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The following article contains new recommendations for colorectal cancer screening, the first set we have published since 2003 (Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale—update based on new evidence. Gastroenterology 2003;124:544–560.) The current recommendations have emerged through the participation of multiple national societies, taking into consideration newly emerging technologies. Please note the US Multi-Society Task Force (USMTF) represents the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy, and the American College of Gastroenterology. Commissioned originally by the American Cancer Society, this compendium will be published concurrently in CA: A Cancer Journal for Clinicians *and reprinted in the June issue of* Radiology.

Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, 2008: A Joint Guideline From the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology

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In the United States, colorectal cancer (CRC) is the third most common cancer diagnosed among men and women and the second leading cause of death from cancer. CRC largely can be prevented by the detection and removal of adenomatous polyps, and survival is significantly better when CRC is diagnosed while still localized. In 2006 to 2007, the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology came together to develop consensus guidelines for the detection of adenomatous polyps and CRC in asymptomatic average-risk adults. In this update of each organization's guidelines, screening tests are grouped into those that primarily detect cancer early and those that can detect cancer early and also can detect adenomatous polyps, thus providing a greater potential for prevention through polypectomy. When possible, clinicians should make patients aware of the full range of screening options, but at a minimum they should be prepared to offer patients a choice between a screening test that primarily is effective at early cancer detection and a screening test that is effective at both early cancer detection and zations that colon cancer prevention should be the primary goal of screening.

In the United States, colorectal cancer (CRC) is the third most common cancer diagnosed in men and women and the second leading cause of death from cancer.[1] In 2008, it is estimated that 148,810 men and women will be diagnosed with CRC and 49,960 will die from this disease.[1] Five-year survival is 90% if the disease is diagnosed while still localized (ie, confined to the wall of the bowel) but only 68% for regional disease (ie, disease

Abbreviations used in this paper: ACR, American College of Radiology; ACRIN, American College of Radiology Imaging Network; ACS, American Cancer Society; CRC, colorectal cancer; CSPY, colonoscopy; CT, computed tomography; CTC, computed tomographic colonography; DCBE, double-contrast barium enema; DIA, DNA integrity analysis; FIT, fecal immunochemical test; FOBT, fecal occult blood test; FSIG, flexible sigmoidoscopy; gFOBT, guaiac-based fecal occult blood test; HPNCC, hereditary nonpolyposis colon cancer; MRI, magnetic resonance imaging; NRDR, National Radiology Data Register; OC, optical colonoscopy; sDNA, stool DNA test; 2D, 2-dimensional; 3D, 3-dimensional; USMSTF, US Multi-Society Task Force on Colorectal Cancer.

with lymph node involvement) and only 10% if distant metastases are present.[2] Recent trends in CRC incidence and mortality reveal declining rates, which have been attributed to reduced exposure to risk factors, the effect of screening on early detection and prevention through polypectomy, and improved treatment.[3] However, in the near term, even greater incidence and mortality reductions could be achieved if a greater proportion of adults received regular screening. Although prospective randomized trials and observational studies have demonstrated mortality reductions associated with early detection of invasive disease, as well as removal of adenomatous polyps,[4–7] a majority of US adults are not receiving regular age- and risk-appropriate screening or have never been screened at all.[8,9]

The goal of cancer screening is to reduce mortality through a reduction in incidence of advanced disease. To this end, modern CRC screening can achieve this goal through the detection of early-stage adenocarcinomas and the detection and removal of adenomatous polyps, the latter generally accepted as a nonobligate precursor lesion. Adenomatous polyps are common in adults over age 50 years, but the majority of polyps will not develop into adenocarcinoma; histology and size determine their clinical importance.[10,11] The most common and clinically important polyps are adenomatous polyps, which represent approximately one half to two thirds of all colorectal polyps and are associated with a higher risk of CRC. Thus, most CRC screening studies evaluate the detection rate of invasive CRCs as well as advanced adenomas, which conventionally are defined as polyps $\geq$10 mm or histologically having high-grade dysplasia or significant villous components. The evidence for the importance of colorectal polyps in the development of CRC is largely indirect, but nonetheless extensive and convincing, and has been described in detail.[11–13]

