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Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer

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This document updates the colorectal cancer (CRC) screening recommendations of the U.S. Multi-Society Task Force of Colorectal Cancer (MSTF), which represents the American College of Gastroenterology, the American Gastroenterological Association, and The American Society for Gastrointestinal Endoscopy. CRC screening tests are ranked in 3 tiers based on performance features, costs, and practical considerations. The first-tier tests are colonoscopy every 10 years and annual fecal immunochemical test (FIT). Colonoscopy and FIT are recommended as the cornerstones of screening regardless of how screening is offered. Thus, in a sequential approach based on colonoscopy offered first, FIT should be offered to patients who decline colonoscopy. Colonoscopy and FIT are recommended as tests of choice when multiple options are presented as alternatives. A risk-stratified approach is also appropriate, with FIT screening in populations with an estimated low prevalence of advanced neoplasia and colonoscopy screening in high prevalence populations. The second-tier tests include CT colonography every 5 years, the FIT–fecal DNA test every 3 years, and flexible sigmoidoscopy every 5 to 10 years. These tests are appropriate screening tests, but each has disadvantages relative to the tier 1 tests. Because of limited evidence and current obstacles to use, capsule colonoscopy every 5 years is a third-tier test. We suggest that the Septin9 serum assay (Epigenomics, Seattle, Wash) not be used for screening. Screening should begin at age 50 years in average-risk persons, except in African Americans in whom limited evidence supports screening at 45 years. CRC incidence is rising in persons under age 50, and thorough diagnostic evaluation of young persons with suspected colorectal bleeding is recommended. Discontinuation of screening should be considered when persons up to date with screening, who have prior negative screening (particularly colonoscopy), reach age 75 or have <10 years of life expectancy. Persons without prior screening should be considered for screening up to age 85, depending on age and comorbidities. Persons with a family history of CRC or a documented advanced adenoma in a first-degree relative age <60 years or 2 first-degree relatives with these findings at any age are recommended to undergo screening by colonoscopy every 5 years, beginning 10 years before the age at diagnosis of the youngest affected relative or age 40, whichever is earlier. Persons with a single first-degree relative diagnosed at ≥60 years with CRC or an advanced adenoma can be offered average-risk screening options beginning at age 40 years.

Colorectal cancer (CRC) screening is the process of detecting early-stage CRCs and precancerous lesions in asymptomatic people with no prior history of cancer or precancerous lesions. The U.S. Multi-Society Task Force of Colorectal Cancer (MSTF) is a panel of expert gastroenterologists representing the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy. The MSTF, like others, has long endorsed systematic offers of CRC screening to average-risk persons (persons without a high-risk family history of colorectal neoplasia) beginning at age 50 years, with general evidence supporting screening reviewed in previous publications.[1] This publication updates the screening recommendations of the MSTF for screening in average-risk persons.[1]

Screening differs from surveillance. Surveillance refers to the interval use of colonoscopy in patients with previously detected CRC or precancerous lesions and interval colonoscopy in patients performed to detect dysplasia in persons with inflammatory bowel disease affecting the colon. Surveillance recommendations from the MSTF on surveillance after cancer[2] and removal of precancerous lesions[3] are available in other documents. Screening is also distinct from diagnostic examinations, which refer to the

Abbreviations used in this paper: CRC, colorectal cancer; FIT, fecal immunochemical test; MSTF, U.S. Multi-Society Task Force on Colorectal Cancer; SSP, sessile serrated polyp.

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investigation of patients with symptoms or positive screening tests other than colonoscopy. Colonoscopy is generally the test of choice for diagnostic examinations.

Methods

Literature Review

The English language medical literature using MEDLINE (2005 to August 1, 2016), EMBASE (2005 to third quarter 2016 update), the Database of Abstracts of Reviews and Effects (2005 to third quarter 2016 update), and the Cochrane Database of Systematic Reviews (2005 to third quarter 2014 update) was searched. In MEDLINE, subject headings for colorectal cancer screening were combined with headings for fecal occult blood test, fecal immunochemical test, colonoscopy, sigmoidoscopy, CT colonoscopy, fecal DNA, serum testing, cost-effectiveness, and quality. Similar searches were performed in EMBASE, the Database of Abstracts of Reviews and Effects, and the Cochrane Database of Systematic Reviews. Case reports and studies performed in patients with inflammatory bowel disease, prior CRC or polyps, or hereditary CRC syndromes were excluded. Review papers, meta-analyses, gastroenterology textbooks, and editorials were searched manually for additional pertinent references. The review includes studies published since 2008 but also incorporates older evidence used to draft the 2008 recommendations.[1] Evidence-based weighted recommendations are provided with supporting discussion to help guide clinicians in the management of these patients.

Process and Levels of Evidence

Guidance statements were developed by consensus obtained through joint teleconferences. The completed article was reviewed and approved by all 3 gastroenterology societies.

The use of GRADE for MSTF guidance papers has been outlined in detail elsewhere.[2] GRADE involves comprehensive literature search and summary (often through meta-analysis) and then a separate review of literature quality and development of recommendations. The MSTF uses a modified qualitative approach based on literature review (as described above for this article) but without formal meta-analysis. GRADE allows for a separate assessment of the quality of the evidence and strength of recommendation. This approach explicitly recognizes the importance of literature in informing clinical recommendations but allows latitude because recommendations may be influenced by other factors, such as patient preference, cost, and expert consensus. "Strong recommendations" are those that would be chosen by most informed patients. "Weak recommendations" are those where patient values and preferences might play a larger role than the quality of evidence. Within the document we preface strong recommendations with phrases such as "we recommend" and weak recommendations with "we suggest."

Approaches to Screening

In the United States CRC screening usually results from an office-based interaction between a healthcare provider and patient. Screening in this setting is termed *opportunistic.*[4]

Programmatic screening (sometimes called *organized* screening) refers to a system-wide, organized approach to offering screening to a population or members of a healthcare plan.[4] Programmatic screening has potential advantages over opportunistic screening, including systematic offers of screening, reduction of overscreening, superior monitoring of quality, and systematic follow-up of testing. National CRC screening programs in Europe[5] and Australia[6] use fecal occult blood testing and include screening colonoscopy in Germany and Poland.[5] The United States has no national program for CRC screening, although several large healthcare plans offer programmatic screening, typically with a fecal immunochemical test (FIT).[7] Despite the potential advantages of programmatic screening, the United States has achieved the world's highest rates of CRC screening compliance at 60% and the greatest CRC incidence and mortality reduction, using an almost entirely opportunistic approach.[8–12] Incidence reductions in the United States were 3% to 4% per year and 30% overall in the first decade of this century.[11,12] High rates of screening in the United States may reflect widespread awareness of CRC and insurance coverage of screening. The MSTF anticipates growth of programmatic screening within healthcare systems but expects at least short-term continued reliance on opportunistic screening in the United States. Reliance on opportunistic screening can affect the preference for CRC screening, because achieving compliance with tests that should be repeated at short intervals is more challenging in the opportunistic setting.[13]

