

Screening Options and Recommendations for Colorectal Cancer

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ABSTRACT

Screening reduces the burden of disease from colorectal cancer through early detection of cancerous lesions and removal of precancerous polyps. The ideal colorectal cancer screening modality should be cost-effective, increase life-years gained, permit long intervals between tests with high patient compliance and low risk to the patient. Although no single colorectal cancer screening method is perfect, several options exist. Government agencies and medical societies have published screening recommendations with differing guidelines; yet, despite the lack of a consistent standard, it is clear that colorectal cancer screening is cost-effective. In this review, the authors address several options for screening, identify risks and benefits, and present methods to risk stratify patients. A thorough discussion with the patient about potential benefits and harms is critical before initiating any screening regimen.

KEYWORDS: Screening, colorectal cancer, colonoscopy, fecal occult blood test, virtual colonoscopy

Objectives: On completion of this article the reader should be able to summarize screening options for colorectal cancer and be able to risk-stratify patients for colorectal cancer screening.

Approximately 145,000 people in the United States were diagnosed with colon or rectal cancer (CRC) in 2008, making it the third most commonly diagnosed cancer. At the same time, it is estimated that CRC leads to ~50,000 deaths per year.¹ The large number of incident cases, long duration of disease manifestation, and high mortality make CRC an excellent disease to apply screening methods. In addition, screening for CRC is effective because of simple methods for disease detection and reasonable treatment options once disease is identified. Most important, screening for CRC not only detects cancer earlier, but also allows the clinician to intervene and interrupt the well-understood pathway of polyp to cancer.

Given the importance placed on CRC screening, several sensitive and reliable tests are available. Unfortunately, having multiple methods to screen for CRC also leads to considerable confusion regarding which method is best and the optimal timing and interval for screening. This confusion may lead many physicians to reduce the importance paid to CRC screening which many patients indicate is the single most important factor in deciding to undergo screening. Physician confusion likely leads to patient confusion, thereby reducing the number of patients who ultimately get screened. Data from the National Cancer Institute reveal that over 42% of patients were unaware of potential screening options for CRC² and only 35% of respondents were aware that colonoscopy could actually detect CRC.

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Much of the confusion regarding CRC screening may also result from the numerous medical societies and government agencies that have published guidelines for screening. From our review, it is clear that no single guideline is perfect and that any method to get patients into their physicians' offices to address CRC screening is critical. Our present addition to the literature is thus geared toward trying to reduce the confusion regarding CRC screening and outline simple strategies for screening. In this review, we will mainly use guidelines from the U.S. Preventive Services Task Force (USPSTF), recently updated in 2008. We will highlight all screening options as clinicians should be aware of the spectrum of tests and future applications of these tests, yet we will specifically highlight screening tests that are effective at both identifying cancer at an earlier point and preventing cancers through intervention.

FECAL AND SERUM TESTS

Fecal Occult Blood Test

The simplest and least invasive method for CRC detection is the fecal occult blood test (FOBT). The test is based on the understanding that adenomas and CRC lesions tend to bleed. A positive test is noted with detection of pseudoperoxidase activity of heme within the stool. Although simple for patients, accurate screening with FOBT can be difficult. To obtain accurate results, patients must voluntarily conform to dietary restrictions, and the test must be administered multiple times (collecting two samples from three consecutive bowel movements) on multiple occasions (annually or biannually). Multiple sampling increases detection rates by factoring the intermittent nature of bleeding from CRC; however, multiple samples also increase the total number of false-positive results.

FOBT is the only CRC screening test that has shown efficacy in prospective randomized controlled trials. A Cochrane review involving over 300,000 participants in the United States, Denmark, Sweden, and United Kingdom³ revealed a 16% mortality reduction from CRC with screening compared with no screening. These trials also revealed an 80% false-positive rate, leading to increased stress and medical costs from further diagnostic workup. Ultimately, the accuracy of FOBT for detecting CRC is determined by compliance, pooled noncompliance rates are between 33 to 46% for the first screening, which can greatly change the mortality reduction benefits of FOBT.

Fecal Immunochemical Based Stool Tests (FIT)

The fecal immunochemical based stool tests (FIT) is based on the principles of FOBT, but using either monoclonal or polyclonal antibodies to detect the globin

protein found in human hemoglobin. By being more specific for hemoglobin, this test avoids some of the false-positive results of FOBT and does not require the same dietary restrictions. In addition, FIT is more sensitive to detecting lower gastrointestinal (GI) bleeding as globin degradation by the upper gastrointestinal tract reduces the likelihood of FIT positivity.

