

# Colorectal Cancer Screening Clinical Applications

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**S**CREENING FOR COLORECTAL CANCER is now recommended by multiple professional organizations for all individuals aged 50 years or older,<sup>1-4</sup> yet screening rates for colorectal cancer remain low. In the accompanying article, we evaluated the evidence for the currently available screening tests and their impact on colorectal cancer mortality. This article condenses the available scientific evidence into useful information about commonly asked clinical questions about colorectal cancer screening.

## CLINICAL QUESTIONS

### What Is the Best Colorectal Cancer Screening Option?

Decision making about colorectal cancer screening is more complicated than for other cancers. For example, breast cancer has 1 standard screening test, mammography, which is recommended for appropriate women. In contrast, several screening tests are available for the detection of colorectal cancer and patients frequently want to know which test is best.

### What Are the Screening Recommendations of Professional Organizations?

All professional organizations that have published clinical guidelines on colorectal cancer screening recommend screening for all adults aged 50 years or older (BOX).<sup>2,3,5,6</sup> Most professional organizations do not emphasize one screening strategy as being supe-

See also p 1288 and Patient Page.

rior to another, but they all emphasize the importance of screening for all eligible adults. Age 50 years is chosen as the starting point because at this age colorectal cancer becomes prevalent enough to warrant widespread screening of the general population. A recent study evaluating colonoscopy among persons aged 40 to 49 years confirmed the low yield of screening colonoscopy among individuals younger than 50 years.<sup>7</sup> Most professional organizations do not make recommendations about the upper age limit of screening.<sup>4</sup>

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### What Is the Quality of the Evidence for Each Screening Test?

For the professional organizations, an important tension exists between the level of evidence available and the potential rationale for each screening test. The most direct evidence that screening reduces colorectal cancer mortality for fecal occult blood testing (FOBT) has been shown in 3 randomized controlled clinical trials.<sup>8-10</sup> Although the rationale for colonoscopy reducing mortality is strong, the evidence is indirect.<sup>11-13</sup>

### What Are the Sensitivity and Specificity of Colorectal Screening Tests?

Colonoscopy is the most sensitive and specific of the all the available colorectal screening tests, whereas the sensitivity and specificity for FOBT and sigmoidoscopy are much lower. Therefore, colonoscopy can detect more cases of colorectal cancer or large polyps than the other screening tests, but that does not mean that it is a better or preferable test. The extent to which the increased sensitivity of colonoscopy will translate into

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**Box. Clinical Guidelines for Colorectal Cancer Screening for Asymptomatic, Average-Risk Adults Aged 50 Years or Older**

**Multidisciplinary Expert Panel<sup>2\*</sup>**

The panel recommends screening

- On the basis of strong evidence, annual FOBT or flexible sigmoidoscopy every 5 years;
- On the basis of theoretical but not proven findings, combined annual FOBT and flexible sigmoidoscopy every 5 years;
- On the basis of no direct evidence of efficacy but strong rationale, double-contrast barium enema every 5 to 10 years or colonoscopy every 10 years.

**American College of Gastroenterology<sup>3</sup>**

They recommend colonoscopy screening every 10 years as the preferred screening strategy when available. An alternative strategy is flexible sigmoidoscopy every 5 years plus annual FOBT.

**US Preventive Services Task Force<sup>5</sup>**

The task force recommends screening all adults aged 50 years or older for colorectal cancer. The benefits from screening substantially outweigh potential harms, but the quality of evidence, magnitude of benefit, and potential harms vary with each method.

**American Cancer Society<sup>6</sup>**

They recommend an annual FOBT and sigmoidoscopy every 5 years, or annual FOBT, or sigmoidoscopy every 5 years, or colonoscopy every 10 years, or double-contrast barium enema every 5 years.

FOBT indicates fecal occult blood testing.

\*This multidisciplinary expert panel convened by the Agency for Health Care Policy and Research evaluated the available evidence and developed an evidence-based set of clinical guidelines. These guidelines have been endorsed by multiple organizations, including the American Cancer Society, the American Society of Colon and Rectal Surgeons, and the Society of American Gastrointestinal Endoscopic Surgeons.

reduced colorectal cancer mortality remains uncertain.

