

SPECIAL REPORT ON COLORECTAL CANCER

Colorectal Cancer Screening Guidelines: A Review of 2008 Updates Which Test is Best?



Introduction

In the 2008 fall issue of the *Cornhusker Family Physician* we reviewed the incidence and mortality of colorectal cancer in the United States and Nebraska¹. To summarize that discussion, Nebraska ranks above the national average in both incidence and mortality rates for colorectal cancer. Nebraska's ranking near the bottom of the nation on the rate of screening can account for both of these dismal statistics. Low screening rates mean fewer colorectal cancers prevented by removing precancerous polyps and later stage at diagnosis which equates with poorer survival. Five year survival for colorectal cancer is 90% if diagnosed while still localized, 68% with lymph node involvement and only 10% if there are distant metastases². We also briefly reviewed common barriers to screening and touched on some resources available to assist in screening uninsured and underinsured Nebraskans.

In 2008 we saw published revisions in colorectal screening guidelines by two prominent groups. In May and June, the American Cancer Society (ACS), the US Multi-Society Task Force on Colorectal Cancer (USMSTF; a group represented by the American College of Gastroenterology, the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy and the American College of Physicians) and the American College of Radiology (ACR) (ACS-USMSTF-ACR) published a joint guideline simultaneously in CA: A Cancer Journal for Clinicians, Radiology and Gastroenterology³⁻⁵ (the Guidelines). In November, the US Preventive Services Task Force (USPSTF) published revised recommendations for colorectal cancer screening in the *Annals of Internal*

Medicine⁶ (the Statement).

This review is meant to briefly summarize the recommendations of the groups, compare where they differ and emphasize where they are similar. As to which test is best, on numerous occasions I have heard John H. Bond, MD, Professor of Medicine and Gastroenterology at the University of Minnesota and the VAMC in Minneapolis state that the "best" test is the one that gets done. The test most likely to get done by any individual patient may be dependent on a number of factors including personal preference, transportation, distance, historical patterns of use, influence of physicians and financial barriers. To that end, this review is intended to assist you in determining which test is most likely to get done by your patients. For more detailed discussions of the recommended tests, please refer to the references cited at the end of this article.

Guidelines of the American Cancer Society

The joint guideline published by the ACS-USMSTF-ACR made two strong points. First, a distinction was drawn between test sensitivity and program sensitivity. Test sensitivity refers to the sensitivity for a single test to detect a cancer or a polyp. Program sensitivity refers to the sensitivity achieved over time through serial testing in a prescribed screening program. For example, the sensitivity for a single fecal occult blood test (FOBT) varies significantly (14% to 79%) depending upon the product utilized. However the program sensitivity of FOBT is calculated to be much higher.

It was the conclusion of the ACS guideline group that only tests capable of attaining at least a 50% sensitivity for cancer as a single test should be utilized for screening. The rationale for this includes recognition of the difficulty in getting patients to participate fully in the recommended programmatic schedule of FOBT on an annual basis. This recommendation eliminates the use of a single in-office digital rectal exam (DRE) test whose sensitivity has been shown to be only 4.9% for advanced polyps and only 9% for cancer⁷. This is so low that in-office DRE should never be used as a screening modality for colorectal cancer. Likewise, many guaiac based FOBT (gFOBT) variants are no longer considered relevant including un-rehydrated Hemoccult II. Acceptable FOBT tests now include high sensitivity tests such as Hemoccult SENSAs or other guaiac based FOBT of similar sensitivity or immunochemical FOBT (iFOBT or FIT) e.g. InSure or Hemoccult ICT.

The second major point made by the ACS group was the prioritization between stool tests that primarily detect cancer early and the structural exams that can not only detect cancer early but can also detect adenomatous polyps

Tests That Primarily Detect Cancer:	Interval
gFOBT with at least 50% test sensitivity for cancer	Annual
FIT with at least 50% test sensitivity for cancer	Annual
sDNA with at least 50% test sensitivity for cancer	Interval Uncertain
Tests That Detect Cancer and Adenomas:	
Flexible Sigmoidoscopy	5 Years
Colonoscopy	10 Years
DCBE	5 Years
CT Colonography	5 Years

Table 1. Differentiating tests that primarily detect cancer and those that detect cancer and adenomatous polyps

allowing for the removal of these premalignant lesions and the prevention of cancer (Table 1). Both physicians and patients should understand that the less invasive stool tests are less likely to prevent cancer compared to the structural exams, require repeating at more frequent and regular intervals and require an invasive structural exam if the test is abnormal.