There have been no randomized controlled trials evaluating the benefits of FIT. In trials comparing FIT to FOBT, the sensitivity for detecting CRC with a single stool sample FIT was 65.8%;⁴ the sensitivity when sampling three consecutive bowel movements was 81.8%.⁵ Despite increased sensitivity of FIT for CRC, it was also noted that FOBT had a higher sensitivity for advanced adenomas than FIT (41.3% versus 29.5%).⁵ Lastly, although patient compliance has not been investigated as rigorously as with FOBT, it is proposed that FIT would have better compliance due to lack of dietary restrictions.

DNA Stool Assays

The mechanism of detection for DNA stool assays (sDNA) is based on the understanding that cells (normal colonocytes, adenomatous cells, and cancerous cells) are constantly shed from the colonic mucosa into feces. These cells contain DNA mutations as described by Fearon and Vogelstein⁶ that can be used as a biologic marker for CRC detection. To obtain a sufficient sample for sDNA, an entire stool specimen must be submitted (minimum of 30 g) and transported in a way to minimize DNA degradation. Special kits have been developed to aid in the process, but there are compliance issues related to the collection process. In addition, costs are higher for sDNA methods as compared with other stool evaluation methods. Yet, studies comparing sDNA to FOBT were very promising with a sensitivity of 91% for cancers and 82% for adenomas⁷ when a multitarget mutation assay was used (21 mutations identified). Unfortunately, follow-up studies have failed to show such accuracy,⁸⁻¹¹ with a mean sensitivity between 50 to 60% for cancers and 40% for adenomas. At this time, there are no prospective randomized control trials investigating sDNA.

Serum Markers

Given the compliance issues related to any stool testing method, serum markers have been intensely investigated for CRC screening. Several serum markers have been studied to find a simple blood test capable of detecting CRC. Presently, the two most studied serum markers for CRC are carcinoembryonic antigen (CEA) and cancer antigen (CA) 19-9. CEA has been used for many years as a biomarker for CRC progression following resection and in the monitoring of metastatic CRC.

Unfortunately, as a CRC detection method, CEA does not have good sensitivity and specificity as it is elevated in many non-CRC conditions, such as liver disease and pulmonary disease. In a study by Duffy et al,¹² a sensitivity for detecting CRC of 30% was reported for a CEA level above 2.5 ng/mL, making CEA a poor screening test. Similar to CEA, CA 19-9 has not been found to be useful for the detection of CRC.¹³

Summary Recommendations for Fecal and Serum Tests

There have been no serious adverse risks found with any of the studies examining fecal detection testing. Risks were related to false-positive results and the associated risk of an unnecessary second test. In addition, FOBT is the only fecal test with randomized controlled studies showing a mortality reduction. In considering the usefulness of any screening test, the most important factor is the compliance rate of each test. FOBT is simple and inexpensive, but high noncompliance rates reduce the effectiveness of this screening method. With respect to the other fecal detection tests, the literature is constantly updated with newer tests, analyzing multiple DNA panels, glycoproteins, cytokines, and proteins. Although these newer tests offer the trade-off of higher sensitivity with lower specificity, further investigation is needed before endorsing these newer stool-testing methods.

IMAGING TESTS

Barium Enema

The double-contrast barium enema (DCBE), sometimes referred to as an air contrast barium enema, identifies CRC and other pathology by coating the mucosa of the colon with barium and then inflating the colon with air. Multiple images are then obtained to evaluate the entire length of the colon and rectum. DCBE is a low cost, simple test that is commonly used for evaluation of CRC in patients who have a contraindication to colonoscopy or following an unsuccessful colonoscopic examination. The test has a relatively low complication rate, but success is dependant on colonic preparation and the experience of the radiologist.

There have been no randomized control trials to demonstrate the efficacy of DCBE for detection of CRC. Observational and case-control studies have varied with respect to CRC sensitivity. In one study by Winawer,¹⁴ DCBE sensitivity for polyps <5 mm was only 32%, for polyps between 6 and 10 mm sensitivity was 53%, and sensitivity was 48% for polyps >1 cm. The sensitivity of DCBE for CRC is better than for polyps as most observational studies show sensitivity between 85 to 97%.^{15,16} Yet as better technology has emerged, the role of DCBE has dwindled appreciably.

