New Screening Guidelines for Colorectal Cancer: A Practical Guide for the Primary Care Physician

James E. Allison, MD, FACP, AGAF[a,*], Michael B. Potter, MD, FAAFP[b]

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- Colorectal cancer • Screening guidelines
- Fecal occult blood tests • Stool DNA tests
- Flexible sigmoidoscopy • Colonoscopy • Virtual colonoscopy

Until recently, most clinical guidelines in the United States were in general agreement about the tests available for colorectal cancer screening, recommending fecal occult blood tests (FOBT) every year, flexible sigmoidoscopy (FSIG) every 5 years, both these tests together, double contrast barium enema (DCBE) every 5 years, or colonoscopy every 10 years.[1–5] However, in 2008, the release of 2 new sets of guidelines[6,7] makes it necessary for primary care physicians to re-examine their approach to screening. The organizations that developed these new guidelines examined the available evidence using different approaches and came to different conclusions about which tests deserve to be recommended and how they should be offered in clinical practice.

Most primary care doctors know that colorectal cancer is the second leading cause of cancer mortality in the United States, and there is strong evidence that screening for this disease saves lives; however, screening rates continue to lag well behind those for other cancers.[8] The reasons for low colorectal cancer screening rates are complex. In particular, busy clinicians may not have the time to explain the rationale for screening or list of testing options with sufficient frequency or detail to motivate patients to complete screening when indicated, or to provide information and assess patient

[a] Division of Gastroenterology, San Francisco General Hospital, 1001 Potrero Avenue, NH-3D, San Francisco, CA 94110, USA
[b] Department of Family and Community Medicine, University of California, San Francisco, Box 0900, San Francisco, CA 94143, USA
* Corresponding author. San Francisco General Hospital, 1001 Potrero Avenue, NH-3D, San Francisco, CA 94110.
E-mail address: jallison@medsfgh.ucsf.edu (J.E. Allison).

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preferences among the various options.[9] Primary care groups often lack office systems to reach out to patients who are due for screening and to support patients in completing tests that are recommended, despite evidence that they can make a difference.[10] Overcoming these obstacles could have tremendous benefits for patients. For example, approximately 50% of adults age 50 years and older are up to date with recommended colorectal cancer screening. If this figure were to increase to 90%, roughly 14,000 lives would be saved each year.[11]

The most influential factor in determining whether a patient is screened is recommendation from a physician.[12,13] The primary goal of this article is to review and critique the new guidelines for average-risk screening in adults older than 50 years. Armed with such information, primary care physicians will be better prepared to address the important issues of how to make sure that every one of their eligible patients is given the education, opportunity, and support to be screened.

THE GROUPS PRODUCING GUIDELINES

One set of guidelines was developed by a group effort of the American Cancer Society (ACS), American College of Radiology (ACR), and the 3 major American gastroenterology professional societies: the American College of Gastroenterology (ACG), the American Gastroenterological Association (AGA), and the American Society for Gastrointestinal Endoscopy (ASGE). Together these societies are referred to as the US Multisociety Task Force on Colorectal Cancer (USMSTF). The committee members included leading experts on the available screening tests and they were drawn from a variety of constituencies, including physician members of professional societies, as well as cancer screening advocates and survivors. The second set of guidelines was developed under the auspices of the Agency for Health Care Research and Quality (AHRQ), a US Government supported organization created to improve the quality, safety, efficiency, and effectiveness of health care for all Americans. AHRQ appoints members to the United States Preventive Services Taskforce (USPSTF), an independent panel of experts in primary care and prevention that systematically reviews the evidence of effectiveness and develops recommendations for clinical preventive services, including guidelines for colorectal cancer screening. **Tables 1** and **2** show the ACS/ACR/USMSTF Guideline and **Table 3** shows the AHRQ/USPSTF Guideline.

PUTTING THE TWO NEW SETS OF GUIDELINES INTO CONTEXT

The ACS/ACR/USMSTF Guideline divides the recommended screening tests into those it identifies as primarily effective at detecting colorectal cancer (CRC), the fecal tests, and those that identify cancer and premalignant adenomatous polyps, the structural exams. Tests belonging to the former group include the sensitive guaiac test (GT), the fecal immunochemical test (FIT), and stool DNA test (sDNA). The Guideline asserts that fecal tests are primarily effective at identifying CRC and that, although some polyps may also be detected, "the opportunity for prevention is both limited and incidental and is not the primary goal of CRC screening with these tests."[6] Tests belonging to the latter, more invasive group, with higher sensitivity for polyps in addition to cancers, are defined as FSIG, colonoscopy (CSPY), DCBE, and computed tomographic colonography (CTC or "virtual colonoscopy"). According to the Guideline, colon cancer prevention should be the primary goal of CRC screening and, thus, these screening tests should be encouraged if resources are available and patients are willing to undergo an invasive test. Given this strong statement, it is important to explore which of these "preferred" screening options are practical choices for most primary care patients, and which tests are backed by strong evidence showing cancer prevention and reduction in mortality.

The AHRQ-sponsored USPSTF performed a systematic review of the literature and found that there is not enough evidence to support sDNA or CTC.[17] They also decided not to review the evidence for DCBE. For the remaining tests, they did not focus on test sensitivity for polyps, but focused on potential population-based mortality reductions that could be achieved using each test in a screening program for adults aged 50 to 75 years.[18] Neither the ACS/ACR/USMSTF Guideline nor the AHRQ/USPSTF Guideline formally took the relative test costs or test availability into account when determining which tests to recommend over others. In the following sections, the evidence to support the use of different CRC screening tests is reviewed.

FLEXIBLE SIGMOIDOSCOPY

There are four high-quality case–control and cohort studies that verify the benefit of FSIG in decreasing mortality from CRC[19–22] but the only large prospective randomized controlled trials investigating the effect of screening FSIG on decreasing CRC incidence have yet to be completed. Whatever the results, in the United States the use of sigmoidoscopy has decreased dramatically from 1993 to 2002. During these years, there was a 54% decrease in sigmoidoscopy use between the earliest and latest periods studied. Over the same period, there was more than a 6-fold increase in colonoscopy usage.[6] The ACS/ACR/USMSTF Guideline proposes that the reasons for this decrease in sigmoidoscopy use include decreased reimbursement and lack of adequately trained examiners. Other possible contributing factors include the publication in 2000 of the Lieberman and Imperiale studies showing the yield of advanced neoplasms discovered at screening colonoscopy and the publicity these studies generated.[23,24] These publications on screening colonoscopy were followed by an editorial that stated "There is suspicion among physicians that in recommending FSIG to screen persons for colorectal cancer, we are promoting a suboptimal approach. Relying on FSIG is as clinically logical as performing mammography of one breast to screen women for breast cancer. The failure of insurance companies to cover the costs of colonoscopic screening is no longer tenable."[25] The American College of Gastroenterology in 2000 proclaimed colonoscopy as the preferred screening option.[3]

The television media were quick to pick up on the push for colonoscopy as the best screening choice. On July 19, 2000, Dr Timothy Johnson, ABC News Medical Editor, said "The results of the Lieberman study may put doctors in an ethical—and possibly legal—bind. How can I in good conscience still advise patients to use sigmoidoscopy given we have evidence it will miss a significant number of early polyps." Katie Couric of the NBC News program the Today Show had her own colonoscopy televised for the viewing audience and, on the program's Web site, there was a picture of her having that colonoscopy and saying "It's considered the most effective test for detecting colon cancer." Her publicity led to documentable increases in screening colonoscopies and this is now known as the "Katie Couric Effect".[16] Soon after the colonoscopy studies and statements by opinion leaders and the press, Congress added colonoscopy to the CRC screening tests covered for Medicare patients, bypassing the usual method of Centers for Medicare and Medicaid Services (CMS) analysis before such approval.