**What Are the Risks and Discomforts of the Colorectal Screening Test?**

Colonoscopic evaluation may be indicated following a positive FOBT result. Complications may ensue from colonoscopy, but no risk of complications from FOBT have been reported. The absolute risk of serious complications with sigmoidoscopy and colonoscopy are both low, but colonoscopy has higher reported risks than sigmoidoscopy.<sup>8,13-16,18</sup> However, the risks posed by endoscopic screening tests are generally immediate, while the clinical benefit may be delayed for many years. In addition to serious risks posed by most of the screening tests, many small discomforts and inconveniences (eg, colonic preparation, dietary modifica-

tion, sedation, time lost from work) exist and these differ among the tests.

**Do Patient Preference and Adherence Vary Among the Tests?**

Few studies have assessed patient preferences about colorectal cancer screening and substantial variation exists, although some evidence suggests that patients in general are quite accepting of endoscopic screening. Factors stated as important by some patients include having strong preferences for sedation and having discomfort with limiting screening to only half the colon.<sup>19</sup> Patient preferences may affect adherence: for example, the benefit of FOBT is that it is repeated over time,<sup>8-10,20</sup> but colonoscopy may be a preferred option for individuals who are concerned about compliance since it can be performed every 10 years instead of annually.

**Do the Screening Tests Differ With Respect to Their Availability Because of Either Differing Resources or Health Insurance Coverage?**

Even if colonoscopy screening was to be performed on all US eligible adults, there is currently insufficient infrastructure and insufficient numbers of colonoscopists available.<sup>21</sup> Although most health insurance companies cover some type of colorectal cancer screening for average-risk individuals, some may not cover all options (ie, colonoscopy screening). As of July 1, 2001, US federal law entitles Medicare beneficiaries to a colonoscopy screening every 10 years.

**How Is the Best Screening Test Chosen?**

Given that there is no one best option, physicians should discuss with eligible individuals the pros and cons of each screening test. Factors to consider include age, actual risk of colorectal cancer, risks of the screening procedure, discomfort, safety, adherence, resources, availability of screening tests, and health insurance coverage. What is most important is for eligible individuals to undergo some type of colorectal cancer screening test. There are a variety of resources available to physicians and patients about colorectal cancer screening, including the American Cancer Society ([http://www.cancer.org/docroot/cricri\\_2x.asp?sitearea=ln&dt=10](http://www.cancer.org/docroot/cricri_2x.asp?sitearea=ln&dt=10)), the National Cancer Institute ([http://www.nci.nih.gov/cancer\\_information/cancer\\_type/colon\\_and\\_rectal/](http://www.nci.nih.gov/cancer_information/cancer_type/colon_and_rectal/)), and the American Gastroenterological Association ([http://www.gastro.org/public/brochures/cc\\_screening.html](http://www.gastro.org/public/brochures/cc_screening.html)).

**Should Colorectal Cancer Screening Recommendations Be Modified for Individuals at Higher Than Average Risk for Colorectal Cancer?**

Having a family history of colorectal cancer is the most important clinical feature that increases an individual's risk of the disease. The magnitude of the risk depends on the number of first-degree

relatives affected and their age at diagnosis. In a recent meta-analysis, it was determined that individuals with a single first-degree relative with colorectal cancer have an increased risk of approximately 2.25 times that of the general population.<sup>22</sup> Individuals with more than 1 first-degree relative with colorectal cancer have an increased risk of approximately 4.25 times that of the general population. Some evidence shows that individuals with a first-degree relative with colorectal adenoma also have an increased risk of colorectal cancer of approximately 2 times that of the general population. Furthermore, evidence shows that individuals with a first-degree relative with a family history of colorectal cancer have a risk of colorectal cancer at age 40 years similar to the risk observed in the general population at age 50 years.<sup>2</sup> No randomized studies have been conducted with mortality end points addressing the question of what is the optimal screening strategy among individuals with a family history of the disease.