In the setting of opportunistic screening, healthcare providers can use several broad strategies to offer screening to patients. One approach is *multiple options*, in which the benefits, risks, and costs of 2 or more tests are discussed and offered to patients (Table 1).[14] Some evidence suggests that when patients are offered both colonoscopy and fecal occult blood testing, more patients undergo screening.[15] Other data suggest no benefit in overall compliance when multiple options are offered.[16–18] In 1 study, offering patients 5 options did not enhance compliance over 2

Table 1. Approaches to Offering Screening in the Opportunistic Setting

Approach	Description
Multiple options	The relative benefits, risks, and costs of 2 or more options are presented
Sequential testing	A preferred test is offered first. If the patients decline another option(s) is offered
Risk stratified approach	Colonoscopy is offered to patients predicted to have a high prevalence of advanced pre-cancerous lesions; other tests are offered to patients predicted at low risk

options.[19] In this regard, at least 9 different screening tests (colonoscopy, FIT, guaiac-based fecal occult blood test, FIT–fecal DNA, sigmoidoscopy, sigmoidoscopy plus fecal occult blood test, CT colonography, barium enema, and the Septin9 serum assay [Epigenomics, Seattle, Wash]) are endorsed or discussed in recent major screening guidelines.[14,20] Thus, the multiple options discussion may best be limited to 2 or 3 preferred options. If patients decline all the offered options, 1 or more of the other options can be offered.

The *sequential* approach to screening involves an offer of a first test that is usually the provider's preferred screening option; if the patient declines the first option, a second test is offered, and so on. In the United States the sequential approach often involves an offer of colonoscopy, followed by FIT if colonoscopy is declined, or another screening test.[9] Separate guidelines from the American College of Gastroenterology[21] and the American Society for Gastrointestinal Endoscopy[22] recommend a sequential approach with colonoscopy offered first. Sequential testing can maximize compliance overall as well as with the test recommended first.[23–25] Clinicians using the colonoscopy-first sequential approach place emphasis on the high efficacy of colonoscopy in preventing CRC and less emphasis on the risks of colonoscopy. Indeed, high-quality colonoscopy has both higher single-time testing efficacy and greater risks than any other screening tests but with absolute risk rates that are still very low when performed by skilled operators.[26] A variant of sequential testing often used in the programmatic setting is to offer patients FIT as the initial or preferred test and have other options such as colonoscopy available to patients who express interest in alternatives.[4]

A third approach to offering screening to average-risk persons is a *risk-stratified* approach. Risk stratification uses evidence that the "average-risk" population actually represents a wide range of risk that can be estimated based on demographic and other risk factors. For example, older age, male gender, obesity, diabetes, and cigarette smoking are all associated with colorectal adenomas and cancer and therefore might be used in stratifying risk within the average-risk population.[21] The goal is to predict subgroups of patients with a high prevalence of important precancerous lesions benefiting most from referral directly to colonoscopy, whereas the subgroups with a predicted lower risk (prevalence) of important precancerous lesions are referred for screening tests with less risk and cost than colonoscopy. Risk stratification has been poorly accepted because of limited accuracy in discriminating high- and low-prevalence subgroups.[27] However, recent validated models appear to be simple to apply and had substantial accuracy in defining high- and low-risk groups for advanced adenomas.[28,29] There are no clinical trials comparing compliance or other outcomes using a risk-stratified approach to the multiple options or sequential approaches. Few data are currently available regarding ease of application of a risk-stratified approach in clinical practice.

The MSTF considers that each of the approaches outlined above is reasonable when offering screening in the opportunistic setting. There is insufficient evidence to identify one approach as superior. Patients undergoing screening tests other than colonoscopy should understand that colonoscopy is used to evaluate these tests when positive. In some instances insurance coverage of colonoscopy performed to evaluate other positive screening tests may be less than coverage of primary screening colonoscopy. Awareness of the different approaches may assist clinicians in understanding screening literature and in selecting an approach to offering screening that seems to be optimal for their practice or for an individual patient.

Recommendations

1. We recommend that clinicians offer CRC screening beginning at age 50 (strong recommendation, high-quality evidence). (See below for adjustments in recommended age for onset of screening based on race and family history.)

2. We suggest that sequential offers of screening tests, offering multiple screening options, and risk-stratified screening are all reasonable approaches to offering screening (weak recommendation, low-quality evidence).

Screening Targets

The object of screening is to reduce CRC incidence and mortality. To accomplish both aims, tests need to detect early-stage (ie, curable) CRCs and high-risk precancerous lesions.[1,21] Detection and removal of precancerous lesions prevents CRC.[30,31] The 2 main classes of precancerous lesions in the colon are conventional adenomas and serrated class lesions (Table 2). These 2 classes of precancerous lesions have distinct endoscopic features and histology and different (though overlapping) distributions within the colorectum. Specific screening tests sometimes have particular strengths or weaknesses detecting 1 or the other class of precancerous lesions, particularly the serrated class. Therefore, we review here the main clinical features of the 2 classes of precancerous lesions.

Adenomas, also known as conventional adenomas, are the precursors of perhaps 70% of all CRCs.[32,33] The adenoma–carcinoma sequence is believed to typically take

Table 2. Histologic Classification of the Two Major Classes of Colorectal Polyps

I. Conventional adenomas
  a. Dysplasia grade
    i. High grade
    ii. Low grade
  b. Villousity
    i. Tubular
    ii. Tubulovillous
    iii. Villous
II. Serrated lesions
  a. Hyperplastic polyps (not considered precancerous)
  b. Sessile serrated polyp
    i. Without cytologic dysplasia
    ii. With cytologic dysplasia
  c. Traditional serrated adenoma

more than 10 years to complete in sporadic cancers, whereas much shorter intervals occur in Lynch syndrome.[34] Correspondingly, colonoscopy is recommended at 10-year intervals in average-risk persons and at 1- to 2-year intervals in those with Lynch syndrome.[1,34] The distribution of adenomas is relatively even throughout the colon, although adenomas with a flat or depressed morphology are distributed more to the proximal colon and pedunculated lesions more to the distal colon.[35] Adenomas are by definition dysplastic, with the overwhelming majority being low grade. The presence of high-grade dysplasia in an adenoma should be noted by a pathologist. Adenomas can also be characterized by tubular versus villous histology, with the overwhelming majority tubular. Lesions with >25% villous elements are termed *tubulovillous* and those with >75% villous elements *villous*. Villous elements and invasive cancer are associated with increasing size of adenomas. Invasive cancer in adenomas ≤5 mm in size is extremely rare, and the prevalence remains well below 1% in adenomas 6 to 9 mm in size.[36] Recent colonoscopic studies have identified lower prevalence rates of cancer in polyps <1 cm in size compared with early studies, probably because improvements in colonoscope technology and performance have led to routine detection of an array of small, flat, low-volume adenomas.[36] Interobserver agreement in differentiation of high- versus low-grade dysplasia by pathologists and tubular versus tubulovillous histology is poor to moderate, particularly in adenomas <1 cm in size.[37] Conversely, interobserver agreement between pathologists is good to excellent in placing lesions within the conventional adenomas versus serrated polyps and in identifying invasive cancer.[38]

