American College of Gastroenterology Guidelines for Colorectal Cancer Screening 2008

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This document is the first update of the American College of Gastroenterology (ACG) colorectal cancer (CRC) screening recommendations since 2000. The CRC screening tests are now grouped into cancer prevention tests and cancer detection tests. Colonoscopy every 10 years, beginning at age 50, remains the preferred CRC screening strategy. It is recognized that colonoscopy is not available in every clinical setting because of economic limitations. It is also realized that not all eligible persons are willing to undergo colonoscopy for screening purposes. In these cases, patients should be offered an alternative CRC prevention test (flexible sigmoidoscopy every 5–10 years, or a computed tomography (CT) colonography every 5 years) or a cancer detection test (fecal immunochemical test for blood, FIT).

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INTRODUCTION

The members of the writing committee carried out a systematic literature review and developed the updated guideline recommendation document. Only peer-reviewed English language articles were included. The criteria used for evaluation of studies and assessment of the category of evidence and strength of recommendation are shown in **Table 1** (1). These guidelines have also been reviewed and approved by the Practice Parameters Committee of the American College of Gastroenterology (ACG) and by the ACG Board of Trustees.

The ACG is an organization of more than 10,000 clinical gastroenterologists and related health professionals. In 2000, the ACG issued colorectal cancer (CRC) screening recommendations that endorsed colonoscopy every 10 years, beginning at age 50, as the preferred CRC screening strategy (2). The ACG was the first organization to recommend colonoscopy as the preferred strategy for the CRC screening; and the American Society for Gastrointestinal Endoscopy (3) and National Comprehensive Cancer Network (4) subsequently endorsed this recommendation.

Other guidelines for CRC screening often utilize an approach called the "menu of options." In this approach, multiple options for screening are presented which differ with regard to their effectiveness, risk, and degree of invasiveness (and, therefore, potentially their acceptability to patients). The menu-of-options approach was first formalized by the "GI consortium" in May 1997 (5), endorsed by the American Cancer Society in 1997 (6), revised by the US Multisociety Task Force in 2003 (7), and revised by a joint committee of the US Multisociety Task Force, the American Cancer Society, and the American College of Radiology in 2008 (8). The ACG participated in and endorsed the menu-of-options approach in 1997, 2003, and 2008. The ACG continues to endorse the menu-of-options approach as appropriate to CRC screening. Publication of this guideline does not rescind the ACG's endorsement of the joint guideline (8). New recommendations, which differ from the earlier ACG guideline, are highlighted in **Table 2**. The rationale for a separate ACG screening guideline is discussed below.

Rationale for a preferred strategy

As in 2000, the ACG recommends that clinicians have access to a "preferred" strategy for making CRC screening recommendations, as an alternative to the "menu of options" approach, if warranted by the performance characteristics of one of the tests. The ACG recommends colonoscopy every 10 years based on the evidence of colonoscopy effectiveness, cost-effectiveness, and acceptance by patients. A "preferred" strategy simplifies and shortens discussions with patients and could also increase the likelihood that screening is offered to patients. One randomized trial showed that patients were more likely to undergo screening with the "preferred" strategy approach compared with the "menu of options" (9). Another study found no improvement in screening rates when multiple options were presented (10). Maintaining simplicity in guidelines may have value, in that recent evidence has suggested that practi-

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Table 1. Grading recommendations

Grade of recommendation/ description	Benefit vs. risk and burdens	Methodological quality of supporting evidence	Implications
1A/Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/Strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/Weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

RCT, randomized controlled trial.

Source: Guyatt *et al.* (1).

Table 2. Changes in this guideline from the 2000 ACG recommendations for screening (see reference 2)

1. Screening tests are divided into cancer prevention and cancer detection tests. Cancer prevention tests are preferred over detection tests.
2. Screening is recommended in African Americans beginning at age 45 years.
3. CT colonography every 5 years replaces double contrast barium enema as the radiographic screening alternative, when patients decline colonoscopy.
4. FIT replaces older guaiac-based fecal occult blood testing. FIT is the preferred cancer detection test.
5. Annual Hemoccult Sensa and fecal DNA testing every 3 years are alternative cancer detection tests.
6. A family history of only small tubular adenomas in first-degree relatives is not considered to increase the risk of CRC.
7. Individuals with a single first-degree relative with CRC or advanced adenomas diagnosed at age ≥60 years can be screened like average-risk persons.

