systematic analysis based on the global burden of disease study 2021. *BMC Med*. 2025;23:34. [DOI] [PubMed] [PMC]
31. Abualkhair WH, Zhou M, Ahnen D, Yu Q, Wu XC, Karlitz JJ. Trends in Incidence of Early-Onset Colorectal Cancer in the United States Among Those Approaching Screening Age. *JAMA Netw Open*. 2020;3:e1920407. [DOI] [PubMed] [PMC]
32. Ystgaard MF, Myklebust TÅ, Smeby J, Larsen IK, Guren TK, Kure EH, et al. Early-onset colorectal cancer incidence in Norway: a national registry-based study (1993–2022) analysing subsite and morphology trends. *ESMO Gastrointest Oncol*. 2024;7:100065. [DOI]
33. Demb J, Kolb JM, Dounel J, Fritz CDL, Advani SM, Cao Y, et al. Red Flag Signs and Symptoms for Patients With Early-Onset Colorectal Cancer: A Systematic Review and Meta-Analysis. *JAMA Netw Open*. 2024;7:e2413157. [DOI] [PubMed] [PMC]
34. Rozani S, Lykoudis PM. Overcoming geographical and socioeconomic limitations in colorectal cancer screening. *World J Gastrointest Oncol*. 2024;16:1683–9. [DOI] [PubMed] [PMC]
35. Vitaloni M, Maguet K, Carlan A, Stack P, de Jong V, Williams R, et al. Clinical challenges and patient experiences in early-onset colorectal cancer: insights from seven European countries. *BMC Gastroenterol*. 2025;25:378. [DOI] [PubMed] [PMC]
36. Huang YN, Munteanu V, Love MI, Ronkowski CF, Deshpande D, Wong-Beringer A, et al. Perceptual and technical barriers in sharing and formatting metadata accompanying omics studies. *Cell Genom*. 2025;5:100845. [DOI] [PubMed] [PMC]
37. Sun C, Mobley E, Quillen M, Parker M, Daly M, Wang R, et al. Predicting Early-Onset Colorectal Cancer in Individuals Below Screening Age Using Machine Learning and Real-World Data: Case Control Study. *JMIR Cancer*. 2025;11:e64506. [DOI] [PubMed] [PMC]
38. Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med*. 1992;326:653–7. [DOI] [PubMed]
39. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med*. 1993;329:1977–81. [DOI] [PubMed]
40. Mandel JS, Bond JH, Church TR, Snover DC, Mary Bradley G, Schuman LM, et al. Reducing Mortality from Colorectal Cancer by Screening for Fecal Occult Blood. *N Engl J Med*. 1993;328:1365–71. [DOI]
41. Atkin WS, Edwards R, Kralj-Hans I, Wooldrage K, Hart AR, Northover JMA, et al.; UK Flexible Sigmoidoscopy Trial Investigators. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. *Lancet*. 2010;375:1624–33. [DOI] [PubMed]

42. Holme Ø, Løberg M, Kalager M, Bretthauer M, Hernán MA, Aas E, et al. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: A randomized clinical trial. *JAMA*. 2014;312:606–15. [DOI]
43. Ladabaum U, Dominitz JA, Kahi C, Schoen RE. Strategies for Colorectal Cancer Screening. *Gastroenterology*. 2020;158:418–32. [DOI] [PubMed]
44. Bretthauer M, Løberg M, Wieszczy P, Kalager M, Emilsson L, Garborg K, et al.; NordICC Study Group. Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death. *N Engl J Med*. 2022; 387:1547–56. [DOI] [PubMed]
45. Pinsky PF, Schoen RE. Contribution of Surveillance Colonoscopy to Colorectal Cancer Prevention. *Clin Gastroenterol Hepatol*. 2020;18:2937–44. [DOI] [PubMed] [PMC]
46. Heisser T, Sergeev D, Hoffmeister M, Brenner H. Contributions of early detection and cancer prevention to colorectal cancer mortality reduction by screening colonoscopy: a validated modeling study. *Gastrointest Endosc*. 2024;100:710–7. [DOI] [PubMed]
47. Cancer Stat Facts: Colorectal Cancer [Internet]. National Cancer Institute; [cited 2025 Oct 1]. Available from: <https://seer.cancer.gov/statfacts/html/colorect.html>
48. Cancer Statistics Review Archive [Internet]. National Cancer Institute; [cited 2025 Oct 1]. Available from: <https://seer.cancer.gov/csr/previous.html>
49. Zilja ES, Leivaditis V, Liolis E, Antzoulas A, Tchabashvili L, Tasios K, et al. Mental Health Disorders in Colorectal Cancer Patients Following Postoperative Complications: Results From a Single Tertiary Center. *Bulg J Psychiatry*. 2025;10:48–9.
50. Zilja ES, Leivaditis V, Liolis E, Antzoulas A, Tchabashvili L, et al. Mental health disorders in colorectal cancer patients following postoperative complications. *J Psychiatry*. 2025;10:49–56.
51. Li J, Ma C. Anxiety and depression during 3-year follow-up period in postoperative gastrointestinal cancer patients: prevalence, vertical change, risk factors, and prognostic value. *Ir J Med Sci*. 2023; 192:2621–9. [DOI] [PubMed]
52. Hu Z, Zhang H, Wang J, Xiong H, Liu Y, Zhu Y, et al. Nomogram to Predict the Risk of Postoperative Anxiety and Depression in Colorectal Cancer Patients. *Int J Gen Med*. 2022;15:4881–95. [DOI] [PubMed] [PMC]
53. Yuan P, Wang D, Xie D. Anxiety and Depression after Colorectal Cancer Surgery: A Systematic Review and Meta-Analysis of Short- and Long-Term Outcomes. *Alpha Psychiatry*. 2024;25:429–39. [DOI] [PubMed] [PMC]
54. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73:17–48. [DOI] [PubMed]
55. Cho MY, Siegel DA, Demb J, Richardson LC, Gupta S. Increasing Colorectal Cancer Incidence Before and After Age 50: Implications for Screening Initiation and Promotion of “On-Time” Screening. *Dig Dis Sci*. 2022;67:4086–91. [DOI] [PubMed] [PMC]
56. Colorectal cancer [Internet]. WHO; c2025 [cited 2025 Oct 1]. Available from: <https://www.who.int/news-room/fact-sheets/detail/colorectal-cancer>
57. Goosenberg E, Kaur A, Babiker HM. A Review of Hereditary Colorectal Cancers. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025. [PubMed]
58. Pallatt S, Nambidi S, Adhikary S, Banerjee A, Pathak S, Duttaroy AK. A brief review of Lynch syndrome: understanding the dual cancer risk between endometrial and colorectal cancer. *Oncol Rev*. 2025;19:1549416. [DOI] [PubMed] [PMC]
59. Sadien ID, Davies RJ, Wheeler J. The genomics of sporadic and hereditary colorectal cancer. *Ann R Coll Surg Engl*. 2024;106:313–20. [DOI] [PubMed] [PMC]
60. Cao Q, Tian Y, Deng Z, Yang F, Chen E. Epigenetic Alteration in Colorectal Cancer: Potential Diagnostic and Prognostic Implications. *Int J Mol Sci*. 2024;25:3358. [DOI] [PubMed] [PMC]