As for the assertion that doing sigmoidoscopy for colorectal cancer screening makes as much sense as screening for breast cancer with mammography on one breast, a recent editorial offered this rebuttal: "There has been the overused analogy

Table 1
ACS/ACR/USMSTF guideline

Test	Interval	Key Issues for Informed Decisions
Tests that detect adenomatous polyps and cancer		
FSIG with insertion to 40 cm or to splenic flexure	Every 5 years	Complete or partial bowel preparation 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 at sigmoidoscopy usually result in referral for colonoscopy
Colonoscopy	Every 10 years	Complete bowel preparation 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 preparation is required; if patients have 1 or more polyps ≥6 mm, colonoscopy will be recommended, and follow-up colonoscopy will require complete bowel preparation; risks of DCBE are low; rare cases of perforation have been reported
CT colonography	Every 5 years	Complete bowel preparation is required; if patients have 1 or more polyps ≥6 mm, colonoscopy will be recommended, but if same-day colonoscopy is not available, a second complete bowel preparation will be required before colonoscopy; risks of CTC are low; rare cases of perforation have been reported; extracolonic abnormalities may be identified at CT colonography that could require further evaluation

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Table 1
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Test	Interval	Key Issues for Informed Decisions
Tests that primarily detect cancer		
gFOBT with high sensitivity for cancer and FIT with high sensitivity for caner	Annual	Depending on manufacture's recommendations, 2–3 stool samples collected at home are needed to complete testing; a single sample of stool gathered during a digital examination in the clinical setting is not an acceptable stool test and should not be done; positive results are associated with an increased risk of colon cancer and advance neoplasia; colonoscopy should be recommended if the test results are positive; if the result is negative, it should be repeated annually; patients should understand that one-time testing is likely to be ineffective
Stool DNA test 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 result is positive, colonoscopy will be recommended; if the result is negative, the appropriate interval for a repeat test is uncertain

From Levin B, Lieberman DA, McFarland, et al. 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. Gastroenterology 2008;134:1570–95.

of FSIG as being similar to screening for breast cancer with mammography of a single breast. The "1 breast" argument, while a catchy sound bite, is grossly misleading. If performing mammography on 1 breast detected 67% to 80% of breast cancers and adding an examination of the other breast required sedation, another specialist, a more difficult preparation, a driver, additional time lost from work, a longer wait for scheduling, carried 15 times the risk of serious complications, and cost 3 to 4 times more, and had substantially less supporting outcomes data, we might be performing (or in the United States, at least discussing) single-breast mammography."[15]

DOUBLE CONTRAST BARIUM ENEMA

The Joint Guideline points out many deficiencies in the studies used to support DCBE as an effective screening test for colorectal cancer and the general lack of enthusiasm

Table 2
Guidelines for screening and surveillance for the early detection of colorectal adenomas and cancer in individuals at increased risk or at high risk

Risk Category	Age to Begin	Recommendation	Comment
Increased risk: patients with history of polyps at prior colonoscopy			
Patients with small rectal hyperplastic polyps[14]	–	Colonoscopy or other screening options at intervals recommended for average-risk individuals	An exception is patients with a hyperplastic polyposis syndrome. They are at increased risk for adenomas and colorectal cancer and need to be identified for more intensive follow up
Patients with 1 or 2 small tubular adenomas with low grade dysplasia[14]	5–10 years after the initial polypectomy	Colonoscopy	The precise timing within this interval should be based on other clinical factors (such as prior colonoscopy findings, family history, and the preferences of the patient and judgment of the physician)
Patients with 3–10 adenomas or 1 adenoma >1 cm or any adenoma with villous features or high-grade dysplasia[14]	3 years after the initial polypectomy	Colonoscopy	Adenomas must have been completely removed. If the follow up colonoscopy is normal or shows only 1 or 2 small, tubular adenomas with low-grade dysplasia, then the interval for the subsequent examination should be 5 years
Patients with >10 adenomas on a single examination[14]	<3 years after the initial polypectomy	Colonoscopy	Consider the possibility of an underlying familial syndrome
Patients with sessile adenomas that are removed piecemeal[14]	2–6 months to verify complete removal	Colonoscopy	Once complete removal has been established, subsequent surveillance needs to be individualized based on the endoscopist's judgment. Completeness of removal should be based on both endoscopic and pathologic assessments

Increased risk: patients with colorectal cancer			
Patients with colon and rectal cancer should undergo high quality perioperative clearing[15]	3–6 months after cancer resection, if no unresectable metastases are found during surgery; alternatively, colonoscopy can be performed intraoperatively	Colonoscopy	In the case of nonobstructing tumors, this can be done by preoperative colonoscopy. In the case of obstructing colon cancers, CTC with intravenous contrast or DCBE can be used to detect neoplasms in the proximal colon
Patients undergoing curative resection for colon or rectal cancer[2]	1 year after the resection (or 1 year following the performance of the colonoscopy that was performed to clear the colon of synchronous disease)	Colonoscopy	This colonoscopy at 1 year is in addition to the perioperative colonoscopy for synchronous tumors. If the examination performed at 1 year is normal, then the interval before the next subsequent examination should be 3 years. If that colonoscopy is normal, then the interval before subsequent examination should be 5 years. Following the examinations at 1 year, the intervals before subsequent examination may be shortened if there is evidence of HNPCC or if adenoma findings warrant earlier colonoscopy. Periodic examination of the rectum for the purpose at 3- to 6-month intervals for the first 2 or 3 years, may be considered after low-anterior resection of rectal cancer
Increased risk: patients with a family history			
Either colorectal cancer or adenomatous polyps in a first-degree relative before age 60 years or in 2 or more first-degree relatives at any age[16]	Age 40 years or 10 years before the youngest case in the immediate family	Colonoscopy	Every 5 years