ACG, American College of Gastroenterology; CRC, colorectal cancer; CT, computed tomography; FIT, fecal immunochemical test.

tioners often do not follow recommended intervals for postpolypectomy surveillance, which may in part be because of their complexity (11–13). The ACG acknowledges that listing quality colonoscopy as a "preferred" CRC prevention strategy places greater emphasis on effectiveness than on risk. Current trends in procedure use in the United States reflect and are consistent with the ACG's recommendation of colonoscopy as the preferred strategy for CRC screening, in that colonoscopy procedure volumes have risen dramatically, whereas flexible sigmoidoscopy and double-contrast barium enema (DCBE) procedure volumes have decreased precipitously, and fecal occult blood test (FOBT) has decreased modestly (14).

Cancer prevention tests vs. cancer detection tests

The recent joint guideline (8) groups CRC screening tests into cancer prevention and cancer detection tests. Cancer prevention tests have the potential to image both cancer and polyps, whereas cancer detection tests have low sensitivity for polyps and typically lower sensitivity for cancer compared with that in cancer prevention tests (imaging tests). The ACG supports the division of screening tests into cancer prevention and cancer detection tests, but recommends a preferred cancer prevention test—colonoscopy every 10 years (Grade 1 B) and a preferred cancer detection test—annual fecal immunochemical test (FIT) to detect occult bleeding (Grade 1 B). All recommendations in this guideline are provided in **Table 3**.

Preferred CRC prevention test: colonoscopy every 10 years (Grade 1 B)

The ACG recommends that quality colonoscopy be offered first to patients aged ≥50 years (**Table 3**). A background discussion of screening colonoscopy, including discussion of quality in technical performance (which is deemed critical to screening

Table 3. CRC screening recommendations

Preferred CRC screening recommendations
• Cancer prevention tests should be offered first. The preferred CRC prevention test is colonoscopy every 10 years, beginning at age 50. (Grade 1 B) Screening should begin at age 45 years in African Americans (Grade 2 C)
• Cancer detection test. This test should be offered to patients who decline colonoscopy or another cancer prevention test. The preferred cancer detection test is annual FIT for blood (Grade 1 B)
Alternative CRC prevention tests
• Flexible sigmoidoscopy every 5–10 years (Grade 2 B)
• CT colonography every 5 years (Grade 1 C)
Alternative cancer detection tests
• Annual Hemoccult Sensa (Grade 1 B)
• Fecal DNA testing every 3 years (Grade 2 B)
Recommendations for screening when family history is positive but evaluation for HNPCC considered not indicated
• Single first-degree relative with CRC or advanced adenoma diagnosed at age ≥60 years
Recommended screening: same as average risk (Grade 2 B)
• Single first-degree with CRC or advanced adenoma diagnosed at age <60 years or two first-degree relatives with CRC or advanced adenomas.
Recommended screening: colonoscopy every 5 years beginning at age 40 years or 10 years younger than age at diagnosis of the youngest affected relative (Grade 2 B)
FAP
• Patients with classic FAP (>100 adenomas) should be advised to pursue genetic counseling and genetic testing, if they have siblings or children who could potentially benefit from this testing (Grade 2 B)
• Patients with known FAP or who are at risk of FAP based on family history (and genetic testing has not been performed) should undergo annual flexible sigmoidoscopy or colonoscopy, as appropriate, until such time as colectomy is deemed by physician and patient as the best treatment (Grade 2 B)
• Patients with retained rectum after subtotal colectomy should undergo flexible sigmoidoscopy every 6–12 months (Grade 2 B)
• Patients with classic FAP, in whom genetic testing is negative, should undergo genetic testing for bi-allelic MYH mutations. Patients with 10–100 adenomas can be considered for genetic testing for attenuated FAP and if negative, MYH associated polyposis (Grade 2 C)
HNPCC
• Patients who meet the Bethesda criteria should undergo microsatellite instability testing of their tumor or a family member's tumor and/or tumor immunohistochemical staining for mismatch repair proteins (Grade 2 B)
• Patients with positive tests can be offered genetic testing. Those with positive genetic testing, or those at risk when genetic testing is unsuccessful in an affected proband, should undergo colonoscopy every 2 years beginning at age 20–25 years, until age 40 years, then annually thereafter (Grade 2 B)