Today there is a range of options for CRC screening in the average-risk population, with current technology falling into 2 general categories: stool tests, which include tests for occult blood or exfoliated DNA, and structural exams, which include flexible sigmoidoscopy (FSIG), colonoscopy (CSPY), double-contrast barium enema (DCBE), and computed tomographic colonography (CTC). Stool tests are best suited for the detection of cancer, although they also will deliver positive findings for some advanced adenomas, while the structural exams can achieve the dual goals of detecting adenocarcinoma as well as identifying adenomatous polyps.[14] These tests may be used alone or in combination to improve sensitivity or, in some instances, to ensure a complete examination of the colon if the initial test cannot be completed. Although screening tests for CRC vary in terms of the degree of supporting evidence, potential efficacy for [illegible] tematic program of regular screening has the potential to significantly reduce deaths from CRC.

Beginning in 1980, the American Cancer Society (ACS) first issued formal guidelines for CRC screening in average-risk adults.[15] Since then, the ACS has periodically updated its CRC guidelines,[16–19] including adding recommendations for high-risk individuals in 1997.[17] Other organizations also have issued recommendations for CRC screening, most notably the US Preventive Services Task Force,[20,21] the American College of Radiology (ACR),[22,23] and the US Multi-Society Task Force on Colorectal Cancer (USMSTF).[12,24] Recently, the ACS and the USMSTF collaborated on an update of earlier recommendations for postpolypectomy and post-CRC resection surveillance in response to reports suggesting significant deviation from existing recommendations.[25,26] Since 1997, the organizational guidelines for average-risk adults have grown increasingly similar and represent a broad organizational consensus on the value, options, and methods for periodic screening for CRC.

In the last decade, there has been an increase in the number of technologies available for CRC screening, and in the case of stool tests, there has been growth in the number of commercial versions of guaiac-based and immunochemical-based stool tests (gFOBT and FIT). This growth in options also has been accompanied by changing patterns in the proportion of adults using different tests, with FSIG rates declining, CSPY rates increasing, use of stool blood tests remaining somewhat constant, and use of the DCBE for screening now becoming very uncommon.[8]

There are pros and cons to having a range of options for CRC screening. Despite the fact that the primary barriers to screening are lack of health insurance, lack of physician recommendation, and lack of awareness of the importance of CRC screening,[27] the historical evidence shows that adults have different preferences and patterns of use among the available CRC screening tests.[28–31] Although population preferences or resistance to a particular technology may change over time or may be influenced by referring physicians, it also may be true that over time some adults may persist in choosing one technology and rejecting another. Furthermore, at this time not all options are available to the entire population, and transportation, distance, and financial barriers to some screening technologies may endure for some time. Although in principle all adults should have access to the full range of options for CRC screening, the fact that simpler, lower-cost options are available in most settings, whereas other more costly options are not universally available, is a public health advantage. However, for average-risk adults, multiple testing options challenge the referring physician to support an office policy that can manage a broad range of testing choices, their follow-up [illegible]

choices is both demanding and time consuming and is complicated by the different characteristics of the tests and the test-specific requirements for individuals undergoing screening.[31] In addition, the description of benefits is complicated by different performance characteristics of the variants of the occult blood tests and uncertain differences between test performance in research settings and test performance in clinical practice. These challenges have been discussed in the past,[19,32] and they still are with us today.