Computed Tomography Colonography

Computed tomography colonography (CTC) has gained much attention since its inception in the 1990s. It combines helical CT scans of the abdomen with a computer imaging program to produce both two-dimensional (2D) and three-dimensional (3D) images of the colon. To increase accuracy, the patient must undergo complete bowel preparation (as with colonoscopy) and have air/CO₂ insufflated through a rectal catheter to distend the entire colon. Some virtual colonographers also use barium per rectum to “tag” any residual stool in the colon.

Benefits of CTC include lack of sedation and a minimal complication rate. In addition, CTC evaluates the entire abdomen to detect extraluminal pathology. The major disadvantage is that this is a nontherapeutic modality; positive findings require flexible colonoscopy (FC) or other intervention. At this time there is considerable debate regarding the size of polyp that should be referred for FC. Although there is no agreement, currently it is felt polyps <6 mm may not need referral for FC. Those referred for polypectomy or biopsy would then be subject to a second test, along with another bowel preparation if FC cannot be arranged subsequently. The final polyp threshold for FC referral will determine the cost-effectiveness of this modality as compared with other screening tests.

Studies comparing CTC to FC have shown a large range of sensitivities (55–94%)^{17–21} A recent meta-analysis demonstrated low sensitivity of CTC for lesions <6 mm, but very good sensitivity for lesions >1 cm (96%).²² The University of Wisconsin group has examined the diagnostic yield from parallel screening programs of CTC versus FC. This study revealed that primary CTC and FC screening strategies resulted in similar detection rates for advanced neoplasia, although the numbers of polypectomies and procedure-related complications was considerably smaller in the CTC group as compared with FC.²¹

Summary Recommendations for Imaging Tests

The use of DCBE has been declining as newer modalities have been introduced. The advent of CTC has changed the focus of radiologists, leading to less enthusiasm for DCBE. With less enthusiasm and declining number of procedures, accuracy rates of DCBE in diagnosing CRC or polyps is likely to decline. The 2002 USPSTF recommendations included DCBE as an effective screening modality for detection of CRC, but in the 2008 recommendations, DCBE has been dropped. This will further the decline in DCBE usage.

CTC has gained much attention for its potential screening of CRC. The clinical accuracy of CTC for lesions 10 mm or larger justifies it as a potential screening tool for CRC. However, there are multiple issues

with CTC screening for CRC. First, there is no standardized protocol for CTC, with numerous 2D and 3D imaging techniques, differences in CT multidetector rows (affecting quality), and the experience of the radiologist significantly affecting the results of the test. The most important issue is what size of polyp warrants polypectomy (i.e., a second procedure). This variable will greatly affect the cost and utility of CTC screening. An additional concern of CTC is the ability to find low rectal lesions. Because the procedure requires a balloon-cuffed rectal tube for CO₂ insufflation of the colon, the distal rectum can be very difficult to examine. The variability in test accuracy and safety needs to be addressed before implementation in the community. Incidental findings of CTC are also a major concern as further studies will be ordered and more procedures performed without documented benefit to the patient. With respect to patient risks, imaging tests have few serious risks. There is a low risk of perforation and bacteremia and there is risk associated with the radiation exposure of the procedure. Given potential harms and observed variability of CTC accuracy, the USPSTF recommends specification, implementation, and monitoring of quality standards before widespread screening with CTC.

OPTICAL TESTS

Flexible Sigmoidoscopy

Flexible sigmoidoscopy (FS) typically involves the use of a sigmoidoscope for examination of the rectum and distal colon. It is often performed in a physician's office without the use of sedation, and can even be administered by nonphysicians with proper training. Advantages of FS include less bowel prep as compared with other modalities such as DCBE or FC. A successful FS should reach 40 cm from the anal verge and into the distal colon, leaving a significant amount of proximal colon unexamined. Thus, the success of FS for CRC detection is dependent on the frequency of CRC in the descending colon as compared with the proximal colon. One of the drawbacks of FS is the increasing prevalence of ascending lesions as a patient ages (over 65 years old), in women compared with men, and in African Americans as compared with Caucasians. Given that FS is only able to examine the distal colon, it is often combined with FOBT testing to increase cancer detection.

At publication of this review, there are four randomized controlled trials examining the sensitivity of FS. In addition, several case-control studies have examined the efficacy of FS in detecting CRC. In the article by Newcombe,²³ the incidence of CRC of the distal colon was reduced by 70%. Overall, most studies demonstrate a 60 to 80% reduction¹⁶ of CRC in the portion of the colon examined. There is little data

examining the combination of FS and FOBT on CRC screening, and the available data are difficult to interpret.