61. Dueñas N, Klinkhammer H, Bonifaci N, Spier I, Mayr A, Hassanin E, et al. Ability of a polygenic risk score to refine colorectal cancer risk in Lynch syndrome. *J Med Genet*. 2023;60:1044–51. [\[DOI\]](#) [\[PubMed\]](#)
62. Mazzone R, Zwergel C, Mai A, Valente S. Epi-drugs in combination with immunotherapy: a new avenue to improve anticancer efficacy. *Clin Epigenetics*. 2017;9:59. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
63. Song J, Yang P, Chen C, Ding W, Tillement O, Bai H, et al. Targeting epigenetic regulators as a promising avenue to overcome cancer therapy resistance. *Signal Transduct Target Ther*. 2025;10:219. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
64. Gao K, Jin H, Yang Y, Li J, He Y, Zhou R, et al. Family history of colorectal cancer and risk of colorectal neoplasia: A systematic review and meta-analysis. *Am J Gastroenterol*. 2025;120:531–9. [\[DOI\]](#)
65. Roshandel G, Ghasemi-Kebria F, Malekzadeh R. Colorectal Cancer: Epidemiology, Risk Factors, and Prevention. *Cancers (Basel)*. 2024;16:1530. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
66. Wu J, Zhang Q, Li X, Bai T, Hou X, Li G, et al. The Effect of the Second Forward View on the Detection Rate of Sessile Serrated Lesions in the Proximal Colon: A Single-Center Prospective Randomized Controlled Study. *Clin Transl Gastroenterol*. 2025;16:e00805. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
67. Wang J, Xu G, Hu X, Li W, Yao N, Han F, et al. The histologic features, molecular features, detection and management of serrated polyps: a review. *Front Oncol*. 2024;14:1356250. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
68. Papier K, Bradbury KE, Balkwill A, Barnes I, Smith-Byrne K, Gunter MJ, et al. Diet-wide analyses for risk of colorectal cancer: prospective study of 12,251 incident cases among 542,778 women in the UK. *Nat Commun*. 2025;16:375. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
69. Yang S, Wang Y, Sheng L, Cui W, Ma C. The effect of fecal bile acids on the incidence and risk-stratification of colorectal cancer: an updated systematic review and meta-analysis. *Sci Rep*. 2025;15:740. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
70. Chu AH, Lin K, Croker H, Kefyalew S, Markozannes G, Tsilidis KK, et al. Dietary-Lifestyle Patterns and Colorectal Cancer Risk: Global Cancer Update Programme (CUP Global) Systematic Literature Review. *Am J Clin Nutr*. 2025;121:986–98. [\[DOI\]](#) [\[PubMed\]](#)
71. Chen Q, Keum N, Giovannucci EL. Post-diagnosis dietary and lifestyle factors and mortality outcomes among colorectal cancer patients: a meta-analysis. *J Natl Cancer Inst*. 2025;[Epub ahead of print]. [\[DOI\]](#) [\[PubMed\]](#)
72. Chen N, Liang H, Huang T, Huang N. Exposome approach for identifying modifiable factors for the prevention of colorectal cancer. *Sci Rep*. 2022;12:21615. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
73. Zepeda-Rivera M, Minot SS, Bouzek H, Wu H, Blanco-Míguez A, Manghi P, et al. A distinct *Fusobacterium nucleatum* clade dominates the colorectal cancer niche. *Nature*. 2024;628:424–32. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
74. Zhang C, Wang Y, Cheng L, Cao X, Liu C. Gut microbiota in colorectal cancer: a review of its influence on tumor immune surveillance and therapeutic response. *Front Oncol*. 2025;15:1557959. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
75. van Zutphen M, Verkaar AJCF, van Duijnhoven FJB, Voortman T, Baskin ML, Chowdhury R, et al. Early-life anthropometry and colorectal cancer risk in adulthood: Global Cancer Update Programme (CUP Global) systematic literature review and meta-analysis of prospective studies. *Int J Cancer*. 2025;157:1094–109. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
76. Tsenkova M, Brauer M, Pozdeev VI, Kasakin M, Busi SB, Schmoetten M, et al. Ketogenic diet suppresses colorectal cancer through the gut microbiome long chain fatty acid stearate. *Nat Commun*. 2025;16:1792. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)
77. Imanbayev N, Iztleuov Y, Bekmukhambetov Y, Abdelazim IA, Donayeva A, Amanzholkyzy A, et al. Colorectal cancer and microbiota: systematic review. *Prz Gastroenterol*. 2024;16:380–96. [\[DOI\]](#) [\[PubMed\]](#) [\[PMC\]](#)

78. Kuru-Yaşar R, Üstün-Aytekin Ö. The Crucial Roles of Diet, Microbiota, and Postbiotics in Colorectal Cancer. *Curr Nutr Rep*. 2024;13:126–51. [DOI]
79. Lin KX, Istl AC, Quan D, Skaro A, Tang E, Zheng X. PD-1 and PD-L1 inhibitors in cold colorectal cancer: challenges and strategies. *Cancer Immunol Immunother*. 2023;72:3875–93. [DOI] [PubMed] [PMC]
80. Cai L, Chen A, Tang D. A new strategy for immunotherapy of microsatellite-stable (MSS)-type advanced colorectal cancer: Multi-pathway combination therapy with PD-1/PD-L1 inhibitors. *Immunology*. 2024;173:209–26. [DOI] [PubMed]
81. Sahin IH, Akce M, Alese O, Shaib W, Lesinski GB, El-Rayes B, et al. Immune checkpoint inhibitors for the treatment of MSI-H/MMR-D colorectal cancer and a perspective on resistance mechanisms. *Br J Cancer*. 2019;121:809–18. [DOI] [PubMed] [PMC]
82. FDA grants accelerated approval to pembrolizumab for first tissue/site-agnostic indication [Internet]. U.S. Food and Drug Administration; [cited 2025 Oct 1]. Available from: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-pembrolizumab-first-tissuesite-agnostic-indication>
83. Lizardo DY, Kuang C, Hao S, Yu J, Huang Y, Zhang L. Immunotherapy efficacy on mismatch repair-deficient colorectal cancer: From bench to bedside. *Biochim Biophys Acta Rev Cancer*. 2020;1874:188447. [DOI] [PubMed] [PMC]
84. Choucrair K, Radford M, Bansal A, Park R, Saeed A. Advances in immune therapies for the treatment of microsatellite instability-high/deficient mismatch repair metastatic colorectal cancer (Review). *Int J Oncol*. 2021;59:74. [DOI] [PubMed] [PMC]
85. Ros J, Balconi F, Baraibar I, Saoudi Gonzalez N, Salva F, Tabernero J, et al. Advances in immune checkpoint inhibitor combination strategies for microsatellite stable colorectal cancer. *Front Oncol*. 2023;13:1112276. [DOI] [PubMed] [PMC]
86. Zhang Y, Rajput A, Jin N, Wang J. Mechanisms of Immunosuppression in Colorectal Cancer. *Cancers (Basel)*. 2020;12:3850. [DOI] [PubMed] [PMC]
87. Alsheridah N, Akhtar S. Diet, obesity and colorectal carcinoma risk: results from a national cancer registry-based middle-eastern study. *BMC Cancer*. 2018;18:1227. [DOI] [PubMed] [PMC]
88. Barnestein R, Galland L, Kalfeist L, Ghiringhelli F, Ladoire S, Limagne E. Immunosuppressive tumor microenvironment modulation by chemotherapies and targeted therapies to enhance immunotherapy effectiveness. *Oncoimmunology*. 2022;11:2120676. [DOI] [PubMed] [PMC]
89. Zheng Z, Wieder T, Mauerer B, Schäfer L, Kesselring R, Braumüller H. T Cells in Colorectal Cancer: Unravelling the Function of Different T Cell Subsets in the Tumor Microenvironment. *Int J Mol Sci*. 2023;24:11673. [DOI] [PubMed] [PMC]
90. Zou D, Xin X, Xu Y, Xu H, Huang L, Xu T. Improving the efficacy of immunotherapy for colorectal cancer: Targeting tumor microenvironment-associated immunosuppressive cells. *Heliyon*. 2024;10:e36446. [DOI] [PubMed] [PMC]
91. Zeng W, Liu H, Mao Y, Jiang S, Yi H, Zhang Z, et al. Myeloid-derived suppressor cells: Key immunosuppressive regulators and therapeutic targets in colorectal cancer (Review). *Int J Oncol*. 2024;65:85. [DOI] [PubMed] [PMC]
92. Clerick J, Van Oosterwyck A, Carton S. Transforming the landscape of colorectal cancer treatment with immunotherapy: Evolution and future horizons. *Cancer Treat Res Commun*. 2024;39:100807. [DOI] [PubMed]
93. Huyghe N, Benidovskaya E, Stevens P, Van den Eynde M. Biomarkers of Response and Resistance to Immunotherapy in Microsatellite Stable Colorectal Cancer: Toward a New Personalized Medicine. *Cancers (Basel)*. 2022;14:2241. [DOI] [PubMed] [PMC]
94. Blair AB, Zheng L, Soares KC. The Landmark Series: Therapeutic Cancer Vaccine Strategies for Cold Tumors. *Ann Surg Oncol*. 2025;32:4957–66. [DOI] [PubMed] [PMC]