In this guideline review, we have reassessed the individual test evidence and comparative evidence for stool tests, including gFOBT, FIT, and stool DNA test (sDNA), and the structural exams, including FSIG, CSPY, DCBE, and CTC, the latter also known as virtual colonoscopy. We have sought to address a number of concerns about the complexity of offering multiple screening options and the degree to which the range of screening options and their performance, costs, and demands on individuals poses a significant challenge for shared decisions. An overriding goal of this update is to provide a practical guideline for physicians to assist with informed decision making related to CRC screening. These guidelines are for individuals at average risk. Individuals with a personal or family history of CRC or adenomas, inflammatory bowel disease, or high-risk genetic syndromes should continue to follow the most recent recommendations for individuals at increased or high risk.[24–26]

Guidelines Development, Methods, and Framework

The guidelines update process was divided into 2 phases. The first phase focused on the stool tests, including gFOBT, FIT, and sDNA. The second phase of the guidelines update process focused on the structural exams, including FSIG, colonoscopy, DCBE,and CTC. Deliberations about evidence and presentations from experts took place during 2 face-to-face meetings of the the collaborating organizations and invited outside experts and through periodic conference calls. The process relied on earlier evidence-based reviews.[12,16–21,24] Literature related to CRC screening and specific to individual tests published between January 2002 and March 2007 was identified using MEDLINE (National Library of Medicine) and bibliographies of identified articles. Expert panel members also provided several unpublished abstracts and manuscripts. Where evidence was insufficient or lacking to provide a clear, evidence-based conclusion, final recommendations were based on expert opinion and are so indicated.

While there is clear experimental evidence that screening for CRC with gFOBT is associ-ated with reduced incidence and mortality from CRC screening,[5,6,33] most of the information supporting the use of the other colo- studies of asymptomatic average-risk or higher-risk populations that were followed by testing with colonoscopy in all or nearly all study participants as a validation measure.

Summary of the Recommendations

In this update of guidelines for CRC screening in average-risk adults, the expert panel concluded that a screening test must be able to detect the majority of prevalent or incident cancers at the time of testing. Here we are drawing a new, important distinction between test sensitivity and program sensitivity, the former being the sensitivity achieved in a single test and the latter being the sensitivity achieved over time through serial testing in a program. While cancer screening tests are expected to achieve acceptable levels of sensitivity and specificity,[34] no specific acceptance threshold for either measure, alone or in combination, has been established for any screening test.[35,36] Thus, this criterion is based on expert opinion and the following considerations. First, in the judgment of the panel, recent evidence has revealed an unacceptably wide range of sensitivity among some gFOBT strategies, with some practices and tests performing so poorly that the large majority of prevalent cancers are missed at the time of screening.[37–39] The observation of very low sensitivity for cancer and advanced neoplasia associated with in-office gFOBT led Sox to speculate that CRC mortality rates might be considerably lower today if the quality of gFOBT testing during the previous decade had been higher.[40] While the literature on other CRC screening tests also reveals a range of sensitivities, even in the presence of significant, correctable, quality-related shortcomings, the majority of invasive cancers still will be detected. Second, a test like gFOBT that demonstrates poor test sensitivity but good program sensitivity depends on high rates of adherence with regular screening. However, many patients have only one test and do not return the following year for programmatic testing.[41,42] Given the lack of systems to ensure or at least facilitate adherence with recommended regular screening intervals, as well as evidence of suboptimal awareness and engagement of primary care in supporting adherence with screening recommendations,[43] the panel concluded that it was not realistic at this time to rely on program sensitivity to overcome limitations in test sensitivity. Physicians and institutions should select stool blood tests that have been shown in the scientific literature to detect the majority of prevalent CRCs in an asymptomatic population. If there is not evidence that an available test has met that benchmark, it should not be offered to patients for CRC screening.