CRC, colorectal cancer; CT, computed tomography, FAP, familial adenomatous polyposis; FIT, fecal immunochemical test; HNPCC, hereditary non-polyposis colorectal cancer.

colonoscopy) is found in Appendix B. Alternative CRC prevention tests are discussed in Appendix C. In clinical settings, in which economic issues preclude primary screening with colonoscopy, or for patients who decline colonoscopy, one of the alternative cancer prevention tests (**Table 3**, Appendix C) or the preferred cancer detection test, occult blood detection through the FIT (**Table 3**) should be offered.

Preferred cancer detection test: annual FIT (Grade 1 B)

The preferred cancer detection test is annual FIT. This test has superior performance characteristics when compared with older guaiac-based Hemoccult II cards (15–17); additionally, there were 10 and 12% gains in adherence with the FIT in the first two randomized controlled trials comparing the FIT with guaiac-based testing (18,19), The overall result of superior performance and improved adherence was a doubling in the detection of advanced lesions, with little loss of positive predictive value (18,19). The ACG supports the joint guideline recommendation that older guaiac-based fecal occult blood testing be abandoned as a method for CRC screening. Alternatives, such as the higher sensitivity guaiac-based Hemoccult Sensa and the fecal DNA test (**Table 3**), are discussed in Appendix D. However, because of more extensive data (compared with Hemoccult Sensa), and the high cost of fecal DNA testing, the ACG recommends the FIT as the preferred cancer detection test (Grade 1 B).

Age to begin screening in average-risk persons

The ACG continues to recommend that screening begin at age 50 years in average-risk persons (i.e., those without a family history of colorectal neoplasia) (Grade 1 B), except for African Americans. The ACG recommends that screening begin at age 45 years in African Americans (Grade 2 C). The rationale for this recommendation has been presented elsewhere (20).

The "average risk" population is large and complex with regard to risk. Certain other subgroups of the average-risk population might warrant initiation of screening at an earlier or later age, depending on their risk. For example, the age-adjusted risk of incident cancers (21) and prevalent adenomas (22–25) is greater in men than in women. However, delaying the onset of screening in women could result in a greater loss of life years in women who develop CRC in their 50s compared with that in men, as women on average live longer than men. Pending further study and evaluation of this issue, the ACG recommends that screening begin at age 50 years for both the genders (at age 45 years for African-American men and women).

In reviewing the literature, the writing committee also identified heavy cigarette smoking and obesity as linked to an increased risk of CRC and to the development of CRC at an earlier age. The clinical evidence supporting the increased risk in these groups is given in Appendix A. The current evidence supports a decision by clinicians in individual patients with an extreme smoking history or obesity to begin screening at an age earlier than 50 years and perhaps as early as 45 years. A formal recommendation to begin screening at an earlier age in smokers and obese patients will be re-evaluated as additional evidence appears.

cancers (99,101). Therefore, flexible sigmoidoscopy is carried out by highly skilled practitioners, it may be recommended at 10-year, rather than 5-year intervals (8).

Double contrast barium enema is no longer recommended as an alternative CRC prevention test, because its use has declined dramatically and also as its effectiveness for polyp detection is less than computed tomography (CT) colonography. The ACG considers that the DCBE could be used as a CRC screening test that is within the standard of care, if it is carried out by high volume operators with special interest and expertise in the technique. The rationale for DCBE over CT colonography is its low cost, but patients clearly prefer CT colonography (121,122). Only a few centers in the United States still perform sufficient volumes of screening DCBE to warrant its continued use.