95. He R, Lao Y, Yu W, Zhang X, Jiang M, Zhu C. Progress in the Application of Immune Checkpoint Inhibitor-Based Immunotherapy for Targeting Different Types of Colorectal Cancer. *Front Oncol.* 2021;11:764618. [DOI] [PubMed] [PMC]
96. Ma S, Li L, Cai H, Guo T, Zhang L. Therapeutic challenge for immunotherapy targeting cold colorectal cancer: A narrative review. *World J Clin Oncol.* 2023;14:81–8. [DOI] [PubMed] [PMC]
97. Zhu Y, Li X, Chen T, Wang J, Zhou Y, Mu X, et al. Personalised neoantigen-based therapy in colorectal cancer. *Clin Transl Med.* 2023;13:e1461. [DOI] [PubMed] [PMC]
98. Cornista AM, Giolito MV, Baker K, Hazime H, Dufait I, Datta J, et al. Colorectal Cancer Immunotherapy: State of the Art and Future Directions. *Gastro Hep Adv.* 2023;2:1103–19. [DOI] [PubMed] [PMC]
99. Martín-García D, García-Aranda M, Redondo M. Biomarker Identification through Proteomics in Colorectal Cancer. *Int J Mol Sci.* 2024;25:2283. [DOI] [PubMed] [PMC]
100. Yang M, Cui M, Sun Y, Liu S, Jiang W. Mechanisms, combination therapy, and biomarkers in cancer immunotherapy resistance. *Cell Commun Signal.* 2024;22:338. [DOI] [PubMed] [PMC]
101. Rachiglio AM, Lambiase M, Fenizia F, Roma C, Cardone C, Iannaccone A, et al. Genomic Profiling of *KRAS/NRAS/BRAF/PIK3CA* Wild-Type Metastatic Colorectal Cancer Patients Reveals Novel Mutations in Genes Potentially Associated with Resistance to Anti-EGFR Agents. *Cancers (Basel).* 2019;11:859. [DOI] [PubMed] [PMC]
102. Wu J, Li X, Liu H, Liu Y, Liu X. Association of *KRAS*, *NRAS*, *BRAF* and *PIK3CA* gene mutations with clinicopathological features, prognosis and ring finger protein 215 expression in patients with colorectal cancer. *Biomed Rep.* 2023;19:104. [DOI] [PubMed] [PMC]
103. Chung J, Xiao S, Gao Y, Soung YH. Recent Technologies towards Diagnostic and Therapeutic Applications of Circulating Nucleic Acids in Colorectal Cancers. *Int J Mol Sci.* 2024;25:8703. [DOI] [PubMed] [PMC]
104. Yao S, Han Y, Yang M, Jin K, Lan H. Integration of liquid biopsy and immunotherapy: opening a new era in colorectal cancer treatment. *Front Immunol.* 2023;14:1292861. [DOI] [PubMed] [PMC]
105. Lone SN, Nisar S, Masoodi T, Singh M, Rizwan A, Hashem S, et al. Liquid biopsy: a step closer to transform diagnosis, prognosis and future of cancer treatments. *Mol Cancer.* 2022;21:79. [DOI] [PubMed] [PMC]
106. 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] [PubMed] [PMC]
107. Adhit KK, Wanjari A, Menon S, K S. Liquid Biopsy: An Evolving Paradigm for Non-invasive Disease Diagnosis and Monitoring in Medicine. *Cureus.* 2023;15:e50176. [DOI] [PubMed] [PMC]
108. Tao X, Li Q, Zeng Y. Clinical application of liquid biopsy in colorectal cancer: detection, prediction, and treatment monitoring. *Mol Cancer.* 2024;23:145. [DOI] [PubMed] [PMC]
109. Herranz-Montoya I, Angulo-Aguado M, Perna C, Zagorac S, García-Jimeno L, Park S, et al. p53 protein degradation redefines the initiation mechanisms and drives transitional mutations in colorectal cancer. *Nat Commun.* 2025;16:3934. [DOI] [PubMed] [PMC]
110. Sikavi DR, Wang K, Ma W, Drew DA, Ogino S, Giovannucci EL, et al. Aspirin Use and Incidence of Colorectal Cancer According to Lifestyle Risk. *JAMA Oncol.* 2024;10:1354–61. [DOI] [PubMed] [PMC]
111. Martling A, Hed Myrberg I, Nilbert M, Grönberg H, Granath F, Eklund M, et al.; ALASCCA Study Group. Low-dose aspirin for PI3K-altered localized colorectal cancer. *N Engl J Med.* 2025;393:1051–64. [DOI] [PubMed]
112. Campbell PT, Patel AV, Newton CC, Jacobs EJ, Gapstur SM. Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. *J Clin Oncol.* 2013;31:876–85. [DOI] [PubMed]

113. Reardon B, Moore ND, Moore NS, Kofman E, AlDubayan SH, Cheung ATM, et al. Integrating molecular profiles into clinical frameworks through the Molecular Oncology Almanac to prospectively guide precision oncology. *Nat Cancer*. 2021;2:1102–12. [DOI] [PubMed] [PMC]
114. Ogino S, Nowak JA, Hamada T, Phipps AI, Peters U, Milner DA Jr, et al. Integrative analysis of exogenous, endogenous, tumour and immune factors for precision medicine. *Gut*. 2018;67:1168–80. [DOI] [PubMed] [PMC]
115. Qi GX, Zhao RX, Gao C, Ma ZY, Wang S, Xu J. Recent advances and challenges in colorectal cancer: from molecular research to treatment. *World J Gastroenterol*. 2025;31:106964. [DOI] [PubMed] [PMC]
116. Gebauer L, Nist A, Mernberger M, Stiewe T, Moll R, Stabla K, et al. Superior Overall Survival in Patients with Colorectal Cancer, Regular Aspirin Use, and Combined Wild-Type PIK3CA and KRAS-Mutated Tumors. *Cancers (Basel)*. 2021;13:4959. [DOI] [PubMed] [PMC]
117. Slattery ML, Lundgreen A, Herrick JS, Caan BJ, Potter JD, Wolff RK. Diet and colorectal cancer: analysis of a candidate pathway using SNPS, haplotypes, and multi-gene assessment. *Nutr Cancer*. 2011;63:1226–34. [DOI] [PubMed] [PMC]
118. Xun D, Li X, Huang L, Zhao Y, Chen J, Qi X. Machine learning-based analysis identifies a 13-gene prognostic signature to improve the clinical outcomes of colorectal cancer. *J Gastrointest Oncol*. 2024;15:2100–16. [DOI] [PubMed] [PMC]
119. Bian J, Li Y, Dang Y, Chen Y. Deep learning for fine-grained molecular-based colorectal cancer classification. *Transl Cancer Res*. 2025;14:3035–46. [DOI] [PubMed] [PMC]
120. Wagner SJ, Reisenbüchler D, West NP, Niehues JM, Zhu J, Foersch S, et al. Transformer-based biomarker prediction from colorectal cancer histology: a large-scale multicentric study. *Cancer Cell*. 2023;41:1650–61. [DOI] [PubMed] [PMC]
121. Jung SY, Yu H, Tan X, Pellegrini M. Novel DNA methylation-based epigenetic signatures in colorectal cancer from peripheral blood leukocytes. *Am J Cancer Res*. 2024;14:2253–71. [DOI] [PubMed] [PMC]
122. Cost of colonoscopy polyp removal [Internet]. Sidecar Health; [cited 2025 Oct 1]. Available from: <https://cost.sidecarhealth.com/n/colonoscopy-cost>
123. Colonoscopy polyp removal cost [Internet]. Sidecar Health; [cited 2025 Oct 1]. Available from: <https://cost.sidecarhealth.com/ts/colonoscopy-cost-by-state>
124. Insurance Coverage for Colorectal Cancer Screening [Internet]. American Cancer Society; c2025 [cited 2025 Oct 1]. Available from: <https://www.cancer.org/cancer/types/colon-rectal-cancer/detection-diagnosis-staging/screening-coverage-laws.html>
125. Affordable care act implementation FAQs - set 12 [Internet]. U.S. Centers for Medicare & Medicaid Services; [cited 2025 Oct 1]. Available from: https://www.cms.gov/CCIIO/Resources/Fact-Sheets-and-FAQs/aca_implementation_faqs12
126. Preventative and screening services. [Internet]. U.S. Centers for Medicare & Medicaid Services; [cited 2025 Oct 1]. Available from: <https://www.medicare.gov/coverage/preventive-screening-services>
127. Klabunde CN, Cronin KA, Breen N, Waldron WR, Ambis AH, Nadel MR. Trends in colorectal cancer test use among vulnerable populations in the United States. *Cancer Epidemiol Biomarkers Prev*. 2011;20:1611–21. [DOI] [PubMed] [PMC]
128. Ward E, Halpern M, Schrag N, Cokkinides V, DeSantis C, Bandi P, et al. Association of insurance with cancer care utilization and outcomes. *CA Cancer J Clin*. 2008;58:9–31. [DOI] [PubMed]
129. Cooper GS, Kou TD, Schluchter MD, Dor A, Koroukian SM. Changes in Receipt of Cancer Screening in Medicare Beneficiaries Following the Affordable Care Act. *J Natl Cancer Inst*. 2015;108:djv374. [DOI] [PubMed] [PMC]
130. Yabroff KR, Reeder-Hayes K, Zhao J, Halpern MT, Lopez AM, Bernal-Mizrachi L, et al. Health Insurance Coverage Disruptions and Cancer Care and Outcomes: Systematic Review of Published Research. *J Natl Cancer Inst*. 2020;112:671–87. [DOI] [PubMed] [PMC]