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Table 2
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Risk Category	Age to Begin	Recommendation	Comment
Either colorectal cancer or adenomatous polyps in a first-degree relative $\geq$60 years or in 2 second-degree relatives with colorectal cancer[16]	Age 40 years	Screening options at intervals recommended for average-risk individuals	Screening should begin at an earlier age, but individuals may choose to be screened with any recommended form of testing
High risk			
Genetic diagnosis of FAP or suspected FAP without genetic testing evidence[16]	Age 10–12 years	Annual FSIG to determine if the individual is expressing the genetic abnormality and counseling to consider genetic testing	If the genetic test is positive, colectomy should be considered
Genetic or clinical diagnosis of HNPCC or individuals at increased risk of HNPCC[16]	Aged 20–25 years or 10 years before the youngest case in the immediate family	Colonoscopy every 1–2 years and counseling to consider genetic testing	Genetic testing for HNPCC should be offered to first-degree relatives of persons with a known inherited MMR gene mutation. It should also be offered when the family mutation is not already known, but 1 of the first 3 of the modified Bethesda criteria is present
Inflammatory bowel disease,[16] chronic ulcerative colitis, and Crohn colitis	Cancer risk begins to be significant 8 years after the onset of pancolitis or 12–15 years after the onset of left-sided colitis	Colonoscopy with biopsies for dysplasia	Every 1–2 years; these patients are best referred to a center with experience in the surveillance and management of inflammatory bowel disease

Abbreviations: CTC, computed tomographic colonography; DCBE, double-contrast barium enema; FAP, familial adenomatous polyposis; FSIG, flexible sigmoidoscopy; HNPCC, hereditary nonpolyposis colon cancer; MMR, mismatch repair.

From Levin B, Lieberman DA, McFarland, et al. 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. Gastroenterology 2008;134:1570–95.

Table 3
AHRQ/USPSTF guideline

Population	Adults Aged 50–75 Years	Adults Aged 76–85 Years	Adults Older Than 85 Years
Recommendation	Screen with high-sensitivity FOBT, sigmoidoscopy, or colonoscopy Grade: A	Do not screen routinely Grade: C	Do not screen Grade: D
	For all populations, evidence is insufficient to assess the benefits and harms of screening with computed tomographic colonography and fecal DNA testing Grade: I (insufficient evidence)		
Screening tests	High-sensitivity FOBT, sigmoidoscopy with FOBT, and colonoscopy are effective in decreasing colorectal cancer mortality The risks and benefits of these screening methods vary Colonoscopy and flexible sigmoidoscopy (to a lesser degree) entail possible serious complications		
Screening test intervals	Intervals for recommended screening strategies: • Annual screening with high-sensitivity FOBT • Sigmoidoscopy every 5 years, with high-sensitivity FOBT every 3 years • Screening colonoscopy every 10 years		
Balance of harms and benefits	The benefits of screening outweigh the potential harms for 50- to 75-year-olds	The likelihood that detection and early intervention will yield a mortality benefit declines after age 75 years because of the long average time between adenoma development and cancer diagnosis	
Implementation	Focus on strategies that maximize the number of individuals who get screened Practice decision making; discussions with patients should incorporate information on test quality and availability Individuals with a personal history of cancer or adenomatous polyps are followed by a surveillance regimen, and screening guidelines are not applicable		
Relevant USPSTF recommendations	The USPSTF recommends against the use of aspirin or nonsteroidal antiinflammatory drugs for the primary prevention of colorectal cancer This recommendation is available at: www.preventiveservices.ahrq.gov		

From US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. Ann Intern Med 2008;149:627–37; with permission.

of radiologists for DCBE due to its labor-intensive nature, low reimbursement rate, and greater interest in newer and more complex technologies such as CTC. There are a lack of randomized controlled trials evaluating the efficacy of DCBE as a primary screening modality to reduce incidence or mortality from CRC in average-risk adults and no case–control studies evaluating its performance. Study designs in the available literature are retrospective and often do not report findings from an asymptomatic or average-risk population. The rate of missed CRC with DCBE is of concern. In 1 large multicenter study published in 1997, it was 14.8%.[14] A more recent study evaluated the miss rate with DCBE in a large population in Ontario, Canada, and found even greater miss rates using this procedure.[26] Little screening for colon cancer by DCBE occurs in the United States and the use of this screening test is declining in the Medicare population, the Department of Veterans' Affairs, and in current clinical practice.[27–29]

COMPUTED TOMOGRAPHIC COLONOGRAPHY OR VIRTUAL COLONOSCOPY

CTC is a noninvasive, rapid imaging method for detecting pathology in the colon and rectum. Publication of the ACS/ACR/USMSTF Guideline marks the first time that CTC has been recommended as a screening choice by any of the United States guideline makers. The evidence for its efficacy in reducing mortality from CRC is indirect and, as pointed out in the ACS/ACR/USMSTF Guideline, no prospective, randomized, controlled clinical trial has been initiated (nor is one currently planned).[6]

Major technology advances have occurred since 1994 when CTC was first introduced, including progression from single-slice scanners and software capable only of displaying 2-dimensional images to multislice scanners allowing for faster imaging and thinner sections. Software now can provide 3-dimensional "fly through" endoluminal views that simulate optical colonoscopy (OC).[30,31]

CTC requires no sedation and can be performed in 10 to 15 minutes. CTC software advances now allow for typical reading times of 10 minutes or less. Final reports can be issued within 2 hours of study completion. There is no risk of bleeding or perforation. A small flexible rectal catheter is used to insufflate air or CO_2. Prone and supine helical thin-section CT scans of the abdomen and pelvis are obtained while the patient holds his/her breath. Three-dimensional reconstructions are made from the images obtained. CTC is performed after colonic cleansing. The test currently requires the same bowel cleansing preparation as OC but "prepless" CTC is under development. In this case water-soluble (Gastrografin) and barium contrast material are used to tag residual fluid and retained stool. Imaging software can then digitally subtract all opacified fluid and stool from the image by a process known as electronic cleansing.[32–34]

Serious questions have been raised about using CTC as a screening test. Critics of CTC cite lack of evidence for effectiveness but many believe there is sufficient evidence to equate the performance characteristics of CTC with that of OC. A large CTC multicenter study of 2600 average-risk individuals, the American College of Radiology Imaging Network (ACRIN) National CT Colonography Trial, compared the accuracy of CTC to OC and revealed evidence that the two technologies were equivalent in identifying polyps and cancers in average-risk patients.[35] Although the evidence for detection equivalency to OC has been fairly well established, many issues surrounding this test remain, including training and technology requirements for high quality examinations, the policy of leaving small polyps in place, appropriate surveillance intervals, and radiation exposure. Radiation exposure is reportedly low for CTC but the effects of low-dose radiation over time remain uncertain. The test must be done by experienced operators using the latest in CTC technology. At present the only state authorizing reimbursement is Wisconsin, where operator experience and technology are "state of the art." CMS did not approve CTC for Medicare reimbursement stating that the evidence is inadequate to conclude that CT colonography is an appropriate colorectal cancer screening test under §1861(pp)(1) of the Social Security Act. (https://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?from2=viewdraftdecisionmemo.asp&;id=220&;).