An important clinical concept is the "advanced" adenoma, defined as a lesion ≥1 cm in size or having high-grade dysplasia or villous elements.[3] Because nonadvanced adenomas have a very low prevalence of cancer and a long adenoma–cancer sequence, screening tests can remain useful if they target cancer and advanced adenomas and not small adenomas. Further, the prevalence of nonadvanced adenomas is so high in modern colonoscopy studies that detection of such lesions by noncolonoscopic screening tests leads to unacceptably low specificity. Colonoscopy has an important benefit over other screening methods because of its ability to detect and remove both advanced and nonadvanced adenomas. Although nonadvanced adenomas have limited clinical importance and are not the target of noncolonoscopic screening methods, colonoscopists strive to identify and remove nonadvanced adenomas. Thus, resecting lesions with any precancerous potential during colonoscopy is safe, seems to be better accepted by patients in the United States, and removes them as a clinical concern.

Serrated colorectal lesions (Figure 1) represent an emerging area in the field of precancerous colorectal lesions. The serrated class of precursor lesions accounts for up to

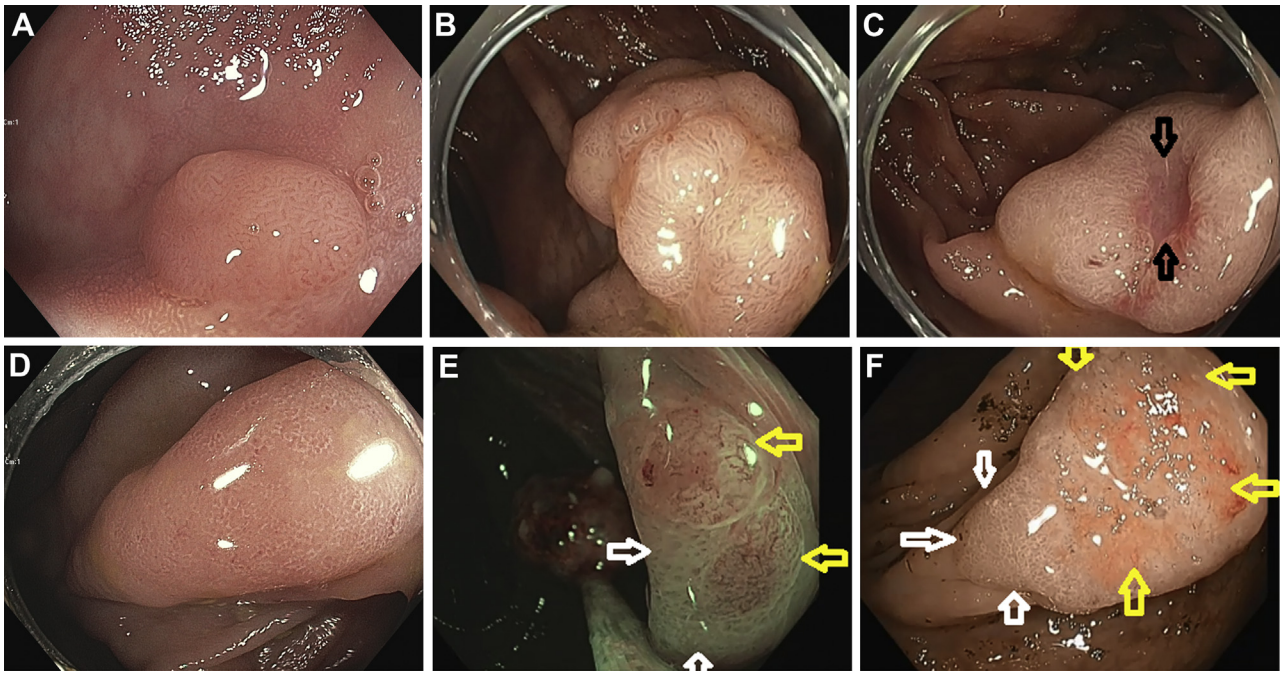

Figure 1. Endoscopic photographs of conventional adenomas and sessile serrated polyps. (*A*), Small (8-mm diameter) conventional adenoma. The red lines are surface blood vessels. (*B*), A portion of a 40-mm advanced conventional adenoma; one of the targets of all screening tests. The prominent blood vessel pattern is again visible. (*C*), A conventional adenoma with a focus of invasive cancer. The prominent blood vessel pattern of a conventional adenoma visible over the lesion except in the ulcerated area. The cancer is located at the ulcer *(arrows)* (*D*), A sessile serrated polyp without cytologic dysplasia. Note the absence of blood vessels on the surface. (*E*), A sessile serrated polyp (visualized in narrow-band imaging) with multiple foci of cytologic dysplasia *(yellow arrows)*. The dysplastic areas have the blood vessel pattern (and the histologic features) of an adenoma. The *white arrows* point to non-dysplastic portions of this sessile serrated polyp. (*F*), A sessile serrated polyp with invasive cancer; *white arrows* designate the residual sessile serrated polyp, whereas *yellow arrows* indicate the ulcerated malignant portion of the lesion.

30% of CRCs.[33] Within the serrated class, hyperplastic polyps are not currently considered precancerous, whereas sessile serrated polyps (SSPs; also known as sessile serrated adenoma) and traditional serrated adenomas are considered precancerous (Table 2).[33] Hyperplastic polyps are usually small lesions and are distributed toward the distal colon.[39] SSPs are common (found in 8%-9% of screening colonoscopies performed by expert detectors)[40,41] and are distributed toward the proximal colon compared with conventional adenomas. SSPs are typically flat or sessile in shape, have few or no surface blood vessels (conventional adenomas by comparison have many surface vessels), and are more difficult to detect at colonoscopy than conventional adenomas.[33,42,43] Because of their prevalence and precancerous potential, SSPs are the major precancerous serrated lesion. There is poor interobserver agreement between pathologists in the differentiation of hyperplastic polyps from SSPs.[44] Consequently, clinicians can see widely varying rates of SSPs in pathology reports, depending on the pathologist or even the center in which they practice.[45] Most SSPs are not dysplastic, and the lesions should consistently be designated as "SSP without cytologic dysplasia" or "SSP with cytologic dysplasia."[46] When a dysplastic component is present, it is often evident endoscopically (Figure 1) and histologically is a region of conventional adenoma within an otherwise serrated lesion.[47] Microdissection studies indicate that the dysplastic area often has microsatellite instability.[48] The SSP with cytologic dysplasia is considered a more advanced lesion in the polyp cancer sequence than SSP without cytologic dysplasia.[3,33,49,50]

The traditional serrated adenoma is a rare lesion, often in the left colon, sessile, and uniformly dysplastic.[33,46] Because traditional serrated adenoma is rare, dysplastic, and has a villous-like growth pattern histologically, it is often misinterpreted as a tubulovillous conventional adenoma.[33]