131. Colorectal Cancer Screening Tests [Internet]. American Cancer Society, Inc.; c2025 [cited 2025 Oct 1]. Available from: <https://www.cancer.org/cancer/types/colon-rectal-cancer/detection-diagnosis-staging/screening-tests-used.html>
132. Greegor DH. Diagnosis of large-bowel cancer in the asymptomatic patient. *JAMA*. 1967;201:943–5. [PubMed]
133. Lee JK, Liles EG, Bent S, Levin TR, Corley DA. Accuracy of fecal immunochemical tests for colorectal cancer: systematic review and meta-analysis. *Ann Intern Med*. 2014;160:171. [DOI] [PubMed] [PMC]
134. Zorzi M, Fedeli U, Schievano E, Bovo E, Guzzinati S, Baracco S, et al. Impact on colorectal cancer mortality of screening programmes based on the faecal immunochemical test. *Gut*. 2015;64:784–90. [DOI] [PubMed]
135. Imperiale TF, Gruber RN, Stump TE, Emmett TW, Monahan PO. Performance Characteristics of Fecal Immunochemical Tests for Colorectal Cancer and Advanced Adenomatous Polyps: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2019;170:319–29. [DOI] [PubMed]
136. 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] [PubMed]
137. Ahlquist DA, Zou H, Domanico M, Mahoney DW, Yab TC, Taylor WR, et al. Next-generation stool DNA test accurately detects colorectal cancer and large adenomas. *Gastroenterology*. 2012;142:248–56. [DOI] [PubMed] [PMC]
138. Dickinson BT, Kisiel J, Ahlquist DA, Grady WM. Molecular markers for colorectal cancer screening. *Gut*. 2015;64:1485–94. [DOI] [PubMed] [PMC]
139. Shaukat A, Levin TR. Current and future colorectal cancer screening strategies. *Nat Rev Gastroenterol Hepatol*. 2022;19:521–31. [DOI] [PubMed] [PMC]
140. FDA panel votes on blood-based test for colorectal cancer screening [Internet]. Haymarket Media, Inc.; c2025 [cited 2025 Oct 1]. Available from: <https://www.empr.com/home/news/fda-panel-vote-s-on-blood-based-test-for-colorectal-cancer-screening/>
141. van den Puttelaar R, Nascimento de Lima P, Knudsen AB, Rutter CM, Kuntz KM, de Jonge L, et al. Effectiveness and Cost-Effectiveness of Colorectal Cancer Screening With a Blood Test That Meets the Centers for Medicare & Medicaid Services Coverage Decision. *Gastroenterology*. 2024;167:368–77. [DOI] [PubMed] [PMC]
142. Screening for Colorectal Cancer - Blood-Based Biomarker Tests (CAG-00454N) [Internet]. U.S. Centers for Medicare & Medicaid Services; [cited 2025 Oct 1]. Available from: <https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&NCAId=299>
143. Katz ML, Loomans-Kropp HA, Reiter PL. Colorectal cancer screening blood test: awareness and willingness among a national sample of adults post-Federal and Drug Administration approval. *BMC Public Health*. 2025;25:1853. [DOI] [PubMed] [PMC]
144. Clark A, Lauzon M, Griffin NM, Baldo L, Spiegel BMR, Almario CV. Patient preferences for a blood-based colorectal cancer screening test: insights from a conjoint analysis survey. *Clin Transl Gastroenterol*. 2025;[Epub ahead of print]. [DOI]
145. Mohandesi Khosrosroshahi E, Bashi Zadeh Fakhar H, Akbari ME, Izadi N. Investigating the expression level of 9-methylated septin 9 in different grades of colorectal cancer—a meta-analysis study. *Egypt J Med Hum Genet*. 2025;26:38. [DOI]
146. Chung DC, Gray DM 2nd, 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] [PubMed]
147. Johnson DA, Barclay RL, Mergener K, Weiss G, König T, Beck J, et al. Plasma Septin9 versus fecal immunochemical testing for colorectal cancer screening: a prospective multicenter study. *PLoS One*. 2014:e98238. [DOI] [PubMed] [PMC]
148. Song L, Jia J, Peng X, Xiao W, Li Y. The performance of the SEPT9 gene methylation assay and a comparison with other CRC screening tests: A meta-analysis. *Sci Rep*. 2017;7:3032. [DOI] [PubMed] [PMC]

149. Lu D, Zhang Q, Li L, Luo X, Liang B, Lu Y, et al. Methylated Septin9 has moderate diagnostic value in colorectal cancer detection in Chinese population: a multicenter study. *BMC Gastroenterol*. 2022;22:232. [DOI] [PubMed] [PMC]
150. Freenome Announces Topline Results for PREEMPT CRC® to Validate the First Version of its Blood-Based Test for the Early Detection of Colorectal Cancer [Internet]. Freenome Holdings, Inc.; c2025 [cited 2025 Oct 1]. Available from: <https://www.freenome.com/newsroom/freenome-announces-topline-results-for-preempt-crc-to-validate-the-first-version-of-its-blood-based-test-for-the-early-detection-of-colorectal-cancer/>
151. Prevention of colorectal cancer through multiomics blood testing (PREEMPT CRC) [Internet]. ClinicalTrials.gov; [cited 2025 Oct 1]. Available from: <https://clinicaltrials.gov/study/NCT04369053>
152. 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] [PubMed] [PMC]
153. Eledkawy A, Hamza T, El-Metwally S. Precision cancer classification using liquid biopsy and advanced machine learning techniques. *Sci Rep*. 2024;14:5841. [DOI] [PubMed] [PMC]
154. Chen H, Zhou Q. Detecting liquid remnants of solid tumors treated with curative intent: Circulating tumor DNA as a biomarker of minimal residual disease (Review). *Oncol Rep*. 2023;49:106. [DOI] [PubMed] [PMC]
155. Nakamura Y, Tsukada Y, Matsuhashi N, Murano T, Shiozawa M, Takahashi Y, et al. Colorectal Cancer Recurrence Prediction Using a Tissue-Free Epigenomic Minimal Residual Disease Assay. *Clin Cancer Res*. 2024;30:4377–87. [DOI] [PubMed] [PMC]
156. 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] [PubMed]
157. Turnbull C, Wald N, Sullivan R, Pharoah P, Houlston RS, Aggarwal A, et al. GRAIL-Galleri: why the special treatment? *Lancet*. 2024;403:431–2. [DOI] [PubMed]
158. Shao SH, Allen B, Clement J, Chung G, Gao J, Hubbell E, et al. Multi-cancer early detection test sensitivity for cancers with and without current population-level screening options. *Tumori*. 2023;109:335–41. [DOI] [PubMed] [PMC]
159. Li L, Sun Y. Circulating tumor DNA methylation detection as biomarker and its application in tumor liquid biopsy: advances and challenges. *MedComm* (2020). 2024;5:e766. [DOI] [PubMed] [PMC]
160. Hoffman RM, Wolf AMD, Raoof S, Guerra CE, Church TR, Elkin EB, et al. Multicancer early detection testing: Guidance for primary care discussions with patients. *Cancer*. 2025;131:e35823. [DOI] [PubMed] [PMC]
161. Imai M, Nakamura Y, Yoshino T. Transforming cancer screening: the potential of multi-cancer early detection (MCED) technologies. *Int J Clin Oncol*. 2025;30:180–93. [DOI] [PubMed] [PMC]
162. Kansal AR, Tafazzoli A, Shaul A, Chavan A, Ye W, Zou D, et al. Cost-effectiveness of a multicancer early detection test in the US. *Am J Manag Care*. 2024;30:e352–8. [DOI] [PubMed]
163. Liu MC. Transforming the landscape of early cancer detection using blood tests-Commentary on current methodologies and future prospects. *Br J Cancer*. 2021;124:1475–7. [DOI] [PubMed] [PMC]
164. Lin D, Shen L, Luo M, Zhang K, Li J, Yang Q, et al. Circulating tumor cells: biology and clinical significance. *Signal Transduct Target Ther*. 2021;6:404. [DOI] [PubMed] [PMC]
165. Walter N, Groth J, Zu Zwerger BVU. Evaluation of an innovative multi-cancer early detection test: high sensitivity and specificity in differentiating cancer, inflammatory conditions, and healthy individuals. *Front Oncol*. 2025;15:1520869. [DOI] [PubMed] [PMC]
166. Vidal J, Fernández-Rodríguez MC, Casadevall D, García-Alfonso P, Páez D, Guix M, et al.; Spanish Cooperative Group for the Treatment of Digestive Tumours (TTD). Liquid Biopsy Detects Early Molecular Response and Predicts Benefit to First-Line Chemotherapy plus Cetuximab in Metastatic Colorectal Cancer: PLATFORM-B Study. *Clin Cancer Res*. 2023;29:379–88. [DOI] [PubMed]