#### **What Are the Recommendations of Professional Organizations?**

Clinical guidelines for colorectal cancer screening were developed by a multidisciplinary expert panel convened by the Agency for Health Care Policy and Research, and they were endorsed by several professional societies, including the American Cancer Society.<sup>2</sup> This panel recommends that the same colorectal cancer screening be performed for individuals at higher risk as for the individuals at average risk, but it recommends that this screening start at age 40 years. In addition, special efforts to ensure compliance should be made, particularly for those who have a first-degree relative who had an adenomatous polyp before the age of 60 years or colorectal cancer before the age of 55 years.

The American College of Gastroenterology recommends a more aggressive approach.<sup>3</sup> For individuals with a strong family history of colorectal cancer (eg, multiple first-degree relatives with colorectal cancer of a single first-

degree relative with cancer diagnosed at age <60 years), they recommend colonoscopy beginning at age 40 years or 10 years younger than the age at diagnosis of the youngest affected relative. They then recommend that colonoscopy be repeated at 3- to 5-year intervals. For those individuals with a single first-degree relative diagnosed with colorectal cancer before age 60 years, they recommend the same screening strategies as for average-risk individuals but beginning at age 40 years; the preferred screening strategy of the American College of Gastroenterology for average-risk individuals is colonoscopy every 10 years.<sup>3</sup>

The US Preventive Services Task Force does not address familial risk outside of the inherited syndromes.<sup>5</sup>

#### **In the Face of Conflicting Recommendations, How Should Physicians Decide About Screening Individuals with a Family History of Colorectal Cancer?**

Since the risk of colorectal cancer in high-risk individuals at age 40 years is similar to that of average-risk individuals at age 50 years, it is generally recommended that screening of high-risk individuals begin at age 40 years.<sup>2,23</sup> Colonoscopy will detect more colorectal cancer for all individuals with a family history of colorectal cancer or adenoma, but at a higher cost, and possibly with more complications. Large numbers of individuals with a family history of colorectal cancer are not being screened; thus, the primary goal is for all individuals with a family history of colorectal cancer to undergo some type of colorectal cancer screening.

#### **Is a Single Negative FOBT Result Obtained at the Time of a Routine Digital Rectal Examination Adequate?**

It is common clinical practice to test stool samples obtained by digital rectal examination using FOBT, but the test results for colorectal cancer using FOBT obtained during digital rectal examination has not been shown to be accurate. Fecal occult blood testing was not

designed to test stool samples obtained at a digital rectal examination, and no evidence is available to indicate that screening for colorectal cancer solely using FOBT at this time will reduce mortality.<sup>24</sup> An increased false positive rate is a theoretic concern given that the patient has not undergone the usual dietary preparation for FOBT and that the digital examination itself might induce bleeding.<sup>25,26</sup> One study reported the positive predictive value for FOBT obtained by digital rectal examination was similar to that obtained from 3 spontaneously passed stools.<sup>27</sup> More importantly, FOBT results of a single stool sample obtained by digital examination would not be expected to be as sensitive as when the FOBT is performed in the standard fashion, and therefore, it should be considered inadequate screening.<sup>28-30</sup>

In summary, a positive FOBT result obtained at digital rectal examination should not be ignored, but it should require follow-up colonoscopy. However, because of the uncertain sensitivity, patients with a negative FOBT result by digital rectal examination should still undergo complete FOBT on 3 spontaneously passed stools.