The features of these 2 classes of precancerous lesions are relevant to the available screening tests. Colonoscopy is the criterion standard for the detection of all precancerous colorectal lesions. Colonoscopy achieves its greatest superiority relative to other screening tests in the detection of conventional adenomas <1 cm in size and serrated class lesions. Detection of SSPs is a major deficiency of flexible sigmoidoscopy because SSPs are predominantly in the proximal colon,[51] of CT colonography because the lesions tend to be flat,[52] and of FIT[53] probably because SSPs have no or few surface blood vessels with less tendency to bleed than conventional adenomas. The combined FIT–fecal DNA test achieves its greatest relative performance compared with FIT alone in the detection of serrated class lesions, related to the poor sensitivity of FIT for these lesions and the inclusion of hypermethylation markers in the DNA panel.[53] Hypermethylation is a feature of serrated lesions.[33]

Specific Screening Tests

Colonoscopy

The advantages of colonoscopy include high sensitivity for cancer and all classes of precancerous lesions, single-session diagnosis and treatment, and long intervals between examinations (10 years) in subjects with normal examinations. One or 2 negative examinations may signal lifetime protection against CRC.[54] Patients who value the highest level of sensitivity in detection of precancerous lesions and are willing to undergo invasive screening should consider choosing colonoscopy. Although no randomized trials of colonoscopy for screening have been completed, extensive evidence from adenoma cohorts,[30,31] cohort studies on incidence and mortality,[55,56] and case-control studies[57–64] support the efficacy of colonoscopy in preventing incident CRC and cancer deaths. One cohort study[56] and 3 case-control studies[58,59,64] were performed in screening populations. Reductions in incidence and mortality are approximately 80% in the distal colon and 40% to 60% in the proximal colon, at least in the United States and Germany.[57,59,61,62,64] Furthermore, indirect evidence from randomized trials of fecal occult blood testing[65] and sigmoidoscopy,[66] as well as studies showing highly variable cancer protection provided by different colonoscopists,[67,68] also supports a protective effect of colonoscopy against CRC. These findings are consistent with the observed population trends in the United States.[11,12]

Disadvantages of colonoscopy include the need for thorough bowel cleansing, a higher risk of perforation relative to the other screening tests, higher risk of aspiration pneumonitis (particularly when the procedure is performed with deep sedation),[69] a small risk of splenic injury requiring splenectomy, and a greater risk of postprocedural bleeding compared with other screening tests. A meta-analysis of population-based studies found risks of perforation, bleeding, and death of .5 per 1000, 2.6 per 1000, and 2.9 per 100,000, respectively.[70] Bleeding after colonoscopy is almost entirely related to polypectomy. When electrocautery is used for resection of all colorectal polyps, most bleeds occur after resection of small lesions. This relates entirely to the high prevalence of these lesions because increasing polyp size and proximal colon location are the major risk factors for bleeding per individual resected polyp.[71] Cold resection techniques are effective and nearly devoid of clinically significant bleeding risk and can be generally advised for nonpedunculated lesions <1 cm in size.[72] Despite these risks, colonoscopy is the preferred approach to management of any benign colorectal polyp regardless of size or location because the alternative of surgical resection has higher mortality and cost compared with colonoscopy.[73,74] To the extent that other screening tests effectively identify large lesions, they result in colonoscopy and do not prevent adverse events related to colonoscopic resection of large lesions.

A major disadvantage of colonoscopy is operator dependence in performance. Operator dependence affects detection of cancer,[67,68,75] adenomas,[76,77] and serrated lesions[40,41,78]; selection of appropriate screening and surveillance intervals after colonoscopy[79]; and effective resection of colorectal polyps.[80] In general, gastroenterologists performing colonoscopy are more effective than non-gastroenterologists in prevention of cancer[62,81–83] and detection of precancerous polyps.[84] However, substantial

Table 3. Tools for Patients to Enhance Colonoscopy Quality

Questions for patients to ask prospective colonoscopists to help ensure a high-quality examination
1. What is your adenoma detection rate? (should be ≥ 25% overall or ≥ 30% for male patients and ≥ 20% for female patients)
2. What is your cecal intubation rate (should be ≥ 95% for screening colonoscopies and ≥ 90% overall)
3. Do you use split-dosing of bowel preparations? (effective bowel preparation requires that at least half the preparation be ingested on the day of the colonoscopy)
Checks of the endoscopy report after the procedure
1. Does the report include photographs of the end of the colon, including the appendiceal orifice and ileocecal valve/terminal ileum? (this demonstrates that the full extent of the colon was examined)
2. Is the bowel preparation quality described? (the preparation must be adequate to ensure effective examination)

operator dependence within gastroenterologists is consistently observed,[42,43,76–78] so that selection of a colonoscopist by specialty is not adequate protection against suboptimal operator performance. Table 3 shows a list of questions that patients can ask potential colonoscopists to judge whether performance is likely to be at a high level. Afterward, the colonoscopy report should contain the items in Table 3 as an additional check on the adequacy of the procedure.

Fecal Immunochemical Test

Advantages of FIT include its noninvasive nature, 1-time sensitivity for cancer of 79% in 1 meta-analysis,[85] fair sensitivity for advanced adenomas (approximately 30%), and low 1-time cost (approximately $20). FIT is recommended annually in the United States. The MSTF has recently issued detailed recommendations on the technical performance of FIT[86] and considers FIT an essential element of the CRC screening armamentarium for all practitioners. FIT is commonly the test of choice in programmatic screening, an excellent second choice for practitioners using sequential testing who offer colonoscopy first, and should likely always be one of the tests included in a multiple-options approach. Disadvantages of FIT include the need for repeated testing, which can be problematic in the nonprogrammatic (opportunistic) setting,[13] and poor or no sensitivity for serrated class precursor lesions.[53] However, there is no evidence that cancers arising through serrated class lesions are less likely to bleed than those arising via adenomas.

FIT–Fecal DNA Test

The U.S. Food and Drug Administration (FDA) approved a CRC screening test that is a combination of a FIT and markers for abnormal DNA[53] (Cologuard; Exact Sciences; Boston, Mass). The Center for Medicaid & Medicare Services approved the test for reimbursement and recommends performance at 3-year intervals. In a large screening colonoscopy study, patients underwent FIT, the combined FIT–fecal DNA test, and colonoscopy. The FIT–fecal DNA test had a 1-time sensitivity for CRC of 92%. The FIT assay tested in the study had 73.8% sensitivity for cancer, suggesting that most cancer sensitivity of the FIT–fecal DNA test can be achieved without addition of DNA markers. Advantages of the FIT–fecal DNA test include the highest single-time testing sensitivity for cancer of any noninvasive, nonimaging CRC screening test. Also, the study demonstrated 40% sensitivity for SSPs >1 cm in size. The sensitivity of FIT for SSPs was equal to the false-positive rate, indicating no sensitivity.