Flexible Colonoscopy

From 1993 to 2002, flexible colonoscopy (FC) usage for detection of CRC increased sixfold.²⁴ The major advantage of FC is the ability to examine the entire colon while performing biopsies or polypectomy at the same session. When other CRC screening modalities yield a positive result, FC is the usual next test of choice. Yet, FC has several disadvantages including the requirement for complete bowel preparation, typically requiring the patient to make dietary changes 1 to 2 days prior to the study and to undergo bowel prep the day before. FC most commonly involves sedation, which limits the patients' ability to work or perform other important activities for a period of 24 to 30 hours.

Despite the invasiveness of the test, loss of time, and intense bowel preparation, FC is considered the gold standard test for detection of CRC. It is considered to have the highest sensitivity and specificity of any CRC detection modality; yet, there are no randomized controlled trials comparing sensitivity of FC for detection of CRC. Most data has been extrapolated from studies examining FOBT with FS, in which patients with lesions subsequently underwent FC. These studies have shown a decrease in the incidence of CRC after FC from 20 to 80%.^{25,26} Case-control studies have also shown a decrease in CRC when compared with a reference population over a 10-year period.^{27,28} The main reason for the decreased incidence is believed to be due to FC removing all polyps seen on examination.

Despite consideration as the gold standard, FC is not without significant issues. The miss rate for adenomas >1 cm has been observed to be between 6 to 12%^{29,30} with a CRC miss rate of near 5%. In addition, there is a higher complication rate as compared with other modalities including bleeding and perforation. Detection rates are highly related to the experience of the operator, adequacy of the bowel prep, and even the time taken on examination.³¹

Summary Recommendations for Optical Tests

Both FC and FS have the benefit of not only detecting polyps and CRC, but being therapeutic (polypectomy). FS has been shown to decrease the risk of CRC by 60 to 80% for the extent of the colon it surveys. But this benefit may not be seen in patients over the age of 65, and in African Americans. FS is also appealing as a screening modality because it requires a less strict bowel preparation (than other modalities), can be performed without sedation, and can be performed by a properly

trained nonphysician. FC is considered the gold standard test and is the test of choice when other screening modalities are positive. In studies looking at FOBT or FS, some have attributed the reduction in CRC to the follow up FC and polypectomy performed.²⁵ FC has the advantage of clearing the colon of polyps and detecting cancers early. The disadvantage of FC is the use of sedation, more extensive bowel prep, and significant procedural risks.

Clinically significant adverse events during FC were seen in 2.9 per 1000 asymptomatic individuals in 12 combined studies.^{19,26,32-41} This included perforation, hemorrhage, diverticulitis, cardiovascular events, severe abdominal pain, and death. FS had a lower rate of significant adverse events as compared with colonoscopy. In six studies,^{20,34,41-44} 0.34 per 1000 incidence was reported. Recent studies comparing colonoscopy to CTC confirm that FC can miss CRC as well as adenomas. Miss rates are 3.4% for CRC and 2.1% for large adenomas based on tandem colonoscopies. The USPSTF recommended both FS and FC as screening modalities for CRC detection, but concluded the need for quality initiatives for colonoscopy along with all operator-dependant screening tools.

SPECIAL POPULATIONS

Familial Adenomatous Polyposis

Familial adenomatous polyposis (FAP) syndrome increases the incidence of CRC to nearly 100% by 40 to 50 years of age. The American Society for Gastrointestinal Endoscopy (ASGE)⁴⁵ recommends annual screening sigmoidoscopy in all patients with a positive mutation of the APC gene, starting at ages 10 to 12 up to age 40. If no polyps are detected by that time, the patient should be changed to an every 3 to 5 year screening examination. Colonoscopy should be performed yearly in patients with the attenuated form of FAP due to a high risk of proximal lesions. Once the patient develops multiple adenomas, colectomy should be considered.

Hereditary Nonpolyposis Colorectal Cancer

Hereditary nonpolyposis colorectal cancer (HNPCC; DNA mismatch repair gene mutation) accounts for ~5% of all CRC diagnoses. However, 80% of patients with HNPCC will go on to develop CRC. They have a tendency to develop cancers proximal to the splenic flexure, and at an earlier age. The median age of onset is 42 years old, with 5% of cancers occurring before the age of 30. The interval between screenings should be shorter for HNPCC than the general population, as cancers can develop within 42 months of a normal exam.⁴⁶ Because of these characteristics, the ACGE

recommends colonoscopy every 1 to 2 years beginning at ages 20 to 25, or 10 years younger than the earliest age of diagnosis of CRC in the affected family members. Once the patient turns 40, they recommend annual colonoscopy.