Stool Tests

Recommendations for tests on stool (those that primarily detect cancer) include gFOBT, FIT (iFOBT) and stool DNA (sDNA). Only FOBT tests with documented sensitivity for cancer (by brand) of greater than 50% on a single test should be utilized.

Stool DNA relies on the presence of known DNA alterations in the adenoma-carcinoma sequence which can be detected in cells that are continuously shed by polyps and cancer into the stool. DNA is stable in stool but since no single gene mutation accounts for colorectal cancer, the process necessarily uses a multi-target DNA stool assay which includes a panel made up K-ras, APC, P53, and BAT-26 mutations and DNA integrity analysis (DIA).

FOBT based stool tests should be done annually. The interval for testing sDNA is uncertain at this time. FOBT testing should follow manufacturer's instructions, requiring 2 to 3 stool samples collected at home. A single FOBT done at time of DRE in an office setting is not acceptable for colorectal cancer screening and should not be done. All positive FOBT tests (guaiac or immunochemical) should undergo colonoscopy. All negative FOBT tests should be repeated annually.

Dietary restrictions have commonly been utilized for gFOBT testing. These include the avoidance of aspirin and NSAIDs, red meat, poultry, fish and some raw vegetables (those with peroxidase activity such as broccoli, cauliflower, horseradish, parsnips, radishes, turnips and melons) for 3 days prior to the testing. All of these may cause a false positive test. The efficacy and necessity of such restrictions is debated. However, vitamin C in excess of 250 mg daily should be avoided for 3 days as this could lead to a false negative test with potentially more dire consequences.

FIT or iFOBT tests are based on the specific detection of human globin and are not affected by peroxidase activity. FIT tests are also not affected by the presence of vitamin C. Thus FIT tests do not require dietary considerations. Because globin is degraded by digestive enzymes in the upper intestinal tract, FIT tests are also more specific for lower intestinal blood loss thus improving specificity for colorectal cancer.

Stool DNA testing requires not just a smear of stool but an entire stool specimen (30 grams minimum). An adequate sample must be obtained and packaged with appropriate preservative agents for shipping to an authorized laboratory. The unit cost is significantly higher than other forms of stool testing. PreGen-Plus (Exact Sciences, Marlborough, MA) is listed at \$795⁸. A positive sDNA test should undergo colonoscopy. If the test is negative, the interval for a repeat test is uncertain.

Structural Exams

The recommended structural exams (those that detect adenomatous polyps as well as cancer) include flexible sigmoidoscopy, colonoscopy, double contrast barium enema (DCBE) and CT colonography (CTC). To be effective as a screening tool, flexible sigmoidoscopy must be inserted to at least 40 cm or to the splenic flexure. A bowel prep is necessary but a partial prep is often adequate. Sedation is generally not utilized. A positive finding requires a full colonoscopy.

All of the other structural exams require a full bowel prep. If DCBE or CTC find polyps > 5 mm in diameter, colonoscopy is recommended. Optimal management of polyps 5 mm or less in diameter is uncertain and a point for extensive discussion and debate which is beyond the scope of this review. This is, however, a critically important discussion which will be ongoing and should be closely followed since the sensitivity of CTC for polyps falls significantly when polyp size is < 10 mm and dramatically when < 6 mm. Follow-up colonoscopy will require another full bowel prep unless same day colonoscopy can be completed in the instance of a positive CTC. Risks of CTC and DCBE are low but rare cases of perforation have been reported for both. CTC may identify extracolonic abnormalities necessitating additional evaluation.

If negative, all of the structural exams are recommended to be repeated at 5 year intervals except for colonoscopy which should be repeated at 10 year intervals. Conscious sedation utilized with colonoscopy requires most patients to miss a day of work and to have an accompanying individual for transportation. Although rare, risks of colonoscopy

include perforation and bleeding, mostly following polypectomy.

Statement of the US Preventive Services Task Force

The recommendations from the USPSTF also include several options. These include "high sensitivity" gFOBT or an immunochemical based FOBT on an annual basis. Flexible sigmoidoscopy screening is recommended every 5 years in conjunction with gFOBT every 3 years. Colonoscopy is recommended at an interval of every 10 years. The same advantages and disadvantages apply as described for these tests in the previous paragraphs.