CT colonography, every 5 years, is endorsed as an alternative to colonoscopy every 10 years because of its recent performance in the American College of Imaging Network Trial 6664 (also known as the National CT Colonography Trial) (123). Results from earlier multicenter trials in the United States ranged from excellent (124) to poor (121,125). The principle performance feature that justifies inclusion of CT colonography as a viable alternative in patients who decline colonoscopy, is that the sensitivity for polyps ≥1 cm in size in the most recent multicenter US trial was 90% (123). In this study, 25% of radiologists who were tested for entry into the trial but performed poorly were excluded from participation, and thus lower sensitivity might be expected in clinical practice. The CT colonography probably has a lower risk of perforation than colonoscopy in most settings, but for several reasons it is not considered the equivalent of colonoscopy as a screening strategy. First, the evidence to support an effect of endoscopic screening on prevention of incident CRC and mortality is overwhelming compared with that for CT colonography (see Appendix B). Second, the inability to detect polyps 5 mm and smaller, which constitutes 80% of colorectal neoplasms, and whose natural history is still not understood, necessitates performance of the test at 5-year, rather than 10-year intervals (8). This is likely to increase overall costs, if CT colonography is used as a primary strategy. Although management of polyps < 1 cm in size is controversial, the ACG continues to recommend that patients with polyps 6 mm or larger be referred for polypectomy, as should patients with three or more polyps of any size read with high confidence (126). Polyps ≤5 mm in size interpreted with high confidence should be described in the CT colonography report (126). Unfortunately, false positives are common, and the specificity for polyps ≥1 cm in size in the National CT Colonography Trial was only 86%, with a positive predictive value of 23% (123). Thus, colonoscopy for polyps detected on CT colonography will often require long procedures, in order to verify absence of other polyps. False positives diminish cost-effectiveness by increasing follow-up colonoscopies and repeat CT colonographies to verify false positive status. The ACG recommends that asymptomatic patients be informed of the possibility of radiation risk associated with one or repeated CT colonography studies, though the exact risk associated with radiation is unclear (127,128). The value of extracolonic findings detected by CT colonography is mixed, with substantial costs associated with incidental findings, but occasional important extracolonic findings are detected such as asymptomatic cancers and large abdominal aortic aneurysms. As a final point, the ACG is also concerned about the potential impact of CT colonography on adherence and thus on polypectomy rates. Thus, if CT colonography substantially improves adherence, it should improve polypectomy rates and thereby reduce CRC, even if only large polyps are detected and referred for colonoscopy. On the other hand, if CT colonography largely displaces patients who would otherwise be willing to undergo colonoscopy, then polypectomy rates will fall substantially, which could significantly increase the CRC incidence (129). Thus, for multiple reasons, and pending additional study, CT colonography should be offered to patients who decline colonoscopy.

APPENDIX D

Alternative cancer detection tests

The alternative cancer detection tests are listed in **Table 3**. Hemoccult Sensa is an improved guaiac-based card for fecal occult blood testing. It has superior sensitivity to older guaiac-based cards, but the overall evidence is less than that supporting the FIT. Furthermore, the FIT resulted in improved adherence for CRC screening over card-based tests in two randomized controlled trials (18,19). Therefore, FITs are preferred over Hemoccult Sensa.

Fecal DNA testing has been evaluated in three different versions. The first (Version 1.0) included tests for point mutations in *k-ras*, APC, P53, mutations in the BAT26 microsatellite instability marker, and the DNA integrity assay. The sensitivity for cancer was superior to traditional guaiac-based occult blood testing, but the absolute sensitivity was 52% and disappointing considering the high cost of the test (130). After completion of the trial, it was learned that the DNA integrity assay, which had appeared to be the most promising element in the assay in early studies (131), was non-informative because of the instability of DNA during shipment. Subsequently, Version 1.1 has been commercialized, which includes the same DNA test used in Version 1.0, but includes technical improvements of gel-based DNA capture and buffer stabilization of long or redundant DNA critical to the DNA integrity assay. No screening test using Version 1.1 has been reported, but a trial in established CRCs identified 70% sensitivity and specificity of ~95%, (specificity similar to Version 1.0) (132). Version 2.0 utilizes a simplified assay consisting of the DNA integrity assay and hypermethylation of the vimentin gene. No screening trial with Version 2.0 has been carried out, but a study in established CRCs shows sensitivity of 87% for cancer, but specificity fell to 82% (133). The latter specificity limits the frequency with which the test can be carried out reasonably. Given that the performance characteristics of the FIT are approximately equal to Versions 1.0, and 1.1, and superior to Version 2.0 with regard to specificity, and that FIT costs much less than fecal DNA testing,