Individuals and health care professionals should also understand that screening tests for CRC broadly fall into 2 categories. In one category are the fecal tests (ie,

Table 1. Testing Options for the Early Detection of Colorectal Cancer and Adenomatous Polyps for Asymptomatic Adults Aged 50 Years and Older

Tests that detect adenomatous polyps and cancer
FSIG every 5 years, or
CSPY every 10 years, or
DCBE every 5 years, or
CTC every 5 years
Tests that primarily detect cancer
Annual gFOBT with high test sensitivity for cancer, or
Annual FIT with high test sensitivity for cancer, or
sDNA, with high sensitivity for cancer, interval uncertain

enomatous polyps may be detected, providing an opportunity for polypectomy and the prevention of CRC, but the opportunity for prevention is both limited and incidental and is not the primary goal of CRC screening with these tests. In the second category are the partial or full structural exams (ie, FSIG, CSPY, DCBE, and CTC)[44] which are tests that are effective at detecting cancer and premalignant adenomatous polyps. These tests differ in complexity and accuracy for the detection of CRC and advanced neoplasia. When performed properly, each of these structural exams has met the standard of detecting at least half of prevalent or incident cancers at the time of testing.

It is the strong opinion of this expert panel that *colon cancer prevention* should be the primary goal of CRC screening. Tests that are designed to detect both early cancer and adenomatous polyps should be encouraged if resources are available and patients are willing to undergo an invasive test. These tests include the partial or full structural exams mentioned above. These tests require bowel preparation and an office or hospital visit and have various levels of risk to patients. These tests also have limitations, greater patient requirements for successful completion, and potential harms. Significant positive findings on FSIG, DCBE, and CTC require follow-up CSPY.

The panel recognized that some patients will not want to undergo an invasive test that requires bowel preparation, may prefer to have screening in the privacy of their home, or may not have access to the invasive tests due to lack of coverage or local resources. Collection of fecal samples for blood or DNA testing can be performed at home without bowel preparation. However, providers and patients should understand the following limitations and requirements of noninvasive tests:

&# These tests are less likely to prevent cancer compared with the invasive tests;

&# These tests must be repeated at *regular* intervals to be effective;

If patients are not willing to have repeated testing or have CSPY if the test is abnormal, these programs will not be effective and should not be recommended.

Based on our review of the historic and recent evidence, the tests in Table 1 are acceptable options for the early detection of CRC and adenomatous polyps for asymptomatic adults aged 50 years and older (also see Table 2).

Screening Tests for the Detection of CRC

Stool Blood Tests—gFOBT and FIT

Stool blood tests are conventionally known as fecal occult blood tests (FOBT) because they are designed to detect the presence of occult blood in stool. FOBT fall into 2 primary categories based on the detected analyte: gFOBT and FIT. Blood in the stool is a nonspecific finding but may originate from CRC or larger (>1 to 2 cm) polyps. Because small adenomatous polyps do not tend to bleed and bleeding from cancers or large polyps may be intermittent or simply not always detectable in a single sample of stool, the proper use of stool blood tests requires annual testing that consists of collecting specimens (2 or 3, depending on the product) from consecutive bowel movements.[18,24,45] FIT generally are processed only in a clinical laboratory, whereas gFOBT are processed either in the physician's office or in a clinical laboratory. When performed for CRC screening, a positive gFOBT or FIT requires a diagnostic workup with CSPY to examine the entire colon in order to rule out the presence of cancer or advanced neoplasia.

gFOBT

gFOBT are the most common stool blood tests in use for CRC screening and the only CRC screening tests for which there is evidence of efficacy from prospective, randomized controlled trials. Guaiac-based tests detect blood in the stool through the pseudoperoxidase activity of heme or hemoglobin, while immunochemical-based tests react to human globin. The usual gFOBT protocol consists of collecting 2 samples from each of 3 consecutive bowel movements at home. Prior to testing with a sensitive guaiac-based test, individuals usually will be instructed to avoid aspirin and other nonsteroidal anti-inflammatory drugs, vitamin C, red meat, poultry, fish, and some raw vegetables because of diet-test interactions that can increase the risk of both false-positive and false-negative (specifically, vitamin C) results.[46] Collection of all 3 samples is important because test sensitivity improves with each additional stool sample.[14]

gFOBT—Efficacy and Test Performance. Three large, prospective, randomized controlled trials with gFOBT have demonstrated that screened patients have