The major disadvantages of the FIT–fecal DNA test are a substantial decrease in specificity (86.6% in persons with normal colonoscopy or nonadvanced lesions and 89.8% in those with normal colonoscopy), compared with 96% for the FIT test alone, and high cost relative to FIT. Specificity decreased with increasing age and was only 83% in persons aged >65 years. The cost of the FIT–fecal DNA test is approximately $600 for privately insured patients and about $500 for Medicare patients, about 10 times the direct costs of annual FIT. Moreover, there is a further increase in relative costs related to higher numbers of colonoscopies per test. However, specificity of every 3-year testing with the FIT–fecal DNA test may be approximately equal to the anticipated specificity over 3 years of annual FIT testing. There is currently no information regarding the programmatic sensitivity of the FIT–fecal DNA test.

Annual FIT is more effective and less costly than FIT–fecal DNA every 3 years,[87] so the FIT–fecal DNA test is unlikely to replace FIT in large organized screening programs. The FIT–fecal DNA test could be particularly appropriate for patients in the 50- to 65-year age group who seek a noninvasive test with very high sensitivity for cancer, because the test has better specificity in this age group. Available evidence suggests that asymptomatic patients with a positive FIT–fecal DNA test and a negative high-quality colonoscopy do not need the colonoscopy repeated or evaluation of the remainder of the GI tract.

CT Colonography

CT colonography has replaced double-contrast barium enema as the test of choice for colorectal imaging for nearly all indications. CT colonography is more effective than barium enema and better tolerated.[88,89]

Advantages of CT colonography include a lower risk of perforation compared with colonoscopy and sensitivity of 82% to 92% for adenomas ≥1 cm in size.[88–91] Disadvantages of CT colonography include the use of bowel preparation in most centers in the United States. CT colonography can be performed with laxative-free protocols, but this results in clear reductions in sensitivity relative to colonoscopy,[91] including for large polyps. The sensitivity of CT

colonography for polyps <1 cm is less than colonoscopy,[88–91] and detection of flat[92] and serrated lesions[93] are major deficiencies of CT colonography. Detection of extracolonic findings by CT colonography is common, and these findings have been classified by the American College of Radiology according to their clinical relevance.[94] Radiation exposure is generally viewed as a disadvantage of CT colonography.[14] Evidence that CT colonography reduces CRC incidence or mortality is lacking.

Even in centers where CT colonography has long been available, the impact of CT colonography is limited. At one university, after full development of a CT colonography program, CT colonography accounted for about 10% of colorectal imaging studies, even with the availability of insurance coverage.[95,96] Primary care physicians view the need for frequent follow-up colonoscopy examinations and management of incidental extracolonic findings as major factors limiting the utility of CT colonography.[96] In general, despite an extensive literature investigating the performance of CT colonography, the test has limited impact on CRC screening compliance.[95] However, CT colonography appeals to a niche of patients who are willing to undergo bowel preparation and are concerned about the risks of colonoscopy. When used, the recommended interval is 5 years in patients with normal CT colonography. We continue to recommend that patients with polyps ≥6 mm in size at CT colonography undergo colonoscopy.[1]

Flexible Sigmoidoscopy

Randomized controlled trials confirm reductions in distal colon or rectosigmoid cancer incidence and/or mortality of 29% to 76% with flexible sigmoidoscopy.[66,97–99] Flexible sigmoidoscopy can prevent a small fraction (14%) of proximal colon cancers, if liberal criteria are used to indicate colonoscopy based on flexible sigmoidoscopy findings.[66] Advantages of flexible sigmoidoscopy include disproportionately lower cost and risk compared with colonoscopy, a more limited bowel preparation, and no need for sedation. Disadvantages of flexible sigmoidoscopy include a lower benefit in protection against right-sided colon cancer compared with the level of protection achieved in case-control and cohort studies using colonoscopy. Also, the absence of sedation leads to a low satisfaction experience for patients, such that they are less willing to repeat the examination compared with colonoscopy.[100] Further, the concept of examining only part of the colon has been unpopular in the United States, so that screening by flexible sigmoidoscopy has almost disappeared from opportunistic screening settings.[9] Some groups have endorsed the combination of flexible sigmoidoscopy plus FIT for screening,[14] but compliance challenges associated with completing 2 screening tests and the dramatic decline in screening flexible sigmoidoscopy make significant uptake of this combination unlikely.

Flexible sigmoidoscopy when used is often recommended at 5-year intervals. However, endoscopic screening in general is more effective in the left than the right side of the colon, and there is no clear reason why flexible sigmoidoscopy should not be recommended at 10-year intervals, similar to the recommendation for colonoscopy. The MSTF considers that either 5- or 10-year intervals are acceptable but favors 10-year intervals.

Capsule Colonoscopy

Capsule colonoscopy has been approved by the FDA for imaging the proximal colon in patients with previous incomplete colonoscopies and more recently for patients who need colorectal imaging but who are not candidates for colonoscopy or sedation. Capsule colonoscopy is not approved by the FDA for screening average-risk persons. Advantages of capsule colonoscopy are the achievement of endoscopic imaging without an invasive procedure and avoiding the risks of colonoscopy. Disadvantages are that the bowel preparation is more extensive than that for colonoscopy. Also, because the logistics of performing same-day colonoscopy on patients with positive capsule studies are quite difficult, most patients with positive studies will require re-preparation and colonoscopy on a separate day. In a large screening trial in 884 patients, capsule colonoscopy had 88% sensitivity for detecting patients with a conventional adenoma ≥6 mm in size but was ineffective for the detection of serrated lesions, and 9% of patients had technically failed examinations for inadequate cleansing or rapid transit of the capsule.[101]

Overall, the burden associated with bowel preparation and the relative superiority of colonoscopy are such that capsule colonoscopy would be expected to appeal to a niche population concerned about the risks of colonoscopy, in a fashion similar to CT colonography. Currently, lack of FDA approval for screening and lack of reimbursement are major obstacles to its use.

Septin9 Assay

The first FDA-approved serum test for CRC screening is the Septin9 assay (Epigenomics, Seattle, Wash). In a large screening colonoscopy study, this test had a sensitivity of 48% for detection of CRC and no sensitivity for detection of precancerous polyps.[102] The test is expensive relative to FIT.

The advantage of the Septin9 test is that it is a serum assay and is at least potentially more convenient for patients. Some patients who refused colonoscopy preferred this test over FIT.[103]

Disadvantages of the Septin9 assay are markedly inferior performance characteristics compared with FIT, including lower sensitivity for cancer, inability to detect advanced adenomas,[104] and low cost-effectiveness relative to other screening tests.[105] The test appears to have higher sensitivity for late-stage compared with early-stage cancer.[102] The willingness of patients with positive Septin9 tests to undergo colonoscopy remains uncertain. The uncertainties regarding the true clinical utility of Septin 9 makes shared decision-making difficult. Clinicians should inform patients of the uncertain benefits of this test on CRC mortality, the inability of the assay to detect polyps, and the array of superior alternatives. The best frequency for performing the

test is uncertain. Given these limitations, the MSTF suggests that Septin9 not be used for screening.