The USPSTF does not recommend sDNA or CT colonography for screening stating that there is "insufficient evidence to recommend for or against" either test at this time. Double contrast barium enema is not addressed in the USPSTF statement.

Common Ground in the Guidelines and the Statement (Table 2)

Both recommendations confirm the efficacy of screening for colorectal cancer and the life saving potential of a properly applied screening program. Both recommend that screening begin at age 50. Both recommend the same intervals for screening with high sensitivity FOBT, flexible sigmoidoscopy or colonoscopy. Both offer statements on limitations of screening in the elderly. The USPSTF states that routine screening between the ages of 76-85 is not recommended. Although on the surface this statement seems quite definitive, the narrative of the statement emphasizes the need to take a patient's individual circumstances into account.

This recommendation does not say that screening should not be done under any circumstances, only that routine screening in this population may not produce benefits that exceed harms. This is not dissimilar from the ACS-USMSTF-ACR guideline which states that screening should end at a point where an individual "is not likely to benefit from screening due to life-limiting co-morbidity". When an adult's health declines resulting in limited life expectancy screening is not advised.

Both guidelines accept that not every 75 year old is the same. There are some in this age group that are healthier than many that are much younger and would benefit from continued screening. Screening history

Recommendation	ACS-USMSTF-ACR	USPSTF
Age to begin and end screening and test prioritization:		
Age to begin and end screening in average risk adults	Begin age 50 and end when life saving therapy not offered due to life limiting co-morbidity	Begin age 50. Routine screening between 76 and 85 not recommended. Screening after 85 not recommended
Screening in high risk individuals	Detailed recommendations based on personal risk and family history	No specific recommendations on age to begin testing or type of testing
Prioritization of tests	Tests grouped into those that detect cancer and those that detect cancer and polyps	No specific prioritization but acknowledge that visualization tests offer benefit over fecal tests
Stool Testing:		
gFOBT	Annual screening with high sensitivity guaiac based tests	Annual screening with high sensitivity guaiac based tests
iFOBT	Annual screening	Annual screening
sDNA	sDNA is an acceptable option	Insufficient evidence to recommend for or against sDNA
Structural Examinations:		
Flexible Sigmoidoscopy	Screening every 5 years alone or every 5 years with annual gFOBT or iFOBT	Screening every 5 years with gFOBT every 3 years
Colonoscopy	Screening every 10 years	Screening every 10 years
CT Colonography	Screening every 5 years	Insufficient evidence to recommend for or against CT colonography
Double Contrast Barium Enema	Screening every 5 years	Not addressed

Table 2. Comparison of 2008 Recommendations between ACS-USMSTF-ACR and USPSTF

should also be considered. An individual in their mid 70s who has been faithfully screened since age 50 with negative results may want to consider discontinuing screening. However that same healthy individual who has never been screened may significantly benefit from a screening at this point in their lives.

Differences Between the Guidelines and the Statement (Table 2)

The USPSTF does not distinguish between tests that detect cancers and tests that detect cancer and polyps. The statement does, however, acknowledge that "direct visualization techniques offer substantial benefit over fecal tests, with greater sensitivity, when considered as a single test"⁶.

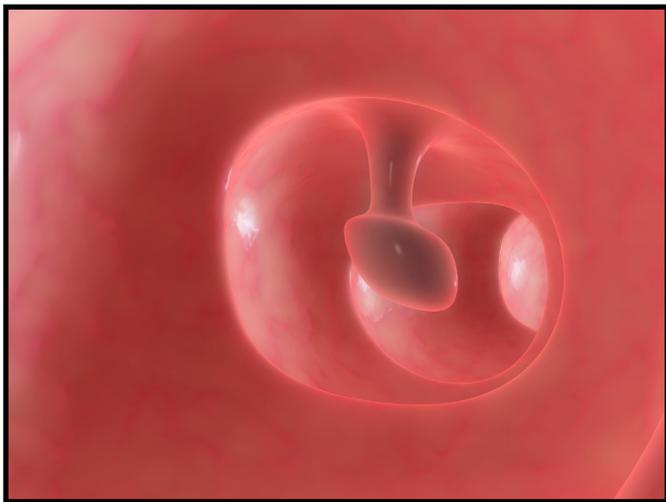
The USPSTF statement recommends against any screening in adults over age 85. The ACS guidelines follow the same approach in these patients as described above for patients aged 76-85.