167. Reichert ZR, Morgan TM, Li G, Castellanos E, Snow T, Dall'Olio FG, et al. Prognostic value of plasma circulating tumor DNA fraction across four common cancer types: a real-world outcomes study. *Ann Oncol.* 2023;34:111–20. [DOI] [PubMed] [PMC]
168. Fischer LE, Stintzing S, Heinemann V, Keilholz U, Keune D, Vollbrecht C, et al. Liquid Biopsy in Colorectal Cancer: Quo Vadis? Implementation of Liquid Biopsies in Routine Clinical Patient Care in Two German Comprehensive Cancer Centers. *Front Oncol.* 2022;12:870411. [DOI] [PubMed] [PMC]
169. Jones GS, Bagga S, Sood P, Hariprasad E, Mangla B, Soni P, et al. MT46 Real World Use of Circulating Tumor DNA (CTDNA) in Colorectal Cancer (CRC): A Targeted Literature Review (TLR). *Value Health.* 2023;26:S305–6. [DOI]
170. Capsule endoscopy [Internet]. The Johns Hopkins University, The Johns Hopkins Hospital, and Johns Hopkins Health System; c2025 [cited 2025 Oct 1]. Available from: <https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/capsule-endoscopy>
171. Rex DK, Adler SN, Aisenberg J, Burch WC Jr, Carretero C, Chowers Y, et al. Accuracy of capsule colonoscopy in detecting colorectal polyps in a screening population. *Gastroenterology.* 2015;148:948–57. [DOI] [PubMed]
172. Colorectal cancer screening [Internet]. Elsevier; c2025 [cited 2025 Oct 1]. Available from: <https://www.sciencedirect.com/topics/medicine-and-dentistry/colorectal-cancer-screening>
173. Jain S, Maque J, Galoosian A, Osuna-Garcia A, May FP. Optimal strategies for colorectal cancer screening. *Curr Treat Options Oncol.* 2022;23:474–93. [DOI] [PubMed] [PMC]
174. Edwards BK, Ward E, Kohler BA, Ehemann C, Zauberg AG, Anderson RN, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer.* 2010;116:544–73. [DOI] [PubMed] [PMC]
175. National coverage determination (NCD) for colorectal cancer screening tests (210.3) [Internet]. U.S. Centers for Medicare & Medicaid Services; [cited 2025 Oct 1]. Available from: <https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=281>
176. Colorectal cancer CRC screening has come of age | DoM grand rounds | 29 March 2023 [Internet]. Google LLC; [cited 2025 Oct 1]. Available from: <https://www.youtube.com/watch?v=bBTmKWTl3Yw>
177. Imperiale TF, Ransohoff DF, Itzkowitz SH, Turnbull BA, Ross ME; Colorectal Cancer Study Group. Fecal DNA versus fecal occult blood for colorectal-cancer screening in an average-risk population. *N Engl J Med.* 2004;351:2704–14. [DOI] [PubMed]
178. Lin JS, Piper MA, Perdue LA, Rutter CM, Webber EM, O'Connor E, et al. Screening for Colorectal Cancer: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA.* 2016;315:2576–94. [DOI] [PubMed]
179. de Kanter C, Dhaliwal S, Hawks M. Colorectal Cancer Screening: Updated Guidelines From the American College of Gastroenterology. *Am Fam Physician.* 2022;105:327–9. [PubMed]
180. Lee JK, Jensen CD, Levin TR, Zauberg AG, Schottinger JE, Quinn VP, et al. Long-term Risk of Colorectal Cancer and Related Deaths After a Colonoscopy With Normal Findings. *JAMA Intern Med.* 2019;179:153–60. [DOI] [PubMed] [PMC]
181. Knudsen AB, Rutter CM, Peterse EFP, Lietz AP, Seguin CL, Meester RGS, et al. Colorectal Cancer Screening: An Updated Modeling Study for the US Preventive Services Task Force. *JAMA.* 2021;325:1998–2011. [DOI] [PubMed] [PMC]
182. Peterse EFP, Meester RGS, de Jonge L, Omidvari AH, Alarid-Escudero F, Knudsen AB, et al. Comparing the Cost-Effectiveness of Innovative Colorectal Cancer Screening Tests. *J Natl Cancer Inst.* 2021;113:154–61. [DOI] [PubMed] [PMC]

183. Doubeni CA, Fedewa SA, Levin TR, Jensen CD, Saia C, Zebrowski AM, et al. Modifiable Failures in the Colorectal Cancer Screening Process and Their Association With Risk of Death. *Gastroenterology*. 2019;156:63–74. [DOI] [PubMed] [PMC]
184. Corley DA, Jensen CD, Marks AR, Zhao WK, Lee JK, Doubeni CA, et al. Adenoma detection rate and risk of colorectal cancer and death. *N Engl J Med*. 2014;370:1298–306. [DOI] [PubMed] [PMC]
185. Kaminski MF, Regula J, Kraszewska E, Polkowski M, Wojciechowska U, Didkowska J, et al. Quality indicators for colonoscopy and the risk of interval cancer. *N Engl J Med*. 2010;362:1795–803. [DOI] [PubMed]
186. Bretthauer M, Kaminski MF, Løberg M, Zauber AG, Regula J, Kuipers EJ, et al.; Nordic-European Initiative on Colorectal Cancer (NordICC) Study Group. Population-Based Colonoscopy Screening for Colorectal Cancer: A Randomized Clinical Trial. *JAMA Intern Med*. 2016;176:894–902. [DOI] [PubMed] [PMC]
187. Kim GH, Lee YC, Kim TJ, Hong SN, Chang DK, Kim YH, et al. Trends in colorectal cancer incidence according to an increase in the number of colonoscopy cases in Korea. *World J Gastrointest Oncol*. 2024;16:51–60. [DOI] [PubMed] [PMC]
188. Galoş D, Gorzo A, Balacescu O, Sur D. Clinical Applications of Liquid Biopsy in Colorectal Cancer Screening: Current Challenges and Future Perspectives. *Cells*. 2022;11:3493. [DOI] [PubMed] [PMC]
189. Beniwal SS, Lamo P, Kaushik A, Lorenzo-Villegas DL, Liu Y, MohanaSundaram A. Current Status and Emerging Trends in Colorectal Cancer Screening and Diagnostics. *Biosensors (Basel)*. 2023;13:926. [DOI] [PubMed] [PMC]
190. Li JW, Wang LM, Ang TL. Artificial intelligence-assisted colonoscopy: a narrative review of current data and clinical applications. *Singapore Med J*. 2022;63:118–24. [DOI] [PubMed] [PMC]
191. Yin Z, Yao C, Zhang L, Qi S. Application of artificial intelligence in diagnosis and treatment of colorectal cancer: A novel Prospect. *Front Med (Lausanne)*. 2023;10:1128084. [DOI] [PubMed] [PMC]
192. Adams LB, Richmond J, Corbie-Smith G, Powell W. Medical Mistrust and Colorectal Cancer Screening Among African Americans. *J Community Health*. 2017;42:1044–61. [DOI] [PubMed] [PMC]
193. Powell W, Richmond J, Mohottige D, Yen I, Joslyn A, Corbie-Smith G. Medical Mistrust, Racism, and Delays in Preventive Health Screening Among African-American Men. *Behav Med*. 2019;45:102–17. [DOI] [PubMed] [PMC]
194. How community outreach can increase access to colorectal cancer screening in underserved populations [Internet]. American Association for Cancer Research; [cited 2024 Oct 29]. Available from: <https://www.aacr.org/blog/2021/03/09/how-community-outreach-can-increase-access-to-colorectal-cancer-screening-in-underserved-populations/>
195. Providing Free At-Home Colorectal Cancer Screening in Underserved Rural Communities [Internet]. CDM Publishing, LLC.; c2025 [cited 2024 Oct 29]. Available from: <https://www.cancerhealth.com/article/expanding-access-cancer-care-providing-free-at-home-colorectal-cancer-screening-underserved-rural-communities>
196. Texting May Help Reduce Disparities in Colorectal Cancer Screening [Internet]. National Cancer Institute; c2025 [cited 2024 Oct 29]. Available from: <https://www.cancer.gov/news-events/cancer-currents-blog/2021/colorectal-cancer-screening-text-message-reduce-disparities>
197. Goal 2: Facilitate Equitable Access to Cancer Screening [Internet]. President’s Cancer Panel; [cited 2024 Oct 29]. Available from: <https://prescancerpanel.cancer.gov/reports-meetings/cancer-screening-report-2022/closing-gaps/goal2-equitable-access>
198. Hirst Y, Skrobanski H, Kerrison RS, Kobayashi LC, Counsell N, Djedovic N, et al. Text-message Reminders in Colorectal Cancer Screening (TRICCS): a randomised controlled trial. *Br J Cancer*. 2017;116:1408–14. [DOI] [PubMed] [PMC]