#### **What Is the Current Adherence and What Are the Barriers to Screenings?**

In 1999, only 20.6% of eligible patients had undergone FOBT within the preceding year, and only 33.6% of eligible patients had undergone sigmoidoscopy and/or colonoscopy in the preceding 5 years.<sup>31</sup>

Many potential barriers to colorectal cancer screening exist. These barriers include factors related to the patient, related to the physician, and related to the health care system. Patient factors include lack of knowledge about colorectal cancer or the screening tests, lack of awareness that colorectal cancer is a prevalent and serious disease, being unaware that screening was due, lack of awareness that they are at risk for colorectal cancer, lack of knowledge of symptoms, being too busy, concerns about the

potential discomforts of colorectal cancer procedures or of the preparations for screening, fear of the consequences of a positive test result, and logistic issues, such as arranging for transportation, for care of a family member, or for time off from work.<sup>32-39</sup> Physician recommendation has been cited as a major factor in determining whether a patient gets screened for colorectal cancer.<sup>40,41</sup> Other potential physician factors include confusion about the conflicting recommendations by

professional organizations, lack of time to communicate with and to educate patients, and lack of preventive priorities. In a recent study of rural primary care practices, discussions about colorectal cancer screening with eligible patients occurred in only 14% of patient visits.<sup>42</sup> In another recent study, physicians incorrectly perceived those features of colorectal cancer screening tests that were important to patients; for example, only 15% of patient stated discomfort as an important test feature af-

fecting their choice, but physicians thought that 64% of patients would state discomfort as an important feature.<sup>43</sup> Health care system factors include insurance coverage for the screening tests and access to the screening service and the screening site.<sup>44,45</sup>

**What Strategies Can Be Implemented to Improve Rates of Colorectal Cancer Screening?**

The majority of studies in the clinical setting have focused on increasing rates

**Table.** Cost-effectiveness Studies of Colorectal Cancer Screening

Study	Goal	Assumptions	Conclusions
Frazier et al <sup>70</sup>	To compare fecal occult blood testing, flexible sigmoidoscopy, double-contrast barium enema, and colonoscopy individually and in combination in individuals aged 50 to 85 years	Screening colonoscopy was assumed to reduce colorectal cancer mortality by 64% Compliance with initial screen was assumed to be 60% and compliance with follow-up or surveillance colonoscopy was assumed to be 80%	Annual fecal occult blood testing plus sigmoidoscopy every 5 years was the most cost-effective strategy A single colonoscopy performed in patients aged 55 years achieved about half the mortality reduction in colorectal cancer mortality as colonoscopy every 10 years
Sonnenberg et al <sup>71</sup>	To compare fecal occult blood testing, sigmoidoscopy, and colonoscopy	Compliance with the various tests will vary Compliance with annual fecal occult blood testing will be less than compliance with colonoscopy every 10 years	Colonoscopy is the most cost-effective screening strategy
Wagner et al <sup>72</sup>	To compare fecal occult blood testing, flexible sigmoidoscopy, double-contrast barium enema, and colonoscopy individually and in combination, with the initial screening beginning at age 50 years and the final screening at age 85 years	Included years of life lost because of detection and treatment of cancers that would have remained harmlessly silent Did not consider imperfect compliance	Screening with any test is in the range of cost-effectiveness commonly accepted for other screening tests—all strategies less than \$20 000 per year of life saved
Khandker et al <sup>73</sup>	To compare several colon cancer screening strategies	Assumptions about polyp dwell time varied	All strategies were cost-effective Fecal occult blood testing was less cost-effective with low compliance Lowering colonoscopy costs increased the cost-effectiveness of colonoscopy screening
Vijan et al <sup>74</sup>	To compare fecal occult blood testing, sigmoidoscopy, fecal occult blood testing plus sigmoidoscopy, and colonoscopy	Compliance with colonoscopy would be optimized with once- or twice-lifetime screenings	Colonoscopy at ages 50 and 60 years is the preferred test
Loeve et al <sup>75</sup>	To explore the costs and savings of sigmoidoscopy every 5 years	Assume that cost of sigmoidoscopy is low at \$100 and that of colonoscopy without polypectomy is \$150 to \$1000	Although colorectal cancer screening is costly, the savings by screening compensate for the costs
Sonnenberg and Delco <sup>76</sup>	To compare single colonoscopy with repeated colonoscopy	Single-screening colonoscopy was assumed to reduce colorectal cancer incidence by 23% and repeated colonoscopy to reduce colorectal cancer by 75% Compliance with initial screening was assumed to be 45% to 100% and compliance with follow-up screening was assumed to be 80%	A single-screening colonoscopy at age 65 years is more cost-effective than fecal occult blood testing or flexible sigmoidoscopy every 5 to 10 years Colonoscopy every 10 years prevents more colon cancer and saves more lives
Ness et al <sup>77</sup>	To assess the utility of one-time colonoscopy at various ages	Sex-related differences in life expectancy and incidence of colorectal neoplasia All colorectal cancers arise from adenomas (important if considering one-time screening only)	A single colonoscopy screening in men before age 60 years and women before age 65 years is more cost-effective than no screening or screening at older ages

