Prevention and Screening of Gastrointestinal Cancers

Suzanne M. Mahon

Objectives: *This article reviews the current recommendations and data supporting various screening and prevention strategies for colorectal cancer (CRC) in average and high-risk individuals.*

Data Sources: *Published research reports, epidemiologic data, and published guidelines from professional organizations.*

Conclusion: *Properly applied screening tools can potentially decrease the morbidity and mortality associated with CRC.*

Implications for Nursing Practice: *Nurses need to be aware of current recommendations for the early detection of CRC so they can provide patients with an accurate assessment of risk for developing CRC and education about the appropriate CRC screening guidelines.*

Key Words: *Colorectal cancer, screening, prevention, risk assessment, colonoscopy.*

TOGETHER, gastrointestinal (GI) cancers comprise a significant percentage of cancers. To date, most efforts in screening and prevention have been directed toward colorectal cancer (CRC), which has a high incidence. Recommendations for the early detection of CRC have been modified over time and there is solid scientific evidence that these measures decrease the morbidity and mortality associated with CRC. More recently, guidelines have been released by the American College of Gastroenterology (ACG) for screening in patients with Barrett's esophagus, and a Japanese group has issued some early guidelines for gastric cancers.[1,2] This article includes an overview of the risk factors and early detection strategies for Barrett's esophagus and gastric cancer and a detailed discussion of risk assessment, prevention, and early detection strategies for CRC.

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0749-2081/09/2501-$32.00/0.
doi:10.1016/j.soncn.2008.10.007

Barrett's Esophagus

Barrett's esophagus (BE) is a progressive metaplasia of the distal esophagus. It often occurs as a result of prolong reflux esophagitis and gastroesophageal reflux. It is considered by many to be a precursor to the development of adenocarcinoma of the esophagus. The exact prevalence of BE in the general population is not known. The overall prevalence of BE is estimated to be 1.6%,

with a prevalence rate of 2.3% in those with reflux symptoms and 1.4% in those without reflux symptoms.[3] Major risk factors for development include male sex, advanced age, chronic gastroesophageal reflux disease (GERD) and, possibly, family history. Screening is further complicated by the fact that a large number of patients lack reflux symptoms and there is not a clear means to identify these persons. BE is a histologic diagnosis. An esophagogastroduodenoscopy (EGD) is performed to obtain tissue samples. Samples are usually taken from the distal esophagus just above the lower esophageal sphincter, where BE primarily occurs. Patients diagnosed with BE should be screened regularly with an EGD with biopsy.

Screening for BE remains controversial because of the lack of a clear algorithm for how and whom to screen and whether screening has a significant impact on mortality.[1] Currently esophageal capsule endoscopy appears to be a promising technique to screen for BE. This video endoscopy is accomplished by having the patient swallow a small camera about the size of a vitamin capsule. The camera emits a light and takes two pictures per second as it traverses the GI tract. The pill is easily swallowed and transmits the images to a recording device worn around the waist. These images are then downloaded to a computer where they are reviewed by a physician to determine if abnormalities are present. It provides a noninvasive means to detect a columnar line esophagus, which is suggestive of BE,[1] but the expense prohibits this test from being utilized routinely. Because of these limitations, the ACG does not routinely recommend screening for BE in the general population.

Once BE is identified in a patient, there should be a discussion regarding the relative strengths of surveillance endoscopy and the risk of developing esophageal adenocarcinoma, which has limited treatment options and poor survival (less than 13% 5-year survival rate).[1,3] It is recommended that persons with GERD be placed on proton pump inhibitor therapy to decrease inflammation so surveillance is more likely to be effective and decrease the cellular changes that result in dysplasia.[3,4] Algorithms are available, depending on the degree of dysplasia, to determine the interval for endoscopy with biopsy. For those patients without dysplasia, endoscopy can be performed every 3 years. Those with low-grade dysplasia should have annual endoscopy until no dysplasia is detected for 2 years. Patients with high-grade dysplasia need aggressive and thorough surveillance every 3 months.

Patients diagnosed with BE require education on how to manage their disease. They need to be aware of the importance of regular endoscopic screening and follow-up. Patients should be informed to avoid foods and beverages that either irritate the esophageal mucosa or decrease lower esophageal sphincter pressure. These include tomato and citrus-based foods, spicy foods, onions, garlic, peppermint, chocolate, caffeine, and alcohol.[4]

Gastric Cancer

Gastric cancer is a significant problem and contributes to 600,000 deaths worldwide,[2,5] In the United States it accounts for 21,500 new cases and 10,880 deaths annually.[6] Risk for gastric cancer is increased in those with Helicobacter pylori (H pylori) infections, and those with certain genetic changes that predispose to developing gastric cancer. These include persons with a family history of gastric cancer as well as persons with a known or suspected mutation for hereditary nonpolyposis colorectal cancer (HNPCC).[5] Other persons at risk include those that consume diets high in salt, smoked, poorly preserved foods, nitrites, and nitrates.