199. Cancer Screening: Multicomponent Interventions — Colorectal Cancer [Internet]. Guide to Community Preventive Services; [cited 2024 Oct 29]. Available from: <https://www.thecommunityguide.org/findings/cancer-screening-multicomponent-interventions-colorectal-cancer.html>
200. Doubeni CA, Corley DA, Zhao W, Lau Y, Jensen CD, Levin TR. Association between Improved Colorectal Screening and Racial Disparities. *N Engl J Med*. 2022;386:796–8. [DOI] [PubMed] [PMC]
201. Smith RA, Mettlin CJ, Eyre H. Cancer Screening and Early Detection. In: Kufe DW, Pollock RE, Weichselbaum RR, editors. *Holland-Frei Cancer Medicine*. 6th edition. Hamilton (ON): BC Decker Inc.; 2003.
202. Smith RA, Andrews KS, Brooks D, Fedewa SA, Manassaram-Baptiste D, Saslow D, et al. Cancer screening in the United States, 2017: A review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin*. 2017;67:100–21. [DOI] [PubMed]
203. Sauer AG, Liu B, Siegel RL, Jemal A, Fedewa SA. Comparing cancer screening estimates: Behavioral Risk Factor Surveillance System and National Health Interview Survey. *Prev Med*. 2018;106:94–100. [DOI] [PubMed]
204. National Colorectal Cancer Roundtable Recognizes Leaders in Colorectal Cancer Screening Efforts with 80% by 2018 National Achievement Award [Internet]. American Cancer Society; [cited 2025 Oct 1]. Available from: <https://pressroom.cancer.org/80x18NationalAward2019>
205. Healthy People 2020 [Internet]. Office of Disease Prevention and Health Promotion; [cited 2025 Oct 1]. Available from: <https://odphp.health.gov/healthypeople/2020>
206. Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2023. *CA Cancer J Clin*. 2023;73:233–54. [DOI] [PubMed]
207. Richardson LC, King JB, Thomas CC, Richards TB, Dowling NF, Coleman King S. Adults Who Have Never Been Screened for Colorectal Cancer, Behavioral Risk Factor Surveillance System, 2012 and 2020. *Prev Chronic Dis*. 2022;19:220001. [DOI]
208. Stanley SL, King JB, Thomas CC, Richardson LC. Factors associated with never being screened for colorectal cancer. *J Community Health*. 2013;38:31–9. [DOI] [PubMed] [PMC]
209. Legato MJ, editor. *Principles of gender-specific medicine*. 3rd ed. Academic Press; 2004.
210. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. *CA Cancer J Clin*. 2024;74:12–49. [DOI] [PubMed]
211. Ladabaum U, Mannalithara A, Meester RGS, Gupta S, Schoen RE. Cost-Effectiveness and National Effects of Initiating Colorectal Cancer Screening for Average-Risk Persons at Age 45 Years Instead of 50 Years. *Gastroenterology*. 2019;157:137–48. [DOI] [PubMed] [PMC]
212. Ladabaum U. Cost-Effectiveness of Current Colorectal Cancer Screening Tests. *Gastrointest Endosc Clin N Am*. 2020;30:479–97. [DOI] [PubMed]
213. HEDIS and Performance Measurement [Internet]. National Committee for Quality Assurance; c2025 [cited 2025 Oct 1]. Available from: <https://www.ncqa.org/hedis/>
214. State of Health Care Quality Report [Internet]. National Committee for Quality Assurance; c2025 [cited 2025 Oct 1]. Available from: <https://www.ncqa.org/report-cards/health-plans/state-of-health-care-quality-report>
215. Rosenthal MB, Frank RG, Li Z, Epstein AM. Early experience with pay-for-performance: from concept to practice. *JAMA*. 2005;294:1788–93. [DOI] [PubMed]
216. Markovitz AA, Ryan AM. Pay-for-Performance: Disappointing Results or Masked Heterogeneity? *Med Care Res Rev*. 2017;74:3–78. [DOI] [PubMed] [PMC]
217. Colorectal cancer screening (COL-e) [Internet]. Horizon Blue Cross Blue Shield of New Jersey; c2025 [cited 2025 Oct 1]. Available from: <https://www.horizonblue.com/providers/resources/patient-quality-outcome-resources/hedis-resources/hedis-measurement-year-my-2024-provider-tips-optimizing-hedis-results/colorectal-cancer-screening-col-e>

218. COL-E - Colorectal Cancer Screening [Internet]. The Johns Hopkins University, The Johns Hopkins Hospital, and Johns Hopkins Health System; c2025 [cited 2025 Oct 1]. Available from: <https://www.hopkinsmedicine.org/johns-hopkins-health-plans/providers-physicians/health-care-performance-measures/hedis/colorectal-cancer-screening>
219. Calculating the Colorectal Cancer Screening Measure in the 2023 Adult and Health Home Core Sets [Internet]. Centers for Medicare & Medicaid Services; [cited 2025 Oct 1]. Available from: <https://www.medicare.gov/quality-of-care/downloads/COL-ta-resource.pdf>
220. Colorectal Cancer Screening (COL) [Internet]. National Committee for Quality Assurance; c2025 [cited 2025 Oct 1]. Available from: <https://www.ncqa.org/report-cards/health-plans/state-of-health-care-quality-report/colorectal-cancer-screening-col/>
221. Bousis D, Verras GI, Bouchagier K, Antzoulas A, Panagiotopoulos I, Katinioti A, et al. The role of deep learning in diagnosing colorectal cancer. *Prz Gastroenterol*. 2023;18:266–73. [DOI] [PubMed] [PMC]
222. Chlorogiannis DD, Verras GI, Tzelepi V, Chlorogiannis A, Apostolos A, Kotis K, et al. Tissue classification and diagnosis of colorectal cancer histopathology images using deep learning algorithms. Is the time ripe for clinical practice implementation? *Prz Gastroenterol*. 2023;18:353–67. [DOI] [PubMed] [PMC]
223. LeCun Y, Bengio Y, Hinton G. Deep learning. *Nature*. 2015;521:436–44. [DOI] [PubMed]
224. Sun L, Zhang R, Gu Y, Huang L, Jin C. Application of Artificial Intelligence in the diagnosis and treatment of colorectal cancer: a bibliometric analysis, 2004–2023. *Front Oncol*. 2024;14:1424044. [DOI] [PubMed] [PMC]
225. AI-driven medical imaging may help fight against rectal cancer [Internet]. AZoNetwork; c2000–2025 [cited 2025 Oct 1]. Available from: <https://www.news-medical.net/news/20211204/AI-driven-medical-imaging-may-help-fight-against-rectal-cancer.aspx>
226. Lo A, Le B, Colin-Escobar J, Ruiz A, Creps J, Kampalath R, et al. Disparities in Diagnostic Imaging for Initial Local Staging for Rectal Cancer. *J Am Coll Radiol*. 2024;21:154–64. [DOI] [PubMed]
227. 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;21:337–46. [DOI] [PubMed]
228. Makar J, Abdelmalak J, Con D, Hafeez B, Garg M. Use of artificial intelligence improves colonoscopy performance in adenoma detection: a systematic review and meta-analysis. *Gastrointest Endosc*. 2025;101:68–81. [DOI] [PubMed]
229. Jia L, Zheng Q, Tian J, He D, Zhao J, Zhao L, et al. Artificial intelligence with magnetic resonance imaging for prediction of pathological complete response to neoadjuvant chemoradiotherapy in rectal cancer: A systematic review and meta-analysis. *Front Oncol*. 2022;12:1026216. [DOI] [PubMed] [PMC]
230. Tayyil Purayil AL, Joseph RM, Raj A, Kooriyattil A, Jabeen N, Beevi SF, et al. Role of Artificial Intelligence in MRI-Based Rectal Cancer Staging: A Systematic Review. *Cureus*. 2024;16:e76185. [DOI] [PubMed] [PMC]
231. Park JH, Kim EY, Luchini C, Eccher A, Tizaoui K, Shin JI, et al. Artificial Intelligence for Predicting Microsatellite Instability Based on Tumor Histomorphology: A Systematic Review. *Int J Mol Sci*. 2022;23:2462. [DOI] [PubMed] [PMC]
232. Hildebrand LA, Pierce CJ, Dennis M, Paracha M, Maoz A. Artificial Intelligence for Histology-Based Detection of Microsatellite Instability and Prediction of Response to Immunotherapy in Colorectal Cancer. *Cancers (Basel)*. 2021;13:391. [DOI] [PubMed] [PMC]
233. Negro S, Pulvirenti A, Trento C, Indraccolo S, Ferrari S, Scarpa M, et al. Circulating Tumor DNA as a Real-Time Biomarker for Minimal Residual Disease and Recurrence Prediction in Stage II Colorectal Cancer: A Systematic Review and Meta-Analysis. *Int J Mol Sci*. 2025;26:2486. [DOI] [PubMed] [PMC]