COLONOSCOPY

There is no direct evidence that screening with colonoscopy reduces mortality from colorectal cancer but many[3] argue that such proof is unnecessary. Central to this argument is the link between identification and removal of precancerous polyps and a subsequent reduction in colon cancer incidence. The reasoning goes that if a test with low sensitivity for cancer and polyps such as FOBT and a test that evaluates only the distal bowel such as FSIG have been shown to decrease colon cancer mortality in randomized controlled and case–control trials, then complete bowel examination with colonoscopy is likely to save more lives. The push for colonoscopy as the screening test of choice has been further fueled by the publication of cross-sectional studies using colonoscopy in asymptomatic, predominantly average-risk persons. Several studies have reported that FSIG, FOBT or the combination of sigmoidoscopy and FOBT have a miss rate of advanced proximal neoplasm of between 25 and 65% compared with colonoscopy.[23,36–38] The miss rate of advanced neoplasms by tests other than colonoscopy raises 3 questions: what is an advanced neoplasm; how likely is it to lead to death from colorectal cancer; and what is the evidence that screening for colorectal cancer with colonoscopy actually decreases the incidence of colorectal cancer in the right colon?

The fear engendered in nonspecialist physicians and patients by the term "advanced neoplasms" is unnecessary and unhelpful for making rational decisions regarding screening test choices. Advanced colonic neoplasms consist of a range of lesions, from large tubular adenomas to early adenocarcinoma, that vary widely in terms of the risk of progression to fatal cancer. Large polyps (>1 cm) become colorectal cancers at a rate of roughly 1% per year.[39] A large polyp, left in situ, has a cumulative risk of malignancy at 20 years of only 24%.[40] The development of invasive cancer from a small (<10 mm) adenoma is extremely unlikely in less than 5 years.[41] The term *advanced adenoma* was originally created not because the clinical course is known to be ominous but rather because researchers needed a surrogate outcome more common than colorectal cancer.[42] Advanced neoplasia may be considered a convenient proxy for colorectal cancer but its use as an outcome measure may be misleading in screening studies because the natural history of this lesion is unknown.[43]

As most polyps, even the "advanced" ones, do not directly lead to death from colon cancer, the most important value of one test over another is the incremental benefit of mortality reduction that test confers on the patient being screened. A person at age 50 years has a 5% lifetime risk of being diagnosed with colorectal cancer and a 2.5% chance of dying from it.[44] (USPSTF http://www.preventiveservices.ahrq.gov) The evidence suggests that if the other available screening tests, such as guaiac FOBT, FIT, and sigmoidoscopy, are employed as recommended, the incremental benefit of colonoscopy in decreasing patient mortality from CRC is small.[18] The concern about missed "advanced neoplasms" in once-only testing with methods other than colonoscopy may not be as important as it has been portrayed. Tests that occur more often, such as FOBT tests or FSIG, leave the potential for discovery of a missed advanced neoplasm on subsequent screens before it has become malignant or lethal.

Even proponents of colonoscopy as the screening test of choice admit that protection against colorectal cancer by colonoscopy is imperfect.[45,46] Others have raised the question of whether colonoscopy is a tarnished gold standard.[47] The questions raised by these investigators are the result of several published studies showing that colonoscopy has a significant miss rate of advanced neoplasia. Furthermore, evidence is growing that protection against cancer afforded by having a negative colonoscopy is quite small (12%–33%) in the proximal colon as compared with the distal colon where it is quite large (80%). These findings are consistent with trends in distal CRC rates in the United States, which have been steadily decreasing since 1985, whereas rates for proximal colon cancers have remained largely unchanged.[14,48–56]

The findings in these studies, especially regarding colorectal cancer prevention in the right colon, are surprising and somewhat counterintuitive. However, there are reasonable explanations. First and foremost is the quality of the colonoscopic examinations. The gold standard study for evaluation of appropriate surveillance intervals is the National Polyp Study (NPS).[57] In the NPS study, if the baseline colonoscopy did not clear the colon with high confidence, the examination was repeated before the patient was entered into the surveillance program. A high confidence examination was defined as one with excellent preparation, complete polypectomy, and slow withdrawal. These standards required repeat examinations in 13% of cases. Quality standards that have been developed include slow withdrawal time (eg, at least 6 minutes in normal colonoscopies in which no biopsies or polypectomies are performed), excellent preparation for maximum visibility, and complete polypectomy for all polyps removed but especially for large sessile adenomas removed by the piecemeal technique. Inherent limitations of colonoscopy include the difficulty of identifying hidden lesions behind folds or flat lesions.[58,59] It is also likely that some cancers are rapidly growing tumors that will not be uncovered soon enough given a recommended 10-year surveillance interval. Mounting evidence indicates that the biology of cancers in the right colon, especially neoplasms characterized by inactivation of a mismatch repair gene, may make right-sided cancers grow more rapidly than left-sided ones. This biologic difference could also explain the difference in cancer reduction observed between the right and left side of the colon in programmatic colonoscopy screening every 10 years.

The effects that population screening with colonoscopy might have on health care policy and the availability of scarce medical resources are legitimate considerations when deciding on screening tests for our citizens because our budget deficit in 2009 is estimated to be more than a trillion dollars. Thirty-seven million American citizens live in poverty and more than 47 million are without health insurance.[60] There are many other worthy causes (eg, prescription drug benefits, screening for breast cancer, childhood vaccinations) that are legitimately competing for health care dollars. A CDC National Health Interview Survey shows that despite all efforts to raise screening rates since colonoscopy has been promoted as the best test in 2000, by 2005, only 50% of Americans of screening age were up to date with screening.[8] More importantly, this finding was only for those with insurance. Those without insurance coverage were found to have a rate of colorectal cancer screening of only 24%. A 2008 publication from the CDC[61] reported no progress in reducing most CRC screening disparities between 2000 and 2005 and emphasized a need to increase CRC screening in all subpopulations, but in particular Hispanic women and uninsured men and women. A highly publicized study in New York City reported a screening program for the uninsured using colonoscopy and a patient navigator to increase compliance.[62] From

November 2003 to May 2006, 351 patients were screened or approximately 140 patients per year. Contrast those results with those of the New York State Department of Health Cancer Services Program's Colorectal Cancer Screening Initiative. From August 1997 to September 2007 between 7000 and 9000 patients were screened with FOBT per year. Of the 97 cancers diagnosed in patients with a positive FOBT, 66% were in stage 1 or 2. Of the 1305 polyps diagnosed and removed, 768 (59%) were adenomatous. At Kaiser Permanente Northern California in 2008, 419,000 FIT were distributed to patients eligible for screening. The response rate was 52%, positivity rate 5.4%, and positive predictive value for cancer 3.4%. To date, 403 cancers have been detected. Clearly, these examples demonstrate that a large screen eligible population is more effectively screened with FIT than OC.