Inflammatory Bowel Diseases

Both Crohn's disease and ulcerative colitis increase the risk of CRC. The ASGE recommends⁴⁵ screening colonoscopy every 1 to 2 years beginning at 8 to 10 years of age after diagnosis of either ulcerative colitis or Crohn's disease involving >one-third of the colon. In addition, they recommend biopsies every 10 cm and in all four quadrants of the colon (from cecum to rectum) to detect advanced disease. The general guideline of when to start screening, and the time interval between screening as defined by the ASGE is also endorsed by the American College of Gastroenterology (ACG), American Gastroenterological Association (AGA), the American Society of Colon and Rectal Surgeons (ASCRS), the British Society of Gastroenterology (BSG), and the Crohn's and Colitis Foundation of America (CCFA).⁴⁷

Personal or Family History of Colon Cancer

In patients who have undergone a curative resection for CRC, the American Cancer Society (ACS) and U.S. Multi-Society Task Force on Colorectal Cancer guidelines recommend a 1-year follow-up for all proximal segmental resections, in the setting of an otherwise normal colonoscopy in the perioperative period. If normal, they recommend a repeat colonoscopic screening in 3 years and then 5 years thereafter. For rectal cancer with a low anterior resection and anastomosis, they recommend the same screening colonoscopic schedule as with proximal resections, but in addition they recommend 3 to 6 monthly proctoscopic examinations or rectal ultrasound (US) examinations. Following endoscopic removal of a cancerous polyp, they recommend repeat colonoscopy in 6 months. The ASGE has the same recommendation as the ACS for proximal colon cancers, but do not recommend the proctoscopic or rectal US screening exams for rectal cancer surveillance. Similarly, a patient with a first-degree relative or two second-degree relatives with colorectal cancer is considered to be at elevated risk and thus should undergo screening at age 40 or 10 years prior to that family member's diagnosis.

Racial Considerations

Patients of African American race have the highest age-adjusted CRC incidence and the highest proportion of CRC occurring in the proximal colon. By further subdividing the location of CRC, African American

males have a higher rate of CRC for all areas of the colon, except the rectum, and females have a higher rate of CRC at all areas of the colon compared with females of other races. The Clinical Outcomes Research⁴⁸ project showed that though African Americans had fewer polyps than Caucasians, these polyps were more likely to be in the proximal colon. African Americans were also proportionately more likely to present before the age of 50 with CRC and at presentation were more likely to have advanced disease. These epidemiologic facts lead to a higher mortality rate for African Americans from CRC and thus some have suggested that screening should begin earlier for African Americans (age 45) with a full colonic exam (colonoscopy instead of sigmoidoscopy). National guidelines are unavailable at this time to recommend a change in screening practices for patients of African American race.

Gender Differences

It has been reported that FC may be preferable over FS for females due to a higher rate of proximal colon CRC as compared with males. However, the literature is controversial, demonstrating a lower rate of proximal advanced neoplasia in females as compared with males (1.2 versus 3.9%),⁴⁹ and a lower rate of finding any proximal neoplasia in females as compared with males (4.9 versus 10.5%). FS would miss 2.4% of advanced proximal neoplasms, which is statistically similar to males (1.9%). Older age, male sex, and distal adenoma were identified as risk factors for proximal neoplasia from multivariate analyses.⁴⁹⁻⁵¹

Age Considerations

Although the incidence of CRC increases with age, the life expectancy decreases, leading to the confusion regarding when CRC becomes less effective. No recommendation prior to the most recent guidelines from the USPSTF in 2008 contained a statement for what age screening should be discontinued. However, in 2008, the USPSTF included considering discontinuing screening for patients aged 75 or older without positive family history and who had been screened starting at age 50 without adenomas, cancers, or any abnormal screening result.⁵² This was based on two computerized modeling techniques, which created a large "asymptomatic population" and evaluated the effect of FC screening at age 75 and 85. The model found that the life years gained by additional colonoscopic exams after age 75 was small. Overall, the USPSTF felt the decrease in CRC detection did not overcome the increase in risk from additional FC exams. This recommendation needs to be followed with caution, as it is based on computer modeling and only considered FC screening. When comorbidities of an average aging population were examined to identify

screening and surveillance of stage 1 cancers, it was felt chronic conditions that effect 5-year survival are more important than age in determining when to stop CRC screening.⁵³