Persons with a known mutation or suspected mutation in their family should be referred to a genetics professional for more detailed evaluation. Genetic testing is readily available for HNPCC, and testing for diffuse gastric cancer is available on a more limited basis. Identifying persons with a hereditary predisposition is important because this population may benefit from aggressive screening including gastroduodenoscopy.[2]

Colorectal Cancer

CRC continues to be a significant health problem in the United States. There is clear evidence that screening is the key to reducing the morbidity and mortality associated with this disease; when screening is performed consistently, correctly, and polyps are removed.[7] Polyps, especially the adenomatous ones, are considered to be precursors to CRC. Screening directly impacts how early a malignancy is detected and long-term survival. The estimated 5-year survival

is 90% if the disease is diagnosed while still localized (confined to the wall of the bowel), but only 68% for regional disease (lymph node involvement), and only 10% if distant metastases are present.[8]

Selection of the appropriate screening interval and modality is based on cancer risk assessment. Guidelines for CRC cannot be uniformly applied to the entire population; some individuals have a greater risk of developing CRC than others. The most important step in CRC screening is an accurate assessment of the risk for developing CRC.

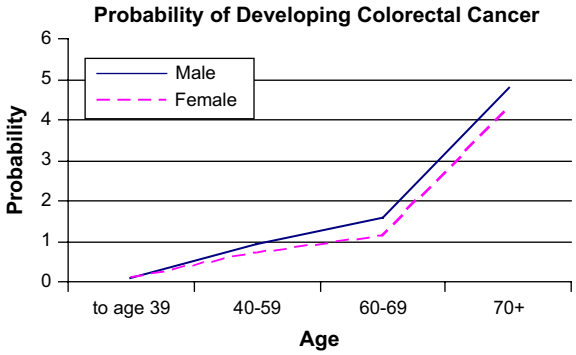

FIGURE 1. **The lifetime probability for males for developing CRC is 5.65 (1 in 18 males) and for females is 5.23 (1 in 19 females). (Source: American Cancer Society.[6])**

Colorectal Cancer Risk Factors

An individual's risk for CRC is stratified into one of three categories. Most of the population has an average risk of developing the disease; some have a slightly higher risk based on personal risk factors. Those with a known or suspected mutation in a cancer susceptibility gene have a very high risk for developing the disease. It is important to note that no one has zero or low risk for developing CRC.

Population at Average Risk

The lifetime risk of developing CRC is approximately 48.2 cases per 100,000 population.[6] Incidence increases with age (90% of cases occur after age 50) and is relatively similar between males and females (as shown in Fig. 1). Table 1 identifies a number of other modifiable and nonmodifiable risk factors for CRC.

There are a variety of myths and misconceptions about CRC that healthcare providers need to address. For instance, it is often incorrectly assumed there are persons at low risk for CRC. At the very minimum, everyone is at average risk. Many individuals are surprised to learn that some risk factors can be adjusted to reduce the risk of developing CRC. When a risk factor can be modified, individuals should be instructed about how to address their particular risk. When it cannot be modified, the healthcare provider should discuss how this risk factor is considered in selecting the appropriate cancer screening modality. People may also be confused about their risk related to a personal or family history of polyps or cancer. Knowing the age of onset can help clarify risk. Individuals with a single first-degree relative diagnosed with CRC or an adenomatous polyp after age 60, or with affected relatives who are more distant than first degree, can be considered to be at average risk.[7-9]

Populations at High Risk

Approximately 15% to 20% of CRCs occur among people at increased risk or high risk (approximately twice the average risk).[6] People who have been diagnosed as having adenomatous polyps are clearly at higher risk. A family history of either CRC or colorectal adenomas increases one's risk of developing CRC.[7] Risk is increased for individuals with a family history involving first-degree relatives, and is even higher if a first-degree relative (parent, sibling, or offspring) has had a CRC or an adenomatous polyp diagnosed before age 60 years, and/or if more than one first-degree relative has been affected at any age. Inflammatory bowel disease, which includes ulcerative colitis and Crohn's disease, is a condition in which the colon is inflamed over a protracted period of time and these conditions have an increased risk of developing CRC.[9]

Hereditary Risk

Persons with a known hereditary mutation are at high risk for developing CRC. The clinical indicators of hereditary CRC syndromes are shown in Table 2. The goal of genetic testing in families is to offer appropriate screening guidelines to individual family members by identifying who carries the mutation and who does not. For those who test positive for a known mutation, screening begins at a very early age (such as age 25 for HNPCC carriers) and is performed at more frequent intervals (annually) throughout their lifetime. Individuals who test negative for a known