The level of resources required to provide a skilled colonoscopic examination for all eligible United States citizens is enormous. Persons age 50 years and older in the United States and eligible for colorectal cancer screening number 75 million. This number has been rising rapidly as the "baby boomers" have come of age. Ladabaum and Song estimate that screening colonoscopy every 10 years would require 8.1 million colonoscopies per year, including surveillance, with other strategies requiring 17% to 58% as many colonoscopies.[63] Evidence suggests the manpower necessary to provide a skilled colonoscopic examination for all eligible United States citizens is inadequate.[64,65] In a letter to the editor of *The New England Journal of Medicine*, a physician at Baylor College of Medicine estimated that screening their 62,000 outpatients aged 50 years and older by colonoscopy would take about 30 years.[66] Since Medicare's decision to reimburse for screening colonoscopy, some gastroenterologists are spending up to 50% of their practice time simply performing colonoscopy.[67] If screening colonoscopy becomes the preferred screening test for CRC, the need for sufficient endoscopists could lead to unqualified examiners absorbing the overflow and the increased inaccuracy and complications could undo the small incremental benefit that the test offers.[68]

A recent review of CRC screening, surveillance, and primary prevention published in *Gastroenterology*[69] cites several recent studies describing the findings of screening colonoscopy in asymptomatic average-risk populations.[38,70–74] The investigators point out that despite differences in the study populations, the fraction of persons with no colorectal neoplasia is consistent, ranging from 75% to 83%. Furthermore; they write that these recent findings are comparable to most of the previously published screening colonoscopy studies and should remind us that most screening colonoscopies will show no adenomas or cancers. Using data from all the screening colonoscopy studies, they calculate that, on average, 9 individuals must undergo screening colonoscopy to detect 1 person with 1 or more nonadvanced adenoma, 23 to detect an advanced adenoma, 20 for advanced neoplasia, and 143 for cancer.

The millions who undergo screening for no apparent gain are subject to harms that could cumulatively outweigh the benefits to the smaller group (those found to have advanced neoplasms) especially if the added benefit is not great compared with other screening options.[68,75] The serious complication rate in the VA colonoscopy screening study, in which the endoscopists were all skilled, was 10 in 3000 or 1 in 300 including stroke and myocardial infarction.[36] In a study of 16,318 primarily diagnostic colonoscopies performed in the Kaiser Permanente Health System in patients older than 40 years, 82 complications occurred or 5 complications for every 1000 colonoscopies. The complication rate was less than 1 in 1000 for colonoscopies without biopsy and about 7 in 1000 colonoscopies with biopsy or polypectomy. Perforations were the least common complication, and bleeding was the most common complication.[76]

The screening colonoscopy findings featured in the recent *Gastroenterology* review[69] highlight the need to identify a way to estimate absolute risk for individual persons so that screening colonoscopy may be more efficiently targeted to those with advanced neoplasia. One way to do that is to use the very tests that the ACS/ACR/USMSTF label as "ineffective for prevention of CRC" and the use of which does not fulfill the primary goal of CRC screening. Let us examine the fecal tests included in the ACS/ACR/USMSTF Guideline and evaluate the evidence for their inclusion.

FECAL DNA TEST

From 2000 to 2007 experts on screening with the fecal DNA test said at national meetings and in print that stool screening has historically relied on detection of occult blood, which has been proven to be an inherently insensitive and nonspecific marker for screen relevant neoplasia.[77] The enthusiasm for this test was generated from results of several small studies of patients with known colorectal neoplasm who were tested with stool DNA tests comprised of multiple neoplastic-specific DNA alterations and called multitarget DNA assays. In one such study using a 21-component DNA panel, the sensitivity of the test for colorectal cancer was reported to be 91% and 82% for adenoma with a respectable specificity of 93%.[78] These promising results led to the first of two large multicenter screening trials comparing this version 1 of the multitarget DNA test, called PreGenPlus, to the standard guaiac-based fecal occult blood test (GT) and the sensitive guaiac-based fecal occult blood test, Hemoccult Sensa.

The results of the first multicenter study, published in 2004,[79] were disappointing. The fecal DNA panel detected 16 of 31 cancers for a calculated sensitivity for cancer of only 52% and the sensitivity of advanced adenoma was only 15%. Although these sensitivities were better than those reported for the standard guaiac test, the results of the study for the GT test were the lowest reported in the literature and were probably the result of lack of quality control in the collection and development of the guaiac test in the many different study sites. Surprisingly, as badly as the GT did with sensitivity, its specificity was better than the stool DNA test (94% for the fecal DNA test and 95% for the GT).

It is reasonable to assume that the ACS/ACR/USMSTF made its recommendation for the stool DNA test based on the findings from this study as it was the only one in the literature to look at a large group of average-risk patients. Thus, the recommendation must have been based on the finding of a 52% reported sensitivity of the PreGenPlus version 1 for cancer. The expert panel said that physicians and institutions should select stool tests that have been shown in the scientific literature to detect most prevalent colorectal cancers in an asymptomatic population. It is important for the primary care physician to understand that this was the finding in only 1 large study of average-risk patients (N = 4404). The results from another large multicenter study sponsored by the Mayo Clinic (N = 3764) was published in the *Annals of Internal Medicine* in October, 2008.[80] The results in this study differed from that of Imperiale and colleagues and the sensitivity for cancer of the fecal DNA test was only 25%, a level that would not qualify PreGenPlus as a recommended stool test by the guideline's authors.

There are other important issues to ponder when considering recommending a stool DNA test for screening. In a report from the Cancer Intervention and Surveillance Modeling Network to the Center for Medicare and Medicaid Services in 2008, the following statement was made: "Only if significant improvements for the DNA stool test characteristics or relative adherence with DNA stool testing compared with other available options can be demonstrated, will stool DNA testing at the current costs of $350 be cost-effective." No data are available to suggest what a safe interval between tests would be. The company has asked CMS for a 5-year screening interval but with sensitivity for cancer only 52% at best, granting a 5-year interval would not be reasonable or safe.

All the above points are made irrelevant because the stool DNA test recommended by the Guideline is not currently available for use in the United States and is not likely to be ever again. LabCorp will be marketing a new stool DNA test called Colosure beginning in September 2008. Colosure was developed with the knowledge gained from the 2 multicenter studies of PreGenPlus. The markers used by Colosure are the DNA integrity assay and vimentin gene methylation. The evidence for its use comes from a study of 40 subjects with known CRC and 122 subjects with a normal colonoscopy. Its sensitivity for cancer was 87.5% and its specificity was 82%.[81] No data are available regarding its performance characteristics for advanced adenomas. Although cheaper than PreGenPlus, Colosure is still more expensive than any of the FOBT and has no supporting data for effectiveness in large average-risk populations. For the primary care physician, the take-home message about use of the fecal DNA test as a colon cancer screening test is that although it is a promising technology, based on evidence from screening studies in large average-risk populations, its present form does not seem to be an improvement over the less costly and more easily performed FIT or sensitive GT.