Table 2. Guidelines for Screening for the Early Detection of Colorectal Cancer and Adenomas for Average-risk Women and Men Aged 50 Years and Older

The following options are acceptable choices for colorectal cancer screening in average-risk adults beginning at age 50 years. Since each of the following tests has inherent characteristics related to prevention potential, accuracy, costs, and potential harms, individuals should have an opportunity to make an informed decision when choosing one of the following options.

In the opinion of the guidelines development committee, *colon cancer prevention* should be the primary goal of colorectal cancer screening. Tests that are designed to detect both early cancer and adenomatous polyps should be encouraged if resources are available and patients are willing to undergo an invasive test.

Tests that Detect Adenomatous Polyps and Cancer

Test	Interval	Key Issues for Informed Decisions
FSIG with insertion to 40 cm or to splenic flexure	Every 5 years	• Complete or partial bowel prep is required • Sedation usually is not used, so there may be some discomfort during the procedure • The protective effect of sigmoidoscopy is primarily limited to the portion of the colon examined • Patients should understand that positive findings on sigmoidoscopy usually result in a referral for CSPY
CSPY	Every 10 years	• Complete bowel prep is required • Conscious sedation is used in most centers; patients will miss a day of work and will need a chaperone for transportation from the facility • Risks include perforation and bleeding, which are rare but potentially serious; most of the risk is associated with polypectomy
DCBE	Every 5 years	• Complete bowel prep is required • If patients have one or more polyps >6 mm, CSPY will be recommended; follow-up CSPY will require complete bowel prep • Risks of DCBE are very low; rare cases of perforation have been reported
CTC	Every 5 years	• Complete bowel prep is required • If patients have one or more polyps >6 mm, CSPY will be recommended; if same day CSPY is not available, a second complete bowel prep will be required before CSPY • Risks of CTC are very low; rare cases of perforation have been reported

Tests that Primarily Detect Cancer

Test	Interval	Key Issues for Informed Decisions
gFOBT with high sensitivity for cancer	Annual	• Depending on manufacturer's recommendations, 2 to 3 stool samples collected at home are needed to complete testing; a single sample of stool gathered during a digital exam in the clinical setting is not an acceptable stool test and should not be done
FIT with high sensitivity for cancer	Annual	• Positive tests are associated with an increased risk of colon cancer and advanced neoplasia; CSPY should be recommended if the test results are positive • If the test is negative, it should be repeated annually • Patients should understand that one-time testing is likely to be ineffective
sDNA with high sensitivity for cancer	Interval uncertain	• An adequate stool sample must be obtained and packaged with appropriate preservative agents for shipping to the laboratory • The unit cost of the currently available test is significantly higher than other forms of stool testing • If the test is positive, CSPY will be recommended • If the test is negative, the appropriate interval for a repeat test is uncertain

FSIG, flexible sigmoidoscopy; CSPY, colonoscopy; DCBE, double-contrast barium enema; CTC, computed tomography colonography; gFOBT, guaiac-based fecal occult blood test; FIT, fecal immunochemical test; sDNA, stool DNA test.

trials demonstrated significant reductions in CRC mortality of 15% to 33%.[5,6,34] Moreover, incidence reduction of 20% was demonstrated in one trial (Minnesota) after 18 years of follow-up, which has been attributed to relatively higher rates of CSPY in the study (38% of subjects in the screened group).[7]

or variant of the test;[47] specimen collection technique;[38] number of samples collected per test;[14] whether or not the stool specimen is rehydrated (ie, adding a drop of water to the slide window before processing);[48]; and variations in interpretation, screening interval, and other factors.[46]

The reported sensitivity of a single gFOBT varies con-

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