Cost Issues

A consistent finding is that CRC screening by any available modality is cost-effective compared with no screening,[106,107] and in some models screening results in cost savings. This finding relates in part to the high costs of CRC treatment. Numerous modeling studies have addressed the relative cost-effectiveness of 2 or more screening tests. The conclusions of the models frequently vary, likely depending in part on the assumptions of the respective models. For example, different models comparing colonoscopy and CT colonography have had variable conclusions.[108] Consistent trends reveal that FIT performs well compared with other screening tests.[106,107,109] Colonoscopy also performs well in most models,[106–108,110] and, in general, the traditional tests are more cost-effective than the newer modalities, including CT colonography, FIT–fecal DNA, capsule colonoscopy, and the Septin9 assay.[105–107,111–113] Newer tests could reach cost-effectiveness by substantially increasing compliance,[112,113] but evidence of improved compliance is lacking. Some models support the cost-effectiveness of risk-stratified approaches to screening.[114] Screening remains cost-effective in patients into their mid-80s if they have few comorbidities and limited prior screening.[115,116]

Quality of Screening

Variable performance of screening tests affects at least colonoscopy, sigmoidoscopy, CT colonography, and FIT. Optimal results in CRC screening cannot be achieved without optimizing the technical performance and reporting of tests and ensuring that patients undergo appropriate follow-up after testing. The MSTF has made detailed recommendations regarding the technical performance of FIT[86] and has previously issued quality recommendations regarding the technical performance of sigmoidoscopy[117] and colonoscopy.[118] The recommendations of the MSTF regarding quality in the technical performance of colonoscopy[118] were largely incorporated in quality recommendations from a combined American College of Gastroenterology–American Society for Gastrointestinal Endoscopy Task Force on quality in 2006[119] and 2015,[120] and the MSTF endorses the American College of Gastroenterology–American Society for Gastrointestinal Endoscopy Task Force recommendations.

The burden of performing high-quality FIT falls largely on primary care physicians and/or the healthcare systems in which they work. In the opportunistic setting there may not be resources allocated to systematically ensure that FIT-positive patients are referred for colonoscopy and that FIT-negative patients are offered repeat testing or to monitor whether compliance with quality targets is adequate.[13] Inability to allocate resources to monitor the quality of FIT testing is a factor favoring reliance on sequential testing with colonoscopy the first test offered.

Unlike primary care physicians, the main role of gastroenterologists in the screening process is to perform colonoscopy on patients referred for primary colonoscopy screening or for colonoscopy to evaluate other positive screening tests. As such, a primary task of gastroenterologists is to perform high-quality colonoscopy and cost-effective follow-up. The adenoma detection rate, originally proposed by the MSTF in 2002,[118] has emerged as the most important and highly variable measure of the quality of mucosal inspection during colonoscopy. Two large studies have validated the adenoma detection rate as a predictor of cancer prevention by colonoscopy.[67,68] Measurement of the adenoma detection rate is mandatory to appreciating whether a colonoscopist should be performing screening colonoscopy. Patients should expect a prospective colonoscopist to provide his or her adenoma detection rate, which should meet or exceed recommended minimum thresholds (Table 3).

Practical Considerations

No published randomized trials have directly compared and reported the relative effects of different tests on CRC incidence or mortality. Several trials are ongoing, but results are not yet available. When compared using simulation models that are dependent on assumptions about natural history of disease, patient acceptance of screening, and test performance, several tests appear to be similarly effective.[121] Therefore, practical considerations are important for informing our recommendations.

A common statement made with regard to CRC screening is that “the best test is the one that gets done.” The MSTF endorses this concept because it is generally better for any person who is eligible to be screened to undergo some screening test rather than not be screened at all. On the other hand, the core concept underlying sequential testing is that offering the “best” test(s) first optimizes the sensitivity and/or cost-effectiveness of screening and still leaves the opportunity to offer other tests when patients decline. As an extreme example, the MSTF considers that equating the Septin9 assay with colonoscopy would be a disservice to patients, because the sensitivity of colonoscopy for cancer and advanced lesions exceeds that of Septin9 by a very large margin. Given these disparities in the performance of individual tests, the MSTF groups the available tests into 3 tiers based on various performance features and costs (Table 4).

The tier 1 tests representing the cornerstone of CRC screening are colonoscopy every 10 years and annual FIT (Table 4). The use of these 2 tests as the primary screening measures provides a framework for screening that is simple and accommodates almost every screening setting. In organized programmatic screening FIT will often be offered as the primary screen, but colonoscopy can be considered as an alternative for patients and physicians who prefer or request it. In the opportunistic setting, colonoscopy will often be preferred when the infrastructure to ensure annual performance of FIT is not available. As noted above, 1 of the most challenging aspects of FIT screening in the

Table 4. Multi-Society Task Force Ranking of Current Colorectal Cancer Screening Tests

Tier 1
Colonoscopy every 10 years
Annual fecal immunochemical test
Tier 2
CT colonography every 5 years
FIT–fecal DNA every 3 years
Flexible sigmoidoscopy every 10 years (or every 5 years)
Tier 3
Capsule colonoscopy every 5 years
Available tests not currently recommended
Septin 9

opportunistic setting is ensuring repeated annual performance. Using a tier 1 approach that focuses on 2 tests makes the discussion of CRC screening tests between physician and patient manageable and feasible, and, as noted above, expanding the number of options in the initial discussion beyond 2 did not increase screening rates.[19] Colonoscopy and FIT can be adapted readily to either the sequential offer of screening (colonoscopy is offered first with FIT reserved for those who decline colonoscopy), the multiple-options approach (colonoscopy and FIT are each discussed with patients, and if both are declined the discussion moves sequentially to tier 2 tests), and the risk-stratified approach (eg, colonoscopy is offered first to men age >60 and women age >65 with no prior screening, and FIT is offered to persons under these ages and persons with negative prior colonoscopy). Risk stratification may also take into account factors such as cigarette smoking, diabetes, and obesity.

The rationale for placing tests in the tier 2 and 3 categories follows from the discussion above of individual tests. The ranking implies equivalence for tests within each category, but this is not the intent of the MSTF. For example, flexible sigmoidoscopy screening has strong evidence to support its use. However, the steady decline in the use of flexible sigmoidoscopy in the United States[9,10] suggests that any strong endorsement of flexible sigmoidoscopy is not consistent with the reality of the test's lack of popularity among patients and poor reimbursement for physicians. The strong evidence base supporting flexible sigmoidoscopy leads us to place the test in the tier 2 category, although we expect that most practitioners using a sequential approach would move to CT colonography or FIT–fecal DNA in patients who decline colonoscopy and FIT, because these tests are less invasive and survey the entire colon.

Performance characteristics alone would place capsule colonoscopy in tier 2. However, offering capsule colonoscopy as a tier 2 test in a sequential methodology currently would often lead to frustration because reimbursement for screening capsule colonoscopy is seldom available at this time, and the test itself is frequently not available. The onerous bowel preparation and the lack of systems to accomplish same-day colonoscopy in most patients with a positive capsule colonoscopy are additional factors placing capsule colonoscopy in the tier 3 category at this time.