GUIDELINES FROM PROFESSIONAL SOCIETIES

United States Preventive Services Task Force

The USPSTF acknowledges that although the idea of customized screening recommendations is "compelling" there is insufficient data to determine the economic or mortality impact of this practice. Routine colorectal cancer screening is recommended in adults beginning at age 50 and continuing only until age 75 (in people with adequate screening histories). The following screening modalities are recommended: high-sensitivity FOBT, sigmoidoscopy with interval FOBT, or colonoscopy. The USPSTF does not recommend routine screening for adults 75 to 85 years of age and recommends against screening adults older than 85 years of age. The USPSTF also concluded that CT colonography and sDNA testing has insufficient evidence to permit a recommendation.⁵⁴

American Society of Gastrointestinal Endoscopy

In 2006 the ASGE published its guidelines for CRC screening.⁴⁵ They recommended that in average-risk individuals CRC screening should begin at age 50. The preferred modality for screening is a colonoscopy performed every 10 years. Alternative modalities were FOBT yearly, flexible sigmoidoscopy every 5 years, or FOBT yearly with flexible sigmoidoscopy every 5 years. Yearly FOBT was recommended to be two samples of three consecutive stools, with a follow-up colonoscopy for a positive test result. They did not recommend barium enema, virtual colonoscopy, or fecal DNA.

U.S. Multi-Society Task Force on Colorectal Cancer

In March 2008, the U.S. Multi-Society Task Force (USMSTF) on Colorectal Cancer recommended CRC screening⁵⁵ starting at age 50 for average risk patients by annual high sensitivity FOBT or FIT, flexible sigmoidoscopy every 5 years, double-contrast barium enema every 5 years, CT colonography every 5 years, colonoscopy every 10 years, or fecal DNA at an "unspecified interval."

Summary Recommendations

We have used the recommendations by the USPSTF, ASGE, and USMSTF on colorectal cancer to provide an

Table 1 Screening Methods and Intervals for Colorectal Cancer

Method	Interval	Society
Fecal occult blood testing	Yearly	USPSTF, ASGE, USMSTF
Fecal DNA	Unspecified	USMSTF
Double-contrast barium enema	Every 5 years	USMSTF
CT Colonography	Every 5 years	USMSTF
Flexible sigmoidoscopy	Every 5 years	USPSTF, ASGE, USMSTF
Flexible colonoscopy	Every 10 years	USPSTF, ASGE, USMSTF

USPSTF, US Preventive Services Task Force; ASGE, American Society for Gastrointestinal Endoscopy; USMSTF, U.S. Multi-Society Task Force (USMSTF) on Colorectal Cancer; DNA, deoxyribonucleic acid; CT, computed tomography.

aggregated list of screening methods and time intervals for screening in the average-risk patient (Table 1).

DISCUSSION

CRC screening is essential to decrease the burden of disease from CRC through early detection of cancerous lesions and removal of precancerous polyps. Increased CRC screening is likely to have led to the reductions in the incidence of CRC since 1998. Controversy, however, remains as to which method of CRC screening is best. Many government agencies and medical societies have published recommendations with differing results. Theoretically, the ideal CRC screening modality would be cost effective, increase life-years gained, and permit long intervals between tests. In addition, it would provide low risks, high patient compliance, and have the highest sensitivity and specificity. Unfortunately, at the present time, our screening modalities have some, but not all of these characteristics. Stool tests have good sensitivity and specificity, with low risk but patient compliance is low, and the time interval between tests is short. Direct visualization tests have high sensitivity and specificity, but higher risk, and compliance remains low. Imaging tests are diagnostic, but not therapeutic leading to more testing.

In the new guidelines of the USPSTF, screening is still recommended to begin at age 50 (unless the patient has a specific inherited syndrome or other high-risk condition), and consideration to stopping routine screening at age 75, when the patient has had adequate screening prior to that time. The numerous recommendations and modalities have helped to establish the basis of screening for CRC. Despite the lack of a consistent standard or agreement between societies, physicians, and other stakeholders, what we can all agree on is that CRC screening is important and that increasing screening while reducing harms is critical. None of

the methods is perfect; each has risks and benefits. A thorough discussion with the patient about potential benefits and harms is critical before initiating any screening program.

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