234. Zeng Y, Xu S, Chapman WC Jr, Li S, Alipour Z, Abdelal H, et al. Real-time colorectal cancer diagnosis using PR-OCT with deep learning. *Theranostics*. 2020;10:2587–96. [DOI] [PubMed] [PMC]
235. Bilal M, Nimir M, Snead D, Taylor GS, Rajpoot N. Role of AI and digital pathology for colorectal immuno-oncology. *Br J Cancer*. 2023;128:3–11. [DOI] [PubMed] [PMC]
236. Yu C, Helwig EJ. The role of AI technology in prediction, diagnosis and treatment of colorectal cancer. *Artif Intell Rev*. 2022;55:323–43. [DOI] [PubMed] [PMC]
237. Stanley EAM, Souza R, Winder AJ, Gulve V, Amador K, Wilms M, et al. Towards objective and systematic evaluation of bias in artificial intelligence for medical imaging. *J Am Med Inform Assoc*. 2024;31:2613–21. [DOI] [PubMed] [PMC]
238. Gao W, Huang Y, Cui D, Yu Z, Liu W, Liang X, et al. Establishing rigorous and cost-effective clinical trials for artificial intelligence models. *arXiv 2407.08554* [Preprint]. 2024 [cited 2025 Oct 1]. Available from: <https://arxiv.org/abs/2407.08554>
239. Wang Y, He X, Nie H, Zhou J, Cao P, Ou C. Application of artificial intelligence to the diagnosis and therapy of colorectal cancer. *Am J Cancer Res*. 2020;10:3575–98. [PubMed] [PMC]
240. Taylor SA, Mallett S, Beare S, Bhatnagar G, Blunt D, Boavida P, et al. Diagnostic accuracy of whole-body MRI versus standard imaging pathways for metastatic disease in newly diagnosed colorectal cancer: the prospective Streamline C trial. *Lancet Gastroenterol Hepatol*. 2019;4:529–37. [DOI] [PubMed] [PMC]
241. Maas M, Rutten IJG, Nelemans PJ, Lambregts DMJ, Cappendijk VC, Beets GL, et al. What is the most accurate whole-body imaging modality for assessment of local and distant recurrent disease in colorectal cancer? A meta-analysis: imaging for recurrent colorectal cancer. *Eur J Nucl Med Mol Imaging*. 2011;38:1560–71. [DOI] [PubMed] [PMC]
242. García-Figueiras R, Baleato-González S, Padhani AR, Marhuenda A, Luna A, Alcalá L, et al. Advanced imaging of colorectal cancer: From anatomy to molecular imaging. *Insights Imaging*. 2016;7:285–309. [DOI] [PubMed] [PMC]
243. García-Figueiras R, Baleato-González S, Padhani AR, Luna-Alcalá A, Marhuenda A, Vilanova JC, et al. Advanced Imaging Techniques in Evaluation of Colorectal Cancer. *Radiographics*. 2018;38:740–65. [DOI] [PubMed]
244. Liu W, Zeng A, Tang H, Qiang J. Radiologic Imaging Modalities for Colorectal Cancer. *Dig Dis Sci*. 2022;67:2792–804. [DOI] [PubMed]
245. Serinsöz S, Aktürk R. Comparison of Imaging Modalities in the Diagnosis and Tumor Staging of Colorectal Adenocarcinoma. *Curr Med Imaging*. 2023;19:612–22. [DOI] [PubMed]
246. Dobos N, Rubesin SE. Radiologic imaging modalities in the diagnosis and management of colorectal cancer. *Hematol Oncol Clin North Am*. 2002;16:875–95. [DOI] [PubMed]
247. Kekelidze M, D’Errico L, Pansini M, Tyndall A, Hohmann J. Colorectal cancer: current imaging methods and future perspectives for the diagnosis, staging and therapeutic response evaluation. *World J Gastroenterol*. 2013;19:8502–14. [DOI] [PubMed] [PMC]
248. Kudo SE, Misawa M, Mori Y, Hotta K, Ohtsuka K, Ikematsu H, et al. Artificial Intelligence-assisted System Improves Endoscopic Identification of Colorectal Neoplasms. *Clin Gastroenterol Hepatol*. 2020;18:1874–81. [DOI] [PubMed]
249. Lui TKL, Leung WK. Is artificial intelligence the final answer to missed polyps in colonoscopy? *World J Gastroenterol*. 2020;26:5248–55. [DOI] [PubMed] [PMC]
250. Sinagra E, Badalamenti M, Maida M, Spadaccini M, Maselli R, Rossi F, et al. Use of artificial intelligence in improving adenoma detection rate during colonoscopy: Might both endoscopists and pathologists be further helped. *World J Gastroenterol*. 2020;26:5911–8. [DOI] [PubMed] [PMC]
251. Zhou D, Tian F, Tian X, Sun L, Huang X, Zhao F, et al. Diagnostic evaluation of a deep learning model for optical diagnosis of colorectal cancer. *Nat Commun*. 2020;11:2961. [DOI] [PubMed] [PMC]

252. Barua I, Wieszczy P, Kudo SE, Misawa M, Holme Ø, Gulati S, et al. Real-Time Artificial Intelligence–Based Optical Diagnosis of Neoplastic Polyps during Colonoscopy. *NEJM Evid.* 2022;1: EVIDoA2200003. [DOI] [PubMed]
253. Hsiao YJ, Wen YC, Lai W, Lin Y, Yang Y, Chien Y, et al. Application of artificial intelligence-driven endoscopic screening and diagnosis of gastric cancer. *World J Gastroenterol.* 2021;27:2979–93. [DOI] [PubMed] [PMC]
254. Messmann H, Bisschops R, Antonelli G, Libânio D, Sinonquel P, Abdelrahim M, et al. Expected value of artificial intelligence in gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. *Endoscopy.* 2022;54:1211–31. [DOI] [PubMed]
255. Wallace MB, Sharma P, Bhandari P, East J, Antonelli G, Lorenzetti R, et al. Impact of Artificial Intelligence on Miss Rate of Colorectal Neoplasia. *Gastroenterology.* 2022;163:295–304. [DOI] [PubMed]
256. Koh FH, Ladlad J, SKH Endoscopy Centre, Teo E, Lin C, Foo F. Real-time artificial intelligence (AI)-aided endoscopy improves adenoma detection rates even in experienced endoscopists: a cohort study in Singapore. *Surg Endosc.* 2023;37:165–71. [DOI] [PubMed] [PMC]
257. Spadaccini M, Massimi D, Mori Y, Alfarone L, Fugazza A, Maselli R, et al. Artificial Intelligence-Aided Endoscopy and Colorectal Cancer Screening. *Diagnostics (Basel).* 2023;13:1102. [DOI] [PubMed] [PMC]
258. Spadaccini M, Troya J, Khalaf K, Facciorusso A, Maselli R, Hann A, et al. Artificial Intelligence-assisted colonoscopy and colorectal cancer screening: Where are we going? *Dig Liver Dis.* 2024;56:1148–55. [DOI] [PubMed]
259. Ferrari R, Mancini-Terracciano C, Voena C, Rengo M, Zerunian M, Ciardiello A, et al. MR-based artificial intelligence model to assess response to therapy in locally advanced rectal cancer. *Eur J Radiol.* 2019;118:1–9. [DOI] [PubMed]
260. Wang P, Deng C, Wu B. Magnetic resonance imaging-based artificial intelligence model in rectal cancer. *World J Gastroenterol.* 2021;27:2122–30. [DOI] [PubMed] [PMC]
261. Villamanca JJ, Hermogino LJ, Ong KD, Pagua B, Abanilla L, Lim A, et al. Predicting the Likelihood of Colorectal Cancer with Artificial Intelligence Tools Using Fourier Transform Infrared Signals Obtained from Tumor Samples. *Appl Spectrosc.* 2022;76:1412–28. [DOI] [PubMed]
262. Gerwert K, Schörner S, Großerueschkamp F, Kraeft AL, Schuhmacher D, Sternemann C, et al. Fast and label-free automated detection of microsatellite status in early colon cancer using artificial intelligence integrated infrared imaging. *Eur J Cancer.* 2023;182:122–31. [DOI] [PubMed]
263. Waljee AK, Weinheimer-Haus EM, Abubakar A, Ngugi AK, Siwo GH, Kwakye G, et al. Artificial intelligence and machine learning for early detection and diagnosis of colorectal cancer in sub-Saharan Africa. *Gut.* 2022;71:1259–65. [DOI] [PubMed] [PMC]
264. Ziegelmayer S, Reischl S, Havrda H, Gawlitza J, Graf M, Lenhart N, et al. Development and Validation of a Deep Learning Algorithm to Differentiate Colon Carcinoma From Acute Diverticulitis in Computed Tomography Images. *JAMA Netw Open.* 2023;6:e2253370. [DOI] [PubMed] [PMC]
265. Peng Y, Deng H. Medical image fusion based on machine learning for health diagnosis and monitoring of colorectal cancer. *BMC Med Imaging.* 2024;24:24. [DOI] [PubMed] [PMC]
266. 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] [PubMed] [PMC]
267. Wang KS, Yu G, Xu C, Meng XH, Zhou J, Zheng C, et al. Accurate diagnosis of colorectal cancer based on histopathology images using artificial intelligence. *BMC Med.* 2021;19:76. [DOI] [PubMed] [PMC]
268. Yu G, Sun K, Xu C, Shi X, Wu C, Xie T, et al. Accurate recognition of colorectal cancer with semi-supervised deep learning on pathological images. *Nat Commun.* 2021;12:6311. [DOI] [PubMed] [PMC]