FECAL OCCULT BLOOD TESTS: GUAIAC AND IMMUNOCHEMICAL

Fecal occult blood tests in the United States have been called the "Rodney Dangerfield" of choices for colorectal cancer screening. "They just don't get respect." The available FOBT tests are variations of 2 types: the guaiac test (GT) and the immunochemical test (FIT).

The Guaiac Test

The GT detects the peroxidase activity of heme either as intact hemoglobin or free heme. In the presence of heme and a developer (hydrogen peroxide), guaiac acid is oxidized producing a blue color. Although there are several GTs available, only 3, Hemoccult II, Hemoccult Sensa (Beckman Coulter Inc.; Primary Care Diagnostics, Los Angeles, CA), and hema-screen (Immunostics, Ocean, NJ), have been extensively evaluated in large screening populations. Hemoccult Sensa (**Fig. 1**) differs from the standard GT because its threshold for detection of peroxidase is set lower than that of the standard GT, thereby increasing sensitivity but decreasing specificity. In screening for colorectal neoplasms, a true positive GT is one that indicates bleeding from a colon cancer or polyp. All other positive results are considered to be false positives. Heme is present in red meat and peroxidase activity is present in fresh fruits and vegetables such as radishes, turnips, and broccoli. These foods, therefore, have the potential to produce false-positive results especially in patients tested with the Sensa test. Some reports suggest that delaying development of GT cards for at least 3 days will decrease the number of false positives due to plant peroxidases and obviate the need for diet restriction of fruits and vegetables.[82,83] Arranging such a processing delay is impractical in most clinical settings and the validity of delaying processing has not been verified in other published studies.[84]

The standard GT has been studied extensively and remains the only test shown by randomized controlled studies to decrease mortality and incidence of colon cancer.[85–91] Accurate interpretation of results for the GT requires training and supervision especially when interpreting borderline results. Results are affected by vitamin C, which inhibits the guaiac reaction.[92–95] The person undergoing screening is required to

Fig. 1. Hemoccult Sensa cards each with 2 windows for guaiac impregnated paper (*Courtesy of* Beckman Coulter, Inc., Fullerton, CA; with permission.) A wooden spatula is used to smear a small stool specimen onto each window. In the presence of heme and a hydrogen peroxide developer, guaiac acid is oxidized producing a blue color. Accurate interpretation of results for GT requires training and supervision especially when interpreting borderline results.

collect the stool sample in the dry state and to sample the feces with a wooden stick. These requirements limit patient acceptance. In a group of motivated volunteers in an Australian population where consumption of red meat is high, a restrictive diet reduced participation by 13%.[96] The standard GT is currently in use in the United Kingdom and the Canadian Province of Ontario as the test of choice for population screening programs. The ACS/USMSTF Guideline does not recommend this test but does say if a GT is to be used; it should be the sensitive GT, Hemoccult Sensa.

The Fecal Immunochemical Test

Recent data have shown that new FOBTs, called fecal immunochemical tests (FIT), are superior to the more commonly used guaiac tests (GT). The operating and performance characteristics of the FIT address many of the weaknesses of the GT. They use specific antibodies to human hemoglobin, albumin, or other blood components. Some use monoclonal and polyclonal antibodies to detect the intact globin protein portion of human hemoglobin. The labeled antibody attaches to the antigens of any human globin present in the stool resulting in a positive test result (**Fig. 2**). Globin does not survive passage through the upper gastrointestinal tract; therefore, FITs detecting globin are specific for occult bleeding from the large bowel. In addition, FITs do not react with nonhuman globin or with food such as uncooked fruits and vegetables that may contain peroxidase activity. Dietary restriction is therefore not necessary when screening with these tests. They are also unaffected by medicines such as nonsteroidal antiinflammatory drugs or vitamin C. All these features may make use of FIT more acceptable to those screened than the GT.

All of the recommendations for an FOBT option in CRC screening guidelines were made on the basis of findings from randomized controlled trials using GT. If, as it seems, the FIT has better performance characteristics and acceptance than the GT, a compelling argument exists for recommending its use as the FOBT of choice in CRC screening programs.[28] In summary, the advantages of FIT over GT include the following:

1. FITs have superior sensitivity and specificity.[84,97]
2. FITs use antibodies specific for human globin and are, unlike the GT, specific for colorectal bleeding and not affected by diet or medications.
3. Some FITs can be developed by automated developers and readers. This innovation allows for management of large numbers of tests in a standardized manner with excellent quality assurance.
4. There is evidence that FIT use improves patient participation in screening for CRC.[98]
5. New technology for FITs allows them to quantify fecal hemoglobin so that sensitivity, specificity, and positivity rates can be adjusted in screening for colorectal neoplasia.[99,100]
6. The developing instrument for some FITs has the ability to read a bar code on the test. This feature ensures accurate identification of the person screened and allows for a print-out of the result as well as a reminder print-out for future compliance.

Once these innovations have been perfected and tested in large asymptomatic populations, government agencies or individual health plans will be able to decide what positivity rate their budget and human resources can accommodate and still have good sensitivity and specificity for advanced neoplasms in an annual screening program.

The new and improved FIT choices are now available and reimbursable by the CMS at $22 per test (including completed test card with 2 samples and analysis). In 2004, CMS concluded that adequate evidence exists to determine that the FIT is an appropriate and effective CRC screening test for detecting fecal occult blood in Medicare beneficiaries aged 50 years or older. The CMS reimbursement decision has led to the approval of several FITs by the US Food and Drug Administration (FDA) for marketing in the United States. These, include InSure (manufactured by Enterix Inc., a Quest Diagnostics company, Lyndhurst, NJ), Hemoccult-ICT (Beckman Coulter, Inc., Primary Care Diagnostics, Los Angeles, CA), Instant-View (Alpha Scientific Designs, Inc., Malvern, PA), immoCARE (Care Products, Inc., Waterbury, CT), MonoHaem (Chemicon International, Inc., Temecula, CA), Clearview Ultra-FOB (Wampole Laboratory, Princeton, NJ), OC Auto Micro 80 (Polymedco, Cortland Manor, NY), Hemosure One Step (WHPM, Inc. Beverly, MA), among others (**Fig. 3**). Magstream HemSp is the automated version of a test previously marketed by the name HemeSelect. The advances provided by the new version are machine reading of the test end point (to avoid problems related to human error), automation that allows a throughput of up to 1000 tests per hour for each