The USPSTF statement recommends flexible sigmoidoscopy every 5 years with the addition of FOBT every 3 years. The ACS guidelines combined approach continues annual FOBT with flexible sigmoidoscopy every 5 years.

Double contrast barium enema is not addressed in the USPSTF statement. CT colonography and sDNA are not recommended tests in the USPSTF statement as they are in the ACS guidelines. Finally, the USPSTF statement does not address screening in high risk adults. The ACS guidelines provide detailed recommendations based on personal risk and family history.

Screening in High Risk Adults

According to the ACS-USMSTF-ACR guidelines, high risk patients should undergo screening/surveillance with colonoscopy at adjusted frequency. These include patients with a personal history of polyps or colorectal cancer, patients with a family history of polyps or colorectal cancer and patients with hereditary syndromes or inflammatory bowel disease (IBD).



Personal History of Polyps

Patients with a personal history of small, isolated hyperplastic polyps should continue screening as an average risk individual. Patients with 1 or 2 small adenomas of low grade dysplasia should have colonoscopy repeated in 5 to 10 years. Patients with 3 to 10 small adenomas or 1 adenoma > 1 cm or any adenoma with villous features or high grade dysplasia should have colonoscopy within 3 years following initial polypectomy and then once every 5 years. Patients with > 10 adenomas on a single examination should repeat colonoscopy in < 3 years and be evaluated for a possible familial syndrome. If no syndrome is found then follow up colonoscopy can be every 5 years if subsequent exams are normal. Patient with sessile adenomas removed piecemeal should have colonoscopy to verify complete removal within 2 to 6 months with subsequent exams following the above guidelines.

Personal History of Colorectal Cancer

Patients with a colorectal cancer should have a colonoscopy in the perioperative period and then one year after resection. If the one year exam is normal, subsequent exams should be done in 3 years and then at 5 year intervals providing the exams are normal. Any findings of additional neoplasia would require adjustments based on the recommendations for polyps as noted above. Patients with rectal cancer may have periodic examination of the rectum following low anterior resection for the purposes

of identifying a local recurrence if it should occur. These exams are usually done every 3 to 6 months for the first 2 to 3 years following resection.

Patients with a Family History of Colorectal Cancer or Polyps

Patients with either colorectal cancer or adenomas in a 1st degree relative before age 60 or in 2 or more 1st degree relatives at any age should begin screening with colonoscopy at age 40 or 10 years before the youngest case in the family and continue at 5 year intervals. Patients with colorectal cancer or adenomas in a 1st degree relative at age 60 or greater or in 2 second degree relatives with colorectal cancer should begin screening at age 40 utilizing any method they choose and continue at intervals recommended for average risk patients utilizing that screening method.

High Risk Patients

Patients with a diagnosis of Familial Adenomatous Polyposis (FAP) or suspected FAP should begin screening at age 10 to 12 with annual flexible sigmoidoscopy. Patients with Hereditary Nonpolyposis Colon Cancer (HNPCC) or suspected HNPCC should begin screening with colonoscopy at age 20 to 25 or 10 years before the youngest case in the family at 1 to 2 year intervals. Patients with a history of IBD should begin screening with colonoscopy and biopsies 8 years after the onset of pancolitis or 12 to 15 years after the onset of left-sided colitis.

Conclusions

Current guidelines on screening for colorectal cancer make it very clear that screening is a valuable tool to decrease both the incidence of and mortality from colorectal cancer. Recommended tests have been divided into those that primarily detect cancer (stool tests) and those that detect both cancer and adenomatous polyps (structural exams). Stool tests are limited in their capacity to prevent cancer. It is the stated opinion of the ACS-UAMSTF-ACR guidelines that, where capacity and financial resources allow, tests that provide for colon cancer prevention should be the primary goal of screening.

When financial resources are limited, stool based testing can provide meaningful reductions in both the incidence and mortality of colorectal cancer. In this time of economic instability, requests for assistance in screening may increase. The Nebraska Colon Cancer Screening Program can assist you with such needs. Please refer to the advertisement on the inside back cover of this issue for more information on this program.

So which test is best? The one that gets done!

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