of FOBT or sigmoidoscopy screening. A variety of strategies have been used, including direct mailing of FOBTs to patients, sending letters from one's own physician about the importance of colorectal cancer screening, and providing educational materials and reminders. One recent intervention of a decision aid, which included patient viewing of a video about colorectal cancer screening and an educational brochure tailored to the patient's readiness to change, resulted in a significant increase in both the ordering and completion of colorectal cancer screening tests.<sup>46</sup> Interventions targeting the physician include providing education about the importance of colorectal cancer screening, educating the physician on communicating educational messages, and/or teaching the physician to offer colorectal cancer screening during an office visit. Academic detailing is an educational outreach strategy in which each physician's concerns or barriers to providing colorectal cancer screening are addressed on an individual basis.<sup>47</sup> One innovative study combined academic detailing with implementation of on-site sigmoidoscopy and showed a large improvement in use of sigmoidoscopy screening.<sup>48</sup> Use of these strategies alone or in combination generally have had modest effects on increasing patient and physician adherence.<sup>38,49-67</sup>

**Does Colorectal Cancer Screening Cost Too Much?**

Although performance of an FOBT is relatively inexpensive, sigmoidoscopy and colonoscopy, which both must be performed by trained endoscopists, are significantly more expensive. Colonoscopy is the most expensive screening test and concerns have been raised about its cost. A study of medical procedures in Canada and in the United States found that the median charge for colonoscopy in Canada was \$606 in US dollars and the median charge in the United States was \$1736.<sup>68</sup> It is possible that the US cost could be reduced by training nurses to perform endoscopies or by a redirection of market

forces, but it would still be an expensive procedure even if these changes were made.<sup>69</sup> If large numbers of individuals were screened now, substantial costs would incur and the clinical benefits may not occur for many years.

**Is Colorectal Cancer Screening Cost-effective?**

Several studies have addressed the cost-effectiveness of colorectal cancer screening (TABLE).<sup>2,70-77</sup> In addition, a systematic review of cost-effectiveness studies recently was conducted for the US Preventive Services Task Force.<sup>4</sup> All studies concluded that screening for colorectal cancer is within the range of cost-effectiveness, which generally is accepted for preventive and therapeutic interventions (\$50 000 per year of life saved).<sup>78</sup> The conclusions of the systematic review were similar; screening is cost-effective compared with no screening, but a single optimal strategy could not be determined.<sup>4</sup>

Depending on the assumptions of the cost-effectiveness model, one screening test may be superior in that model. For many of the assumptions (eg, reduction in mortality with each screening test, estimated compliance) the evidence is incomplete. Estimating the true mortality reduction from sigmoidoscopy or colonoscopy screening is less precise in the absence of clinical trial data. Although cost-effectiveness models can be useful, they must be interpreted with caution in the absence of true evidence of clinical effectiveness.

**COMMENT**

Screening for colorectal cancer reduces colorectal cancer mortality, yet rates of screening remain low. Clinicians should be familiar with the current options for colorectal cancer screening and should discuss these options with all eligible patients. Physicians should particularly ensure that individuals at high risk for colorectal cancer undergo appropriate screening. Clinicians should be aware of the current low levels of patient compliance with screening and should implement strategies within their own prac-

tices to improve compliance. Most importantly, rather than focusing on which screening test is the best, clinicians should ensure that all eligible patients undergo some type of colorectal cancer screening.

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