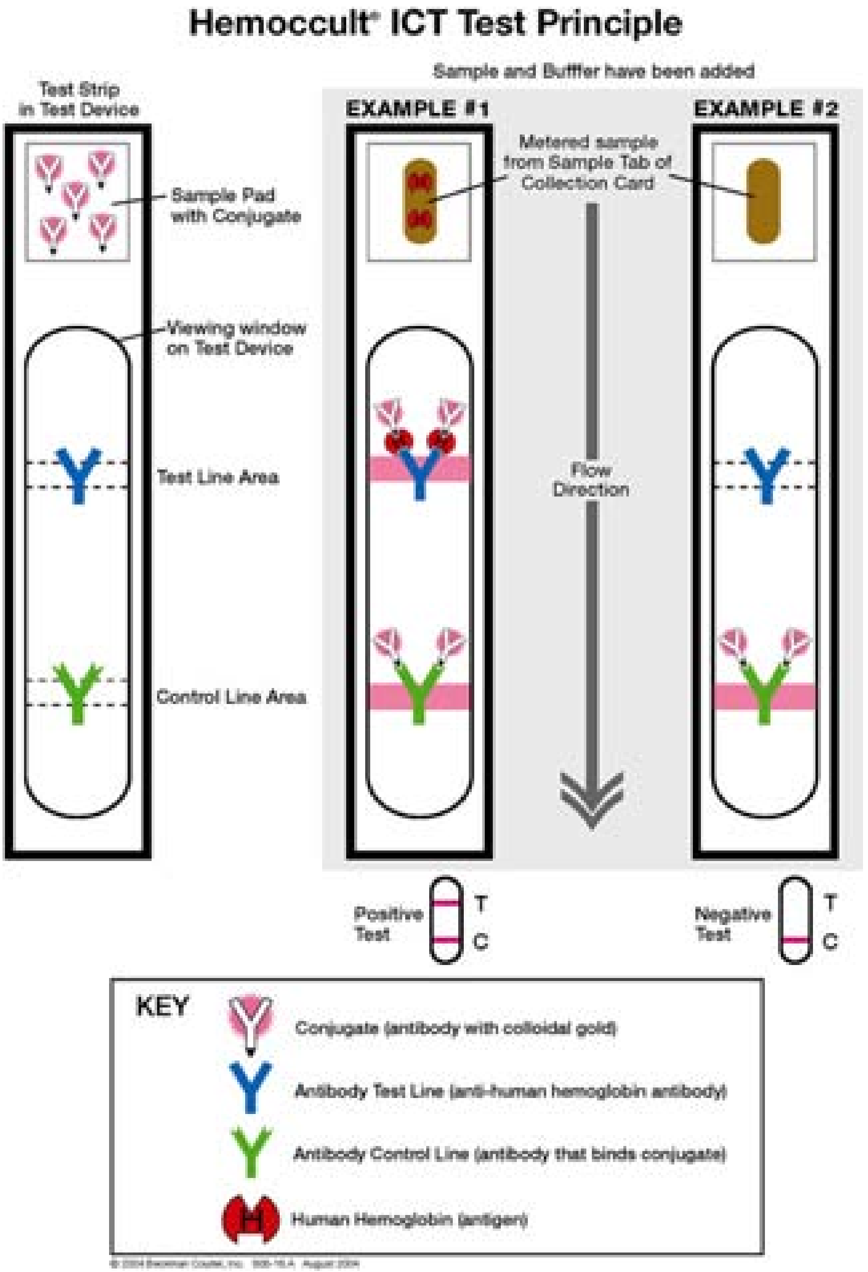

Fig. 2. Cartoon demonstrating FIT methodology for Hemoccult ICT. (*Courtesy of* Beckman Coulter, Inc., Fullerton, CA; with permission.)

auto-analyzer, and the ability to choose test performance characteristics rather than having to rely on the end point chosen by the manufacturer. Magstream 1000/Hem SP (Fujirebio Inc. Tokyo, Japan) is marketed in Australia and Europe by Bayer Diagnostics as Bayer Detect but it is not yet available in the United States.

Fig. 3. Fecal immunochemical tests with different sampling methods: brush (*Courtesy of* Enterix Inc., A Quest Diagnotcis Co., Edison, NJ; with permission.), stick (*Courtesy of* Beckman Coulter, Inc., Fullerton, CA; with permission.), probe.

Although it would be helpful to be able to recommend 1 or a few of these FIT choices as the best option, there is, as yet, insufficient information to do so. Only FlexSure OBT (currently marketed as Hemoccult ICT), HemeSelect (SmithKline Diagnostics, Palo Alto, CA), InSure, MagStream1000/Hem SP, and recently Polymedco/OC Sensor (Cortland Manor, NY, and Eiken Chemical, Japan) have been evaluated in large numbers (thousands) of average-risk patients with results published in United States peer-reviewed journals.[74,97,100,101] Head-to-head comparisons in large average-risk populations are not yet available. The methodology for stool handling and sampling differ among these tests regarding how (automated or by technician) and where (office or laboratory) the tests are developed. Because the immunochemistry seems to be similar for all of the tests, the advantages for one over another may be in sampling methods and development. The following sampling and development issues are important:

1. Is the sample representative of the whole stool specimen?
2. Are multiple stool specimens important given the known intermittent bleeding that occurs in colonic neoplasms? If so, how many is enough? One study suggests that at least 2 days of sampling is important.[102]
3. What features of the FIT make it more suitable for maximum subject participation?
4. What is the stability of the collected sample, and how can it be transported to the laboratory?
5. What is the acceptability of the FIT for laboratory development? Ease of development by technician or automation?
6. Is the test capable of quantifying the hemoglobin concentration and allowing for differentiation between significant and insignificant colorectal neoplasms and non-neoplastic bleeding lesions?

Representative information about a few of these tests is shown in **Tables 4** to **6**.

Table 4
FIT sampling and testing

FIT	Stools Tested	Sampling Method (Per Stool)	Tests Per Stool	Sample Stability	Safety and Transport
Clearview Instant View (Wampole Laboratory, Princeton, NJ)	One	Spike/pin into exposed surface	One test on 1 sample	Refrigerated as soon as possible	Risk of spill, courier?
InSure FIT (produced by Enterix, Australia; distributed by Quest Diagnostics, Lyndhurst, NI)	Two	Brush, water around whole stool	One test on 2 samples	Dry, stable >14 days	Mail
Hemocult-ICT (Beckman Coulter, Inc., Primary Care Diagnostics, Los Angeles, CA)	Three	Stick, 2 smears of exposed surface	Three tests on 3 samples	Dry, stable >14 days	Mail

Abbreviation: FIT, focal immunochemical test.
Data from Allison JE, Lawson M. Screening tests for colorectal cancer 2006. A menu of options remains relevant. Current Oncol Rep 2006;8:492–8; Mahl, V. Practical Gastroenterology June 2007.

A GUIDELINES-BASED, PRIMARY CARE APPROACH TO COLORECTAL CANCER SCREENING

When considering the evidence for each test and what to recommend in clinical practice, it is worth identifying the similarities and differences between the AHRQ/USPSTF and ACS/ACR/USMSTF Guidelines. Both sets of guidelines still recommend screening for average-risk individuals starting at age 50 years. The USPSTF now recommends taking into account the patient's competing comorbidities before recommending screening after the age of 75 years and states that few people can benefit from screening after the age of 85 years. The ACS/ACR/USMSTF does not give a specific age at which to stop screening, but recommends that competing comorbidities and life expectancy should be considered before ordering cancer screening at any age. Both guidelines should remind clinicians to focus their efforts on patients who are young enough and healthy enough to benefit from treatment of any cancers that are diagnosed through screening.