269. Ho C, Zhao Z, Chen XF, Sauer J, Saraf SA, Jialdasani R, et al. A promising deep learning-assistive algorithm for histopathological screening of colorectal cancer. *Sci Rep.* 2022;12:2222. [DOI] [PubMed] [PMC]
270. Ju Y, Zheng L, Zhao P, Xin F, Wang F, Gao Y, et al. Artificial intelligence recognition of pathological T stage and tumor invasion in rectal cancer based on large panoramic pathological sections. *Intell Med.* 2022;2:141–51. [DOI]
271. Neto PC, Montezuma D, Oliveira SP, Oliveira D, Fraga J, Monteiro A, et al. An interpretable machine learning system for colorectal cancer diagnosis from pathology slides. *NPJ Precis Oncol.* 2024;8:56. [DOI] [PubMed] [PMC]
272. Saillard C, Dubois R, Tchita O, Loiseau N, Garcia T, Adriansen A, et al. Validation of MSIntuit as an AI-based pre-screening tool for MSI detection from colorectal cancer histology slides. *Nat Commun.* 2023;14:6695. [DOI] [PubMed] [PMC]
273. Bilal M, Tsang YW, Ali M, Graham S, Hero E, Wahab N, et al. Development and validation of artificial intelligence-based prescreening of large-bowel biopsies taken in the UK and Portugal: a retrospective cohort study. *Lancet Digit Health.* 2023;5:e786–97. [DOI] [PubMed]
274. Griem J, Eich M, Schallenberg S, Pryalukhin A, Bychkov A, Fukuoka J, et al. Artificial Intelligence-Based Tool for Tumor Detection and Quantitative Tissue Analysis in Colorectal Specimens. *Mod Pathol.* 2023;36:100327. [DOI] [PubMed]
275. Prezja F, Äyrämö S, Pölönen I, Ojala T, Lahtinen S, Ruusuviuori P, et al. Improved accuracy in colorectal cancer tissue decomposition through refinement of established deep learning solutions. *Sci Rep.* 2023;13:15879. [DOI] [PubMed] [PMC]
276. Kather JN, Krisam J, Charoentong P, Luedde T, Herpel E, Weis CA, et al. Predicting survival from colorectal cancer histology slides using deep learning: A retrospective multicenter study. *PLoS Med.* 2019;16:e1002730. [DOI] [PubMed] [PMC]
277. Pai RK, Banerjee I, Shivji S, Jain S, Hartman D, Buchanan DD, et al. Quantitative Pathologic Analysis of Digitized Images of Colorectal Carcinoma Improves Prediction of Recurrence-Free Survival. *Gastroenterology.* 2022;163:1531–46. [DOI] [PubMed] [PMC]
278. Pham TD, Ravi V, Fan C, Luo B, Sun X. Classification of IHC Images of NATs With ResNet-FRP-LSTM for Predicting Survival Rates of Rectal Cancer Patients. *IEEE J Transl Eng Health Med.* 2022;11:87–95. [DOI] [PubMed] [PMC]
279. Pham TD, Ravi V, Luo B, Fan C, Sun X. Artificial intelligence fusion for predicting survival of rectal cancer patients using immunohistochemical expression of Ras homolog family member B in biopsy. *Explor Target Antitumor Ther.* 2023;4:1–16. [DOI] [PubMed] [PMC]
280. 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] [PubMed]
281. L'Imperio V, Wulczyn E, Plass M, Müller H, Tamini N, Gianotti L, et al. Pathologist Validation of a Machine Learning-Derived Feature for Colon Cancer Risk Stratification. *JAMA Netw Open.* 2023;6:e2254891. [DOI] [PubMed] [PMC]
282. Yang T, Liang N, Li J, Yang Y, Li Y, Huang Q, et al. Intelligent Imaging Technology in Diagnosis of Colorectal Cancer Using Deep Learning. *IEEE Access.* 2019;7:178839–47. [DOI]
283. Mao Y, Chen B, Wang H, Zhang Y, Yi X, Liao W, et al. Diagnostic performance of magnetic resonance imaging for colorectal liver metastasis: A systematic review and meta-analysis. *Sci Rep.* 2020;10:1969. [DOI] [PubMed] [PMC]
284. Parsa N, Rex DK, Byrne MF. Colorectal polyp characterization with standard endoscopy: Will Artificial Intelligence succeed where human eyes failed? *Best Pract Res Clin Gastroenterol.* 2021;52–53:101736. [DOI] [PubMed]
285. Wang X, Huang J, Ji X, Zhu Z. Application of artificial intelligence for detection and classification of colon polyps. *Nan Fang Yi Ke Da Xue Xue Bao.* 2021;41:310–3. Chinese. [PubMed] [PMC]

286. Yin P, Zhou Z, Liu J, Jiang N, Zhang J, Liu S, et al. A generalized AI method for pathology cancer diagnosis and prognosis prediction based on transfer learning and hierarchical split. *Phys Med Biol*. 2023;68:175039. [DOI] [PubMed]
287. Pham TD. Prediction of Five-Year Survival Rate for Rectal Cancer Using Markov Models of Convolutional Features of RhoB Expression on Tissue Microarray. *IEEE/ACM Trans Comput Biol Bioinform*. 2023;20:3195–204. [DOI] [PubMed]
288. Tsai PC, Lee TH, Kuo KC, Su F, Lee TM, Marostica E, et al. Histopathology images predict multi-omics aberrations and prognoses in colorectal cancer patients. *Nat Commun*. 2023;14:2102. [DOI] [PubMed] [PMC]
289. Ladabaum U, Shepard J, Weng Y, Desai M, Singer SJ, Mannalithara A. Computer-aided Detection of Polyps Does Not Improve Colonoscopist Performance in a Pragmatic Implementation Trial. *Gastroenterology*. 2023;164:481–3. [DOI] [PubMed] [PMC]
290. Huang Y, Liu Z, He L, Chen X, Pan D, Ma Z, et al. Radiomics Signature: A Potential Biomarker for the Prediction of Disease-Free Survival in Early-Stage (I or II) Non-Small Cell Lung Cancer. *Radiology*. 2016;281:947–57. [PMID: 27347764 DOI: 10.1148/radiol.2016152234.
291. Cheng CH, Shi SS. Artificial intelligence in cancer: applications, challenges, and future perspectives. *Mol Cancer*. 2025;24:274. [DOI] [PubMed] [PMC]
292. Mulita F, Verras GI, Anagnostopoulos CN, Kotis K. A Smarter Health through the Internet of Surgical Things. *Sensors (Basel)*. 2022;22:4577. [DOI] [PubMed] [PMC]
293. Panda S, Kumar R, Panda B, Nanda L, Pradhan A, Jena C. Medical Applications of the Internet of Things (IoT): A Literature Review. *Proceedings of the 1st International Conference on Innovative Sustainable Technologies for Energy, Mechatronics, and Smart Systems (ISTEMS); Dehradun, India. IEEE; 2024. pp. 1–5. [DOI]*
294. Pandurangan P, Rakshi AD, Arun Sundar MS, Samrat AV, Meenambiga SS, Vedanarayanan V, et al. Integrating cutting-edge technologies: AI, IoT, blockchain and nanotechnology for enhanced diagnosis and treatment of colorectal cancer – A review. *J Drug Deliv Sci Technol*. 2024;91:105197. [DOI]
295. Alanazi A. The Potential, Applications, and Challenges of Internet of Things (IoT) Technologies From the Perspectives of Clinicians. *Cureus*. 2025;17:e85847. [DOI] [PubMed] [PMC]
296. Thottempudi P, Konduru RM, Valiveti HB, Kuraparthi S, Kumar V. Digital health resilience: IoT solutions in pandemic response and future healthcare scenarios. *Discov Sustain*. 2025;6:144. [DOI]
297. Save money (\$\$\$) on your colonoscopy! | Insider insurance SECRETS [Internet]. Google LLC; [cited 2025 Oct 1]. Available from: <https://www.youtube.com/watch?v=3rzDK6yykF0>
298. Aleissa MA, Luca M, Singh JP, Chitragari G, Drelichman ER, Mittal VK, et al. Current status of artificial intelligence colonoscopy on improving adenoma detection rate based on systematic review of multiple metanalysis. *Artif Intell Gastroenterol*. 2025;6:106149. [DOI]
299. Soleymanjahi S, Rajashekar N, Chung S, Grimshaw AA, Tvedt MJK, Foroutan F, et al. Provider Attitudes and Perceptions on Using Artificial Intelligence in Colonoscopy: A Systematic Review and Meta-Analysis. *Gastro Hep Adv*. 2025;4:100746. [DOI] [PubMed] [PMC]
300. Lee MCM, Parker CH, Liu LWC, Farahvash A, Jeyalingam T. Impact of study design on adenoma detection in the evaluation of artificial intelligence-aided colonoscopy: a systematic review and meta-analysis. *Gastrointest Endosc*. 2024;99:676–87. [DOI] [PubMed]
301. Park JB, Bae JH. Effectiveness of a novel artificial intelligence-assisted colonoscopy system for adenoma detection: a prospective, propensity score-matched, non-randomized controlled study in Korea. *Clin Endosc*. 2025;58:112–20. [DOI] [PubMed] [PMC]
302. 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] [PubMed] [PMC]

303. Imaging informatics [Internet]. Academic; c2000–2025 [cited 2025 Oct 1]. Available from: https://en.wikipedia.org/wiki/Imaging_informatics