In summary, we suggest that the tiered system (Table 4) has numerous advantages. Predominant reliance on tier 1 tests offers modalities with optimal effectiveness, cost-effectiveness, complete colon screening, proven popularity with patients, and a simplified discussion (compared with offering 5-7 different tests) and still leaves room to offer other tests in a sequential fashion. If patients decline colonoscopy and FIT, all tests in tier 2 are acceptable CRC screening tests, but each has deficiencies relative to the tier 1 tests.

Recommendations

1. We recommend colonoscopy every 10 years or annual FIT as first-tier options for screening the average-risk persons for colorectal neoplasia (strong recommendation; moderate-quality evidence).
2. We recommend that physicians performing screening colonoscopy measure quality, including the adenoma detection rate (strong recommendation, high-quality evidence).
3. We recommend that physicians performing FIT monitor quality (strong recommendation, low-quality evidence). The recommended quality measurements for FIT programs are detailed in a prior publication.[86]
4. We recommend CT colonography every 5 years or FIT–fecal DNA every 3 years (strong recommendation, low-quality evidence) or flexible sigmoidoscopy every 5 to 10 years (strong recommendation, high-quality evidence) in patients who refuse colonoscopy and FIT.
5. We suggest that capsule colonoscopy (if available) is an appropriate screening test when patients decline colonoscopy, FIT, FIT–fecal DNA, CT colonography, and flexible sigmoidoscopy (weak recommendation, low-quality evidence).
6. We suggest against Septin9 for CRC screening (weak recommendation, low-quality evidence).

Family History of CRC and Polyps

We recommend that screening in most average-risk persons be initiated at age 50 years. A family history of CRC or certain polyps can modify the recommended starting age and the frequency of screening. The MSTF has previously issued recommendations for screening in persons with Lynch syndrome,[34] which is a genetically defined inherited syndrome caused by mutations in 1 or more mismatch repair genes. Patients in families that meet the clinical criteria for hereditary nonpolyposis CRC but have microsatellite-stable CRCs have family colon cancer syndrome X, which has not been genetically defined.[122] Persons in families with syndrome X should undergo colonoscopy at least every 3 to 5 years, beginning 10 years before the age at diagnosis of the youngest affected relative.

A family history of CRC in a first-degree relative increases the risk of CRC regardless of the age at diagnosis of

Table 5. MSTF Recommendations for Persons With High-Risk Family Histories Not Associated With Polyp Syndromes

Family history	Recommended screening
Lynch Syndrome Family Colon Cancer Syndrome X	See reference 34
Colorectal cancer or an advanced adenoma in two first-degree relatives diagnosed at any age OR colorectal cancer or an advanced adenoma in a single first-degree relative at age < 60 years	Colonoscopy every 3-5 years beginning 10 years before the age at diagnosis of the youngest affected relative Colonoscopy every 5 years beginning 10 years before the age at diagnosis of the youngest affect interval or age 40, whichever is earlier; for those with a single first-degree relative with colorectal cancer in whom no significant neoplasia appears by age 60 years, physicians can offer expanding the interval between colonoscopies
Colorectal cancer or an advanced adenoma in a single first-degree relative diagnosed at age ≥ 60 years	Begin screening at age 40 years; tests and intervals are as per the average-risk screening recommendations (Table 4)

the affected relative.[123–125] There is a gradient of risk such that the younger the age of the affected relative, the greater the risk.[123–125] The MSTF has previously used age 60 as a threshold of risk elevation, so that a single first-degree relative diagnosed with CRC at age <60 years warrants both earlier screening and at more-frequent intervals.[1] Recent population-based studies[123,124] and reviews of risk associated with a positive family history[125] support using age at diagnosis of CRC above or below 60 years in the affected first-degree relative as a risk stratifier. We continue to recommend that persons with a family history of CRC in a first-degree relative diagnosed at <60 years undergo colonoscopy every 5 years beginning at age 40 years or 10 years before the age the relative was diagnosed, whichever comes first (Table 5). In a randomized controlled trial, there was a nonsignificant trend toward detection of more advanced neoplasia in subjects with a positive family history who underwent colonoscopy compared with FIT.[126] Thus, patients with a positive family history who decline colonoscopy should be offered FIT screening.[126]

The greatest relative risk of CRC appears to be in persons <50 years who have a first-degree relative with CRC diagnosed at <50 years.[123-125] Compliance in young persons with a family history of CRC is suboptimal, and clinicians should make special efforts to ensure that screening occurs. Recent evidence suggests if persons with a single first-degree relative with a family history of CRC reach the age of approximately 60 years without manifesting significant colorectal neoplasia,[127] then they are unlikely to be at increased risk of CRC and can be offered the option of expanding the interval between examinations.

When first-degree relatives have documented advanced serrated lesions (SSPs ≥10 mm in size, or an SSP with cytologic dysplasia, or a traditional serrated adenoma ≥10 mm in size), there is no clear evidence as to how to proceed, unless the relative meets criteria for serrated polyposis.[46] Currently, we recommend that screening for first-degree relatives of persons with advanced serrated lesions should be similar to the screening of first-degree relatives of persons with advanced conventional adenomas.

Persons with a single first-degree relative with CRC who was diagnosed at age ≥60 years are recommended to begin screening at 40 years.[128] However, the tests and intervals for testing are the same as the average-risk screening recommendations (Tables 5 and 4).

We no longer recommend that persons with a family history of adenomas in a first-degree relative undergo early screening, unless there is clear documentation of an advanced adenoma in a first-degree relative. In most cases the patient has no information regarding whether the family member's adenoma was advanced, and in this case we recommend that it be assumed the adenomas or polyps were not advanced. If a colonoscopy and/or pathology report(s) is available for a family member that documents an advanced adenoma or there is a report of a polyp requiring surgical resection, an advanced adenoma in a family member is considered established. These considerations regarding adequate documentation of advanced precancerous neoplasms in first-degree relatives before intensifying screening apply to documentation of both advanced adenomas and advanced serrated lesions. First-degree relatives with advanced adenomas are recommended to be weighted the same as first-degree relatives with CRC (Table 5). The yield of colonoscopic screening in first-degree relatives of persons with advanced adenomas is substantially increased.[129–131]

Recommendations

1. We suggest that persons with 1 first-degree relative with CRC or a documented advanced adenoma diagnosed at age <60 years or with 2 first-degree relatives with CRC and/or documented advanced adenomas undergo colonoscopy every 5 years beginning 10 years younger than the age at which the youngest first-degree relative was diagnosed or age 40, whichever is earlier (weak recommendation, low-quality evidence).

2. We suggest that persons with 1 first-degree relative diagnosed with CRC or a documented advanced adenoma at age ≥60 years begin screening at age 40. The options for screening and the recommended intervals are the same as those for average-risk persons (weak recommendation, very-low-quality evidence).