Table 5
FIT sampling and FIT performance

Sampling Time	Sensitivity, %	Specificity, %
One day	67.9	97.5
Two days	88 (+20)	95.6 (−1.9)
Three days	90.8 (+2.8)	92.1 (−3.5)

Abbreviation: FIT, focal immunochemical test.
Data from Nakama H, Kamijo N, Fujimori K, et al. Relationship between fecal sampling times and sensitivity and specificity of immunochemical fecal occult blood tests for colorectal cancer: a comparative study. Dis Colon Rectum 1997;40:781–4.

Table 6
FIT performance characteristics

FIT	Sensitivity for CRCA, %	Sensitivity for Polyps >1 cm, %	Specificity for CRCA, %	Specificity for Polyps >1 cm, %
HemeSelect (Fujirebio, Inc., Tokyo, Japan)[a]	69	67	95	95
Hemoccult-ICT (Beckman Coulter, Inc., Primary Care Diagnostics, Los Angeles, CA)[b]	82	30	97	97
Magstream 1000 HP (Tokyo, Japan)[b]	66	20	95	95

Abbreviations: CRCA, colorectal cancer lesions; FIT, fecal immunochemical test.
[a] Estimated by long-term follow-up in patient testing negative.
[b] Estimated by gold standard endoscopy sigmoidoscopy or colonoscopy of patients testing negative.
Data from Refs.[74,84,97]

The ACS/ACR/USMSTF continues to recommend colonoscopy as the test of choice for patients who are higher than average risk for colorectal cancer (see **Table 3** for the definition of high-risk patients from the ACS/ACR/USMSTF Guideline). The AHRQ/USPSTF has not issued guidelines for high risk individuals. High-risk individuals include adults who have a personal history of colorectal cancer, a first-degree relative who has been diagnosed with colorectal cancer or a tubular adenoma before the age of 60 years, as well as patients with inflammatory bowel disease, familial adenomatous polyposis, or hereditary familial nonadenomatous polyposis (Lynch syndrome). The guidelines controversy should not obscure the fact that high-risk patients of all ages need to be identified through a periodic and systematic review of personal and family history.

Whereas the ACS/ACR/USMSTF considers any type of stool testing to be inferior to colonoscopy, the decision analysis done by the AHRQ/USPSTF suggests that yearly testing with the newer highly sensitive FOBT (when done consistently) can be as effective as colonoscopy in reducing mortality, which is the ultimate goal of all colorectal cancer screening programs.[18] When offering CRC screening to patients, clinicians should continue to offer whatever CRC screening tests are available in their clinical settings. For example, patients who are unable or unwilling to complete annual FOBT should be reminded of screening options that can be done less frequently, and patients resistant to the cost or invasiveness of colonoscopy should be told about the potential benefits of yearly home FOBT. In clinical settings where the options are limited, clinicians and patients should be reassured that mortality can be reduced with the less expensive stool tests if done consistently with careful follow-up. However, clinicians and patients should be aware that for either type of FOBT to be an effective screening test, it must be done as a home test (not as an in-office test), and for best results it must be done yearly. In addition, any single abnormal test must be followed up with colonoscopy even when other samples are normal or when there is concern that the patient may not have followed the instructions properly. For annual screening to reach a high proportion of eligible patients, proactive approaches should be adopted.[103,104] Similarly, most experienced clinicians are aware that adherence to tests such as FSIG, DCBE, and colonoscopy can be low, even when a referral is written and telephone numbers provided to schedule appointments. Primary care practices that rely on these tests should be proactive in providing patients with appointment times before they leave the office, including appropriate information about the bowel preparations that are required to follow through with the tests. Primary care clinicians can overcome obstacles to referral by establishing standard protocols to help patients successfully navigate their way to complete CRC screening tests.[105]

Another important point is that the AHRQ/USPSTF and ACS/ACR/USMSTF Guidelines now agree that, whereas the first-generation home stool tests such as Hemoccult II can reduce CRC mortality, the newer and more sensitive guaiac and immunochemical tests represent a significant advance in terms of sensitivity for the lesions that we would like to detect. The modest increase in cost for these newer stool tests should be within the reach of even the most resource-limited public health settings, and primary care physicians can play an important role in advocating for more widespread adoption of these tests, especially in settings where costlier and more invasive screening tests are not available. On the other hand, resource-limited settings that perform any type of screening must also ensure that patients diagnosed get the follow-up they need, whether it be colonoscopy after an abnormal FOBT, or oncologic evaluation after a cancer has been diagnosed. As for all types of medically necessary care, primary care clinicians have an obligation to advocate for universal availability of cost-effective clinical services that can save lives.

The practical role of FSIG and DCBE in clinical practice may be somewhat limited by recent evidence showing that they are less preferred by patients than either stool tests or colonoscopy.[106] This, coupled with the low reimbursement rates for these procedures compared with colonoscopy, likely has contributed to declining use of these tests in clinical practice. However, some patients may still prefer these tests, and therefore DCBE and FSIG should remain as screening options, particularly for patients resistant to or unable to complete annual stool testing and who have limited access to other options such as colonoscopy.

Klabunde and colleagues have suggested that colorectal cancer screening rates may be improved by following a New Model of Primary Care that emphasizes (1) a team approach including ancillary staff within a clinical practice, (2) information systems that identify eligible patients at the point of care and prompt clinicians to offer screening when it is due, (3) involving patients in shared decision making about colorectal cancer screening, (4) monitoring practice performance with systems to help target patients most likely to benefit from screening; (5) reimbursement for services provided outside the context of usual care, and (6) training opportunities for staff at all levels of the practice to improve the frequency and quality of culturally appropriate communication that occurs with patients with regard to colorectal cancer screening.[107] Sarfaty and Wender recently published a comprehensive review of evidence-based strategies that correspond with these categories, many of which can be implemented with limited resources in practices with a high degree of motivation.[12] Additional information and specific tools to increase colorectal cancer screening in primary care may be found online in “How to Increase Colorectal Cancer Screening Rates in Practice: a Primary Care Clinician’s Evidence-Based Toolbox and Guide” at www.cancer.org/colonmd under the “For Your Clinical Practice” heading. Armed with these resources and the information reviewed in this article, primary care clinicians should be well prepared to translate the tremendous potential of screening to reduce colorectal cancer mortality into tangible benefits for their patients.

SUMMARY

We have come a long way since screening for colorectal cancer was recommended without supporting evidence. Recommending colorectal cancer screening for all eligible adults is a core obligation for all primary care clinicians. If there is a preferred or best test of those currently available, its superiority must be proven by studies in progress. New developments in stool tests, blood tests, and radiology technology will offer more choices in the future. In the meantime, we must keep an open mind on which test to recommend for our patients and use evidence to make and support that decision, remembering that there are several screening test options with proven efficacy for individuals at average risk for colorectal cancer.

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