TABLE 1.
Risk Factors for Developing Colorectal Cancer

Risk Factor	Etiologic Basis	Modifiable	Significance
Age	As the body ages, all tissues are at increased risk for cellular changes leading to cancer	No	90% of colon cancers are diagnosed after age 50. Implication for screening to begin at age 50
Polyps	Many polyps progress in an orderly fashion from a polyp to malignancy over a period of years	Probably not	Polyps need to be removed during colonoscopy. Depending on findings, interval for screening may be decreased
Personal history of cancer	Same risk factors that led to the first cancer can lead to a second CRC in another section of the colon	No	Risk is higher in those with cancer diagnosed before age 60
Inflammatory bowel disease and Crohn's disease	Associated with dysplasia and increased risk of developing CRC especially if the disease is long-term	No	Screening is probably indicated at a younger age and more frequently
Family history of CRC	20% of persons diagnosed with CRC have at least one relative with the disease which is probably related to modifier genes	No	Risk increases with the number of relatives with adenomatous polyps or CRC
Persons with a mutation in FAP	Form hundreds of polyps; most start to occur about age 20	No	Penetrance is nearly 100% and accounts for about 1% of all CRC
Persons with HNPCC syndromes	Polyp to CRC syndrome is short; often occurs before age 40	No	Penetrance is 80% to 85% and accounts for about 4% of all CRC
Ethnicity	African Americans have highest incidence and mortality; about 6% of Ashkenazi Jews have mutations that put them at increased risk	No	Develop screening programs targeting high-risk populations
Dietary factors	Risk is increased in persons who consume a diet high in red and processed meats	Yes	Risk is decreased in persons who eat a diet rich in fruits and vegetables
Physical inactivity	Reason for increased risk is not clear	Yes	Risk is increased in inactive persons
Obesity	Reasons for increased risk is not clear	Yes	Risk is increased in both men and women, but even higher in men
Smoking	Carcinogenic substances enter the gastrointestinal system	Yes	Risk increases with the number of pack years
Alcohol use	Those who consume increased amounts of alcohol may have lower levels of folic acid	Yes	Consume no more than 1 alcholic beverage per day
Type II Diabetes	Reason for increased risk is not completely understood	Possibly	May be associated with a poorer prognosis, once the cancer is diagnosed

Abbreviations: CRC, colorectal cancer; FAP, familial adenomatous polyposis gene; HNPCC, hereditary non-polyposis colorectal cancer gene.
Data from Bernard et al,[7] American Cancer Society,[8] Levin et al,[9] and Lynch and de la Chapelle.[10]

mutation in their family can pursue the screening recommendations for those at average risk.

The most common hereditary CRC syndrome is an autosomal dominant syndrome known as HNPCC, which accounts for 3% to 5% of all CRC.[10] It is also associated with endometrial cancer, ovarian cancer, gastric cancer, bile duct cancer, and small bowel, renal pelvis, and ureter cancer.[11] The majority of mutations responsible for HNPCC occur in four mismatch repair genes, MSH2, MLH1, PMS2, and MSH6.[12] Patients with a mutation in MLH1 and MSH2 have an 80% lifetime risk of developing CRC as compared with a 6% risk in the general population. Women with mutations in these genes have a 60% lifetime risk for developing endometrial cancer and a 12% lifetime risk for developing ovarian cancer.[13]

Persons with HNPCC-related cancers are more likely to have poorly differentiated tumors with an excess of mucoid and signet-cell features.[11]

Although not associated with large numbers of polyps, persons with HNPCC who do form adenomatous polyps are more likely to do so at an earlier age, to develop right-sided colon cancer, and to exhibit a rapid progression to malignancy (ie, 1 to 3 years instead of the 5- to 10-year pattern seen in the general population).[11,14]

Risk assessment is the key to identifying families with an HNPCC mutation. There are several strategies to consider in identifying these patients and any suspected family should be referred to a genetics professional to identify the most cost-effective and efficient strategy for genetic testing. The Amsterdam and Bethesda criteria (Table 3) assess the number of relatives affected by CRC or other HNPCC-related cancers, with particular emphasis on the age of onset.[10,15,16]

Immunohistochemistry staining can be performed on tumor tissue from persons who fulfill Bethesda criteria to determine the presence or absence of MLH1, MSH2, MSH6, and PMS2 proteins. This can predict a mismatch repair defect and thereby avoid unnecessary, expensive, and time-consuming DNA analyses.[12] If immunohistochemistry is positive for all four proteins in a family that fulfills Amsterdam criteria, the next strategy to determine if it is appropriate to test an individual is to perform an MSI (microsatellite) assay on the affected family member's colorectal tumor.[10] In HNPCC, mutations in the DNA repