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Review Article

Current Status and Future Perspectives on Early Detection and Diagnosis of Colorectal Cancer in China

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Abstract

Colorectal cancer (CRC) is the second most commonly diagnosed cancer in China. Early detection and diagnosis of CRC are essential for improving survival rates. However, socioeconomic factors such as regional disparities, economic conditions, and varying levels of awareness impact the uptake of screening programs. Recently, rapid advancements in non-invasive tests, including high-quality fecal immunochemical tests and the emergence of stool and blood biomarkers for CRC, have facilitated improvements in early detection and diagnosis. Additionally, image-enhanced endoscopy, a group of advanced imaging technologies, has been developed to assist in the early identification of colorectal lesions, including narrow band imaging and linked-color imaging. The emergence of artificial intelligence also offers promising opportunities to improve early diagnosis and treatment of CRC. This review mainly introduces screening technologies and the current status of CRC screening in China, provides an overview of CRC early detection and diagnosis, and discusses the limitations and future prospects.

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide and the second leading cause of cancer death, significantly impacting public health.[1] According to data from the National Cancer Center of China in 2024, CRC ranks second in incidence, with 517,100 new cases and 240,000 cancer-related deaths, representing a major public health issue that needs to be addressed.[1] Although the survival rate of CRC in China is gradually increasing, it remains lower than that in the United States, Europe, and other Asian countries (such as Japan and South Korea), primarily due to the low rate of early diagnosis.[2–5]

Most CRCs arise from polyps and develop through two major precursor lesion pathways over an estimated period of 10–15 years: the traditional adenoma-carcinoma pathway and the serrated neoplasia pathway.[6] The five-year survival rate for CRC can exceed 95% in stage I, but drops to only 14% in stage IV. However, CRC is generally asymptomatic until it progresses to an advanced stage.[6] Moreover, the incidence of early-onset CRC, defined as cases diagnosed before age 50, has risen alarmingly in recent years, challenging the adequacy of current screening and treatment strategies.[7] This underscores the critical importance of early diagnosis and intervention. Early diagnosis and treatment not only facilitate the use of less invasive therapeutic modalities, reducing potential side effects, but also significantly improve patient survival rates and maintain overall quality of life.

CRC screening efforts focus on the removal of precancerous polyps via colonoscopy and the detection of early-stage CRC, both of which have been shown to effectively reduce CRC incidence and mortality, making it one of the most preventable and treatable cancers.[8] Due to the large population base of China, implementing simple and efficient screening methods is essential to reduce the economic burden. This review introduces the current status of CRC screening, screening techniques, and artificial intelligence (AI)-assisted screening in China, and discusses the limitations and future prospects.

Current status of CRC screening in China

China does not have an organized national screening program, but individuals can access CRC screening through various organized programs, opportunistic screening, and physical examinations. There are two central government-funded cancer screening programs involving CRC: Cancer Screening Program in Rural China, initiated in 2005 for rural populations, and Cancer Screening Program in Urban China, launched in 2012 for urban populations. Additionally, there are four provincial and municipal programs—one each in Tianjin (2012), Shanghai (2013), Guangzhou (2015), and Zhejiang (2020)—covering all residents of the respective provinces/municipalities (Table 1).[9] These programs

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Table 1. Colorectal cancer screening programs in China

Screening program	Starting year	Age range (years)	Primary screening tests	No. target population (x100,000)	No. invited (x100,000)	Coverage rate (%)	No. screening participants (x100,000)	Screening participation rate (%)
National pilot								
The CanSPRC	2005	40–74	Questionnaire assessment + gFOBT	2,482.7	42.0	1.7	11.1	26.4
The CanSPUC	2012	45–74	Questionnaire assessment + FIT	3,362.3	22.7	0.7	4.6	20.2
Provincial or municipal level								
Tianjin	2012	40–74	Questionnaire assessment + FIT	61.6	20.5	33.3	3.6	17.5
Shanghai	2013	50–74	Questionnaire assessment + FIT	73.9	24.6	33.3	5.9	23.9
Guangzhou	2015	50–74	Questionnaire assessment + FIT	55.9	18.6	33.3	1.2	6.4
Zhejiang	2020	50–74	Questionnaire assessment + FIT	192.2	38.4	20.0	22.3	58.1

CanSPRC, Cancer Screening Program in Rural China; CanSPUC, Cancer Screening Program in Urban China; FIT, fecal immunochemical test; gFOBT, guaiac fecal occult blood test.

offer screening using both questionnaire-based risk assessments and fecal tests, with colonoscopy serving as the gold standard for diagnosis for participants with positive screening results. The coverage rate of organized screening, opportunistic screening, and physical examinations for the Chinese population aged 40–74 is relatively low.[9] Economic constraints present a major challenge to implementing a nationally organized CRC screening program, similar to those in developed countries. Many other provinces are also rolling out CRC screening and working toward extending full implementation. Opportunistic screening could become a vital component of CRC detection, and physical examinations for CRC have been in place for some time. Further efforts are needed to improve population access to CRC screening in China.

Screening techniques for CRC in China

CRC screening techniques can be broadly categorized into non-invasive and invasive procedures. Non-invasive tests include stool-based tests (fecal immunochemical test [FIT] and multitarget stool DNA [mts-DNA] test) and blood-based tests. Invasive tests primarily include colonoscopy. Non-invasive screenings are appreciated for their simplicity and non-intrusiveness; however, their limited sensitivity and specificity can lead to misdiagnoses or missed conditions. In contrast, invasive tests offer direct visual inspection of the intestinal tract, facilitating the biopsy of potential lesions. However, colonoscopy is a demanding and costly procedure, requiring advanced medical facilities and skilled personnel, which can result in reduced patient adherence. A practical and effective approach for China would involve using a more cost-effective method to stratify the target population's risk, followed by colonoscopies for high-risk individuals.[10–12] The main screening methods currently in use are shown in Figure 1 and Table 2.[13–17] A timeline diagram of major events in the development of CRC screening techniques is shown in Figure 2.

Fecal immunochemical test

Fecal occult blood tests can be divided into chemical (guaiac-based) and immunochemical (FIT) methods. The sensitivity of the guaiac-based method is poor and it is easily influenced by factors such as diet, so it is no longer widely used in CRC screening. FIT represents an advancement over the guaiac method. It utilizes antibodies specific to human hemoglobin rather than a non-specific peroxidase reaction, and it is not affected by diet.[18] Growing evidence has shown that FIT-based screening programs reduce CRC incidence and mortality. A prospective cohort study indicated that quantitative FIT screening significantly reduced the incidence of advanced CRC by 34% and CRC mortality by 40%.[13] When employing quantitative FIT, the sensitivity and specificity can be adjusted by varying the cut-off value. In a meta-analysis, the FIT sensitivity for CRC was 75% at 20 μg/g and 91% at 10 μg/g, while the specificity was 95% at 20 μg/g and 90% at 10 μg/g. FIT sensitivity and specificity for advanced adenomas (AAs) were 40% and 90% at 10 μg/g, and 25% and 95% at 20 μg/g, respectively.[19]

The positive test threshold can be adjusted to align colonoscopy demand with available capacity. Therefore, China should place more emphasis on the crucial role of quantitative FIT in CRC screening. Additionally, hypersensitive quantitative FIT is a new generation of fecal occult blood detection methods capable of quantifying extremely low hemoglobin concentrations, achieving

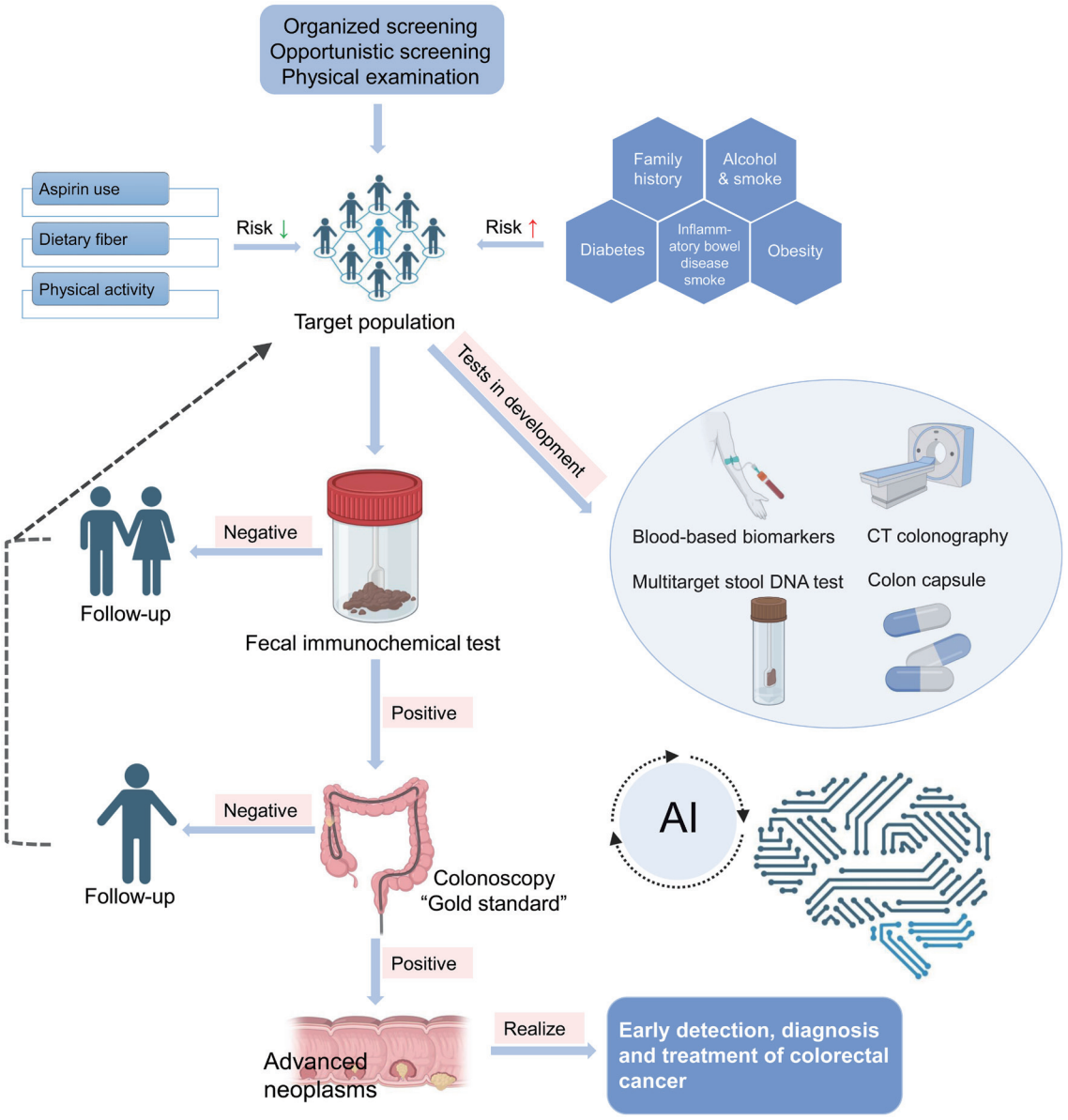

Fig. 1. Current status of colorectal screening methods. AI, artificial intelligence; CT, computed tomography.

higher sensitivity and specificity in CRC screening. The diagnostic efficacy for AAs is significantly higher than that of ordinary FIT, with an optimal cut-off value sensitivity of 66.0% and specificity of 85.3%, which has been well-verified in the Chinese population.[20,21] Previous studies have also confirmed that lowering the cut-off value for quantitative FITs could not only improve AA and CRC detection rates but also achieve comparable levels of sensitivity and specificity to mts-DNA tests.[22,23]

Factors such as older age, smoking, and the use of aspirin/non-steroidal anti-inflammatory drugs are associated with lower specificity for FIT. Additionally, conditions linked to gastrointestinal bleeding, such as fissures, hemorrhoids, and inflammatory bowel disease, are strongly associated with false positive results.[24,25] The benefits of screening are highly dependent on screening compliance. Unfortunately, not all patients with a positive FIT result will undergo a colonoscopy. A community-based CRC screening program initiated by the Shanghai Municipal Government in 2012 revealed that only 39.8% of participants with a positive initial screening result completed a colonoscopy.[26] However, a study comparing colonoscopy, FIT, and a risk-adapted approach in a screening population.[27] showed that FIT had a surprisingly high uptake rate (99.3%), although the compliance with diagnostic colonoscopy among FIT-positive individuals was not optimal. Moreover, compared to offering colonoscopy alone, combining FIT with colonoscopy increased participation in CRC screening.[28] Therefore, combining the high diagnostic yield of colonoscopy with the high participation rate of FIT would be optimal for CRC screening in China. At the grassroots level, efforts need to be made to raise public awareness about the importance of colonoscopy after a positive FIT result.

Table 2. Summary of colorectal cancer screening techniques

Test	Efficacy	Advantage	Limitation	Recommended frequency	Reference
FIT	Sensitivity for CRC 75% and specificity 95% at 20 μg/g	Convenient and non-invasive screening for CRC; positive threshold can be adjusted	Limited sensitivity for detecting precancerous lesions	Every year	13
Multitarget stool DNA test	sensitivity for CRC 93.9% and specificity for advanced neoplasia 90.6%	Non-invasive with high sensitivity and specificity	High cost and lower specificity than FIT	Every three years	14
Blood biomarkers	83% sensitivity for CRC and 90% specificity for advanced neoplasia	Non-invasive with good acceptance and adherence; great potential application value	High cost and limited sample sizes	Screening interval not established	15
Colonoscopy	Gold standard	Direct visualization of the colon for accurate detection of abnormalities	Invasive; bowel perforation; severe complications	Every five to ten years	–
Flexible sigmoidoscopy	–	Less invasive and visualization of the rectum and sigmoid colon	Invasive and bowel perforation	Every five years	–
Colon capsule	Sensitivity for polyps ≥ 6 mm 88% and specificity 82%	No radiation exposure, sedation, or gas insufflation	Bowel perforation and high cost; incapability to biopsy and a high rate of miss rate	Every five years	16
CT colonography	Sensitivity for adenomas ≥ 6 mm 73–98% and specificity 89–91%	Less invasive than colonoscopy and not require sedation	Low detection rate for sessile and flat polyps; bowel preparation and radiation exposure	Every five years	17

CRC, colorectal cancer; CT, computed tomography; FIT, fecal immunochemical test.

mts-DNA test

The detection of methylated tumor DNA in stool, in combination with the detection of occult blood, represents a promising strategy for enhancing the sensitivity of FIT. In a prospective study of 9,989 individuals undergoing screening colonoscopy, mts-DNA test showed 92% sensitivity for CRC and 42% sensitivity for AAs.[14] The National Medical Products Administration in China has approved several novel mts-DNA test kits for CRC detection.[22,29,30] In a study by Jin *et al*.,[22] which enrolled 2,842 participants, the sensitivity and specificity for advanced neoplasms using the mts-DNA test were 42.2% and 93.3%, respectively, which was not inferior to FIT performance. The mts-DNA test demonstrated better performance in detecting CRC but was less effective in predicting adenomas. One of the initial obstacles to implementing this test is its high cost. A cost-effectiveness analysis comparing the mts-DNA test concluded that both FIT and colonoscopy were more cost-effective. Another drawback is the complex stool collection process. In the prospective trial, nearly 6% of participants were unable to collect or submit a sufficient stool sample for the mts-DNA test, compared to just 0.6% for FIT.[31] Recently, a next-generation

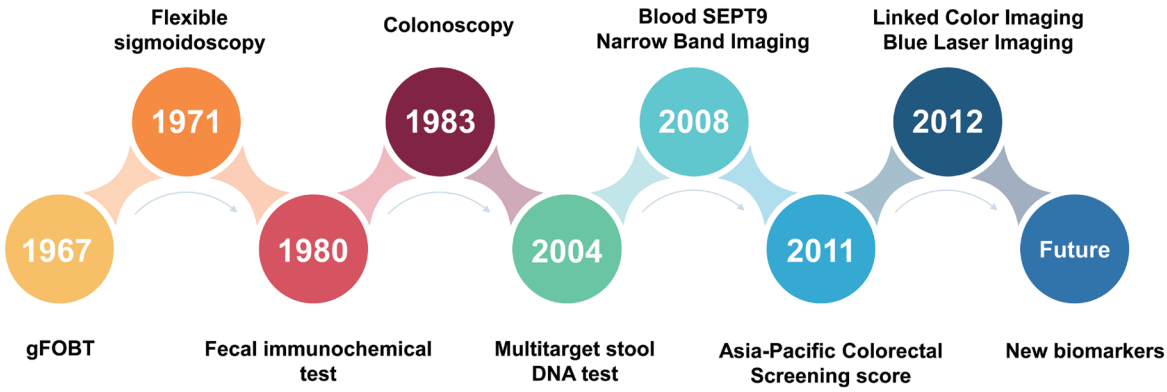

Fig. 2. The timeline diagram of major events in the development of colorectal cancer (CRC) screening techniques. gFOBT, guaiac fecal occult blood test; SEPT9, septin 9.

mts-DNA test has shown greater sensitivity for CRC and advanced precancerous lesions compared to FIT, although it exhibited lower specificity.[32] The mts-DNA test could function as a "prescreening" tool to detect individuals at risk for CRC, facilitating additional evaluations, such as endoscopy, for this population, which may help reduce screening expenses.[24]

Colonoscopy

Colonoscopy is considered the gold standard for the detection and treatment of colorectal neoplastic lesions and serves as a fundamental examination for CRC screening. The diagnosis and removal of precancerous lesions during colonoscopy are crucial for reducing CRC incidence and mortality. Multiple case-control and prospective cohort studies have shown that CRC mortality is 29–68% lower in individuals who undergo screening colonoscopy compared to those who do not, providing protection against both proximal and distal CRC.[33–35] Disadvantages of colonoscopy include its invasive nature, the potential for complications (such as perforation and bleeding), the need for bowel preparation, and the associated resource burden and costs. Due to financial and psychosocial barriers, randomized trials have indicated that compliance with colonoscopy is lower than that for FIT, with only 42% adherence reported in one screening colonoscopy trial.[36] In most screening programs in China, colonoscopy is typically used as a follow-up procedure after a positive result from an initial screening test.

A recent meta-analysis found miss rates of 26% for adenomas, 9% for advanced adenomas, and 27% for serrated polyps.[37] To achieve high-quality colonoscopy assessments, advanced imaging technologies such as image-enhanced endoscopy (IEE) have been developed to assist in the identification of colorectal lesions. IEE can be either traditional dye-based chromoendoscopy or electronic. Dye-based chromoendoscopy improves the visibility of the mucosal surface and assists in lesion removal or biopsies; however, it is operator-dependent, time-intensive, and requires technical expertise.[38] Electronic IEEs, such as narrow band imaging (NBI), blue light imaging (BLI), and linked-color imaging (LCI), offer high-contrast images by utilizing optical filtering or software processing, significantly contributing to the enhancement of diagnostic techniques.[39]

NBI and BLI are commonly used in the optical assessment of neoplastic and non-neoplastic colorectal polyps. Furthermore, NBI combined with magnified observation can help assess the invasive depth of colorectal tumors using the Japan NBI Expert Team classification.[40] However, the detection performance of NBI and BLI during colonoscopy remains uncertain, and their utility in detecting serrated lesions is questionable. Generally, inadequate bowel preparation is observed in 20–25% of colonoscopy procedures. Residual fluid in the colon can hinder polyp detection by NBI and BLI, as it alters the color of this fluid to dark red, which affects visibility. LCI is a newly developed image-enhanced endoscopy modality that improves subtle color differences in the red region while visualizing the mucosa. LCI maintains the color of residual fluid as yellow, similar to white-light imaging (WLI), thereby enhancing visibility and lesion detection.[41] The latest meta-analysis, which included 124 trials, revealed that LCI improved the adenoma detection rate (ADR) by 1.2-fold compared with high-definition WLI.[42] Moreover, Suzuki *et al*.[43] performed a multicenter randomized controlled trial that showed detection rates of serrated polyps and sessile serrated lesions increased by 1.6- to 1.8-fold when LCI was utilized compared with WLI. Thus, LCI could be proposed as the primary modality for general clinical colonoscopy during the scope withdrawal phase to detect more CRC precursors.[44] Nevertheless, LCI has been shown to shorten the recommended surveillance intervals, resulting in more frequent colonoscopies.[43] More extensive studies are needed to investigate its cost-effectiveness.

Blood-based tests

In recent years, blood-based biomarkers have gained attention as potential diagnostic tools for CRC.[45] Various types of CRC biomarkers have been investigated, including circulating tumor DNA, microRNAs, DNA methylation markers, and protein-based markers. Recently, Chung *et al*.[15] evaluated a cell-free DNA blood-based test in an average-risk screening population. This study, which enrolled 7,861 individuals, showed promising results, with 83% sensitivity for CRC, 90% specificity for advanced neoplasia, and 13% sensitivity for advanced precancerous lesions.[15] However, these tests remain expensive and are not widely adopted as part of an organized screening program. Most studies have been retrospective and have limited sample sizes, with few evaluating these tests in a screening population. As a non-invasive examination, blood-based tests are more acceptable to patients and potentially reduce labor and material costs. The development of new proteomic or metabolomic techniques could allow for the identification of profiles associated with CRC. While this technology holds great promise and potential application value, larger studies are needed. Ongoing rigorous research may lead to the development of new advanced non-invasive tests that will improve CRC early detection and diagnosis.

Other CRC screening tests in development

An alternative option for direct visualization of the distal colon is flexible sigmoidoscopy, with a referral for colonoscopy in cases where polyps are detected. Additionally, colon capsule endoscopy utilizes a wireless, disposable pill-sized camera capsule that is swallowed and activated in the terminal ileum.[46] The capsule captures images of the colonic mucosa without the need for radiation exposure, sedation, or gas insufflation. However, obstacles to this test include the need for colonic preparation, its incapability to biopsy lesions, and a relatively high miss rate. Furthermore, computed tomography colonography enables the detection and localization of polyps and cancers in the colon through 3D or 4D reconstruction. It offers the advantages of being less invasive, eliminating the need for procedural sedation, and having a low complication rate. However, it also requires bowel preparation, involves radiation exposure, and may result in extracolonic findings that necessitate further testing and potential overtreatment.[47]

AI

With the explosion of clinical and omics data, along with pioneering research in machine learning, AI applications—including computer-aided detection (CADe) and computer-aided characterization (CADx)—have shown considerable potential in the clinical field of CRC. These technologies offer novel methods to identify high-risk patients, tailor precise and personalized treatment plans, and forecast prognoses.

CADe can detect previously unrecognized lesions and acts as "a second set of eyes", continuously monitoring the process without being influenced by the distraction and fatigue of endoscopists. A meta-analysis of 50 randomized trials has shown that CADe

Table 3. Quality indicators for colonoscopy

Quality indices	Standard
Cecal intubation rate	Minimum standard ≥ 90% Target standard ≥ 95%
Rate of adequate bowel preparation	Minimum standard ≥ 90% Target standard ≥ 95%
Withdrawal time	Minimum standard ≥ 6 m
Adenoma detection rate	Minimum standard ≥ 25%

systems demonstrate superior detection performance compared to standard colonoscopy, regardless of the location, size, and morphology of adenomas.[48] Furthermore, the use of CADe has led to a notable rise in ADR by 44%, outperforming other advanced endoscopy techniques.[48] In a randomized study by Wang *et al*.,[49] patients were assigned to undergo colonoscopy with or without CADe, followed immediately by the other procedure. The adenoma miss rate was significantly lower in the CADe group compared to routine colonoscopy (14% vs. 40%, $p < 0.001$).[49] CADx systems are designed to enhance the precision of optical diagnosis for colorectal polyps, thereby decreasing unnecessary polyp removal through methods such as "resect-and-discard" (omitting histological evaluation) and "leave-in-situ" (avoiding resection of non-neoplastic lesions in the rectum and sigmoid).[50] Research has shown that CADx systems have a negative predictive value for detecting neoplastic lesions exceeding the 90% threshold required for the diagnosis-and-leave criterion established by the American Society for Gastrointestinal Endoscopy.[51] A meta-analysis of 18 studies on predicting polyp histology utilizing CADx models showed a pooled sensitivity of 92.3% (95% CI 88.8–94.9%) and specificity of 89.8% (95% CI 85.3–93.0%).[52]

Stringent quality indicators are essential for ensuring the high quality of all screening colonoscopies. These include not only the ADR of the endoscopist but also factors such as withdrawal time, cecal intubation rate, identification of high-risk individuals, and adequacy of bowel preparation (Table 3). The implementation of an automatic quality control system (AQCS) has been shown to increase mean withdrawal times from 5.68 m to 7.03 m ($p < 0.001$), as demonstrated in a study by Su *et al*.[53] The AQCS produces audio cues to prompt the endoscopist to reduce the withdrawal speed when encountering unstable or blurry frames, or when a colonic segment has suboptimal bowel preparation (Boston Bowel Preparation Scale < 2). Employing this automated system, the rate of adequate bowel preparation increased from 80.6% to 87.3% ($p = 0.023$). When combined with CADe, the AQCS led to an increase in the ADR (28.9% vs. 16.5%, $p < 0.001$). Gong *et al*.[54] conducted a randomized controlled trial involving 704 patients utilizing the ENDOANGEL system, which provides automated monitoring of withdrawal time, speed, and mucosal exposure. The real-time feedback led to a significantly longer mean withdrawal time in the ENDOANGEL group (6.38 m vs. 4.76 m, $p < 0.001$), and the ADR in the ENDOANGEL group was significantly higher (16% vs. 8%).

Despite these advances, several issues remain regarding the widespread implementation of AI in colonoscopy. First, obtaining a representative dataset may be challenging due to the numerous variables involved.[55] Another area that needs improvement is the establishment of legal regulations for the application of AI in healthcare.[56] The lack of transparency in AI use also presents legal concerns. Lastly, the high sensitivity of CADe systems may result in higher rates of unnecessary removal of non-neoplastic polyps, as well as increased withdrawal times and medical costs.[57] Prospective randomized controlled trials with high-quality clinical data and robust outcomes are essential to substantiate the cost-effectiveness of AI applications.

Challenges and outlook

Colonoscopy is currently recommended as the first-line CRC screening method in China.[58] However, the overall participation rate is relatively low compared to developed countries, and the reality of a sizable population, inadequate healthcare resources, and limited colonoscopy capacity cannot be ignored.[9] Thus, reducing the financial burden of CRC screening and improving its accessibility are essential priorities in the current CRC screening landscape. Having health insurance is positively associated with higher uptake of screening tests,[59,60] yet only around one-third of the population has health insurance. Local health authorities should consider providing financial support to facilitate CRC screening for high-risk but socioeconomically disadvantaged populations and incorporate screening into the healthcare system in the future. Additionally, governments and healthcare institutions should enhance awareness initiatives to educate the public about the significance of CRC screening and develop targeted policies to encourage high-risk individuals to undergo screening. The rising incidence of early-onset CRC—defined as cases diagnosed before age 50—has become an alarming trend in recent years. Researchers need to actively pursue innovative screening strategies and identify high-risk factors specifically associated with early-onset CRC. Lastly, several blood-based tests for CRC screening are under development, potentially increasing patient adherence and reducing screening costs. Rapid advancements in cancer biomarker research, along with the swift evolution of novel non-invasive testing methods, are likely to lead to significant breakthroughs in the screening and prevention of CRC.

Limitations

This study has several limitations. First, it lacks data to assess the cost-effectiveness of these screening or diagnostic methods. Second, emerging novel technologies show great potential for CRC opportunistic screening in China as supplementary tests, but further studies are needed to verify their efficacy in real-world screening practices. Third, this review was conducted from the perspective of service providers. Future studies could focus on the participants of CRC screening programs, as they may provide additional opinions on the CRC screening programs in China.

Conclusions

CRC screening in China has made notable advancements, despite facing several challenges. Through continued exploration, innovation in screening technologies, increased promotional activities,

optimization of service processes, and other strategic measures, we can systematically address the challenges in CRC screening and provide more cost-effective screening strategies. Furthermore, AI holds promise for enhancing early CRC diagnosis. Prospective population-based studies are essential to evaluate the impact of AI-driven improvements in adenoma detection on CRC prevention. The future outlook for CRC screening is optimistic, with advancements in technology and enhanced medical practices set to drive significant transformations.

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Conflict of interest

Yanqing Li is an Associate Editor of *Cancer Screening and Prevention*. The other authors have no conflict of interest to declare.

Author contributions

Study concept (YQL), drafting of the manuscript (ZXH), critical revision of the manuscript for important intellectual content (QZK, YQL), and study supervision (YQL). All authors have made significant contributions to this study and have approved the final manuscript.

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