3. We suggest that persons with 1 or more first-degree relatives with a documented advanced serrated lesion (SSP or traditional serrated adenoma ≥10 mm in size or an SSP with cytologic dysplasia) should be screened according to above recommendations for persons with a family history of a documented advanced adenoma (weak recommendation, very-low-quality evidence).

4. We recommend that persons with 1 or more first-degree relatives with CRC or documented advanced adenomas, for whom we recommend colonoscopy, should be offered annual FIT if they decline colonoscopy (strong recommendation, moderate-quality evidence).

Considerations Regarding Age and CRC Risk

CRC screening is recommended to begin at age 50 years in most average-risk persons, including in prior recommendations from the MSTF.[1] Recent modeling supports this recommendation.[121] Several issues related to age and CRC risk warrant specific discussion.

The incidence of CRC is strongly age related and continues to rise with increasing age. Partly because of widespread screening in the United States, the incidence of CRC in falling by 3% to 4% per year in persons age ≥50 years.[12] The incidence of CRC in persons under age 50 is increasing in the United States.[132,133] Although the reasons for this rising incidence remain unclear and the relative incidence in persons under age 50 remains low, the increasing incidence of CRC in young people is a major public health concern.

The best course of action with regard to the rising incidence of CRC in young people is currently not certain. When a young person develops fatal CRC, the loss of life years is great. The first step in reducing CRC morbidity and mortality in persons age <50 years is aggressive evaluation (usually colonoscopy) of patients with colorectal symptoms, specifically those with bleeding symptoms: hematochezia, iron deficiency anemia, and/or melena with a negative upper endoscopy. Persons with bleeding symptoms evaluated with tests other than colonoscopy (eg, sigmoidoscopy) should have a bleeding source identified and treated, and the patient should be followed to resolution of the symptom. Patients who have nonbleeding symptoms (eg, abnormal bowel habit, change in bowel habit or shape, or abdominal pain) and who have no evidence of bleeding do not have an increased risk of CRC when they undergo colonoscopy.[134,135]

There is currently insufficient evidence to recommend systematic screening in asymptomatic persons <50 years old who lack specific risk factors related to family history or Lynch syndrome. The yield of screening colonoscopy in this age group is low in available studies,[136] and the biologic reasons for the increasing incidence of CRC in persons under age 50 years are uncertain. Additional study of the benefits and harms of screening in persons <50 years is warranted, perhaps particularly in persons with known colorectal risk factors such as cigarette smoking, diabetes mellitus, and obesity.[137-139]

Relative to other races, African Americans have lower screening rates for CRC, higher incidence rates, earlier mean age at onset, worse survival and late-stage presentation, and a higher proportion of cancers before age 50.[140–143] These various effects result from both socioeconomic and biologic factors.[144] Two of the member organizations of the MSTF endorsed beginning average-risk screening in African Americans at age 45,[22,145] and the American College of Physicians recommended beginning at age 40.[146] The scientific rationale for beginning screening earlier includes the higher overall incidence rates and younger mean age at onset of CRC in African Americans.[140–143] A recent joinpoint regression analysis[147]and a MISCAN-Colon microsimulation model[148] both supported screening African Americans approximately 5 years earlier compared with whites. There are few data on the yield of screening in African Americans before age 50 or whether earlier screening improves outcomes. In persons over age 50, some reports have identified a higher risk of advanced polyps in African Americans.[149] The recommendations to begin screening earlier have served an important role in stimulating discussion of and research on CRC in African Americans, increasing awareness in physicians of an important public health problem and racial disparity in health outcomes in the United States, and increasing awareness of CRC in African Americans. Increasing screening rates in African Americans generally is an area of obvious importance. Provider recommendation is key,[150] and navigation can improve compliance to colonoscopy screening.[151] Additional study of the yield of screening in persons under age 50 is needed, particularly in African Americans.

The age to stop screening can be individualized. Screening is potentially beneficial in persons up to age 86 if there has not been previous screening[116] but should be considered in the context of comorbidities and life expectancy. Persons with previously negative screening tests, particularly negative screening colonoscopy, could consider stopping at age 75 years.[14] In a variation of this recommendation, the MSTF has recommended that persons with previous negative screening stop when their life expectancy is less than 10 years.[1] Thus, the recommendation to stop screening can be reasonably based on patient age and comorbidities.

The wishes of the patient should be considered in uncertain cases. These considerations do not necessarily apply in the surveillance setting, where patients with advanced neoplasia may benefit from surveillance colonoscopy even at an advanced age, depending on comorbidities and the confidence in neoplasia clearing at colonoscopy.

Recommendations

1. We recommend that screening begin in non–African American average-risk persons at age 50 years (strong recommendation; moderate-quality evidence).

2. We suggest that screening begin in African Americans at age 45 years (weak recommendation, very-low-quality evidence).

3. We recommend that adults age <50 years with colorectal bleeding symptoms (hematochezia, unexplained iron deficiency anemia, melena with a negative upper endoscopy) undergo colonoscopy or an evaluation sufficient to determine a bleeding cause, initiate treatment, and complete follow-up to determine resolution of bleeding (strong recommendation, moderate-quality evidence).
4. We suggest that persons who are up to date with screening and have negative prior screening tests, particularly colonoscopy, consider stopping screening at age 75 years or when life expectancy is less than 10 years (weak recommendation, low-quality evidence).
5. We suggest that persons without prior screening should be considered for screening up to age 85, depending on consideration of their age and comorbidities (weak recommendation, low-quality evidence).

Summary

CRC screening should begin at age 50 years in asymptomatic persons. Colonoscopy every 10 years and annual FIT are currently the first considerations for screening. Colonoscopy every 10 years has advantages in the opportunistic screening setting. Annual FIT is likely to be preferred in organized screening programs. Positioning of the 2 tests can be reasonably based on a sequential offer (colonoscopy first with FIT offered to patients who decline colonoscopy, followed by second-tier tests for patients who decline FIT), a multiple-options approach where both tests are discussed with patients (followed by a sequential offer of second-tier tests to patients who decline both colonoscopy and FIT), or a risk-stratified approach (colonoscopy is offered to patients with a higher pretest probability of neoplasia, and FIT is used in persons with a lower pretest probability of neoplasia).

Persons with a history of CRC or a documented advanced adenoma in a first-degree relative age <60 years or 2 first-degree relatives with these findings at any age are recommended to undergo screening by colonoscopy every 5 years, beginning 10 years before the age at diagnosis of the youngest affected relative, or at age 40, whichever is earlier. Persons with a single first-degree relative diagnosed at ≥60 years with CRC or an advanced adenoma can be offered average-risk screening options beginning at age 40 years.

The incidence of CRC is rising in persons under age 50. Patients under age 50 with bleeding symptoms consistent with a colorectal source should be aggressively evaluated and treated. We suggest that screening begin at age 45 in African Americans. Discontinuation of screening should be considered when patients who are up to date with screening and have had negative screening tests, particularly colonoscopy, reach age 75 years or when life expectancy is <10 years. Persons without prior screening should be considered for screening up to age 85 years, depending on comorbid conditions and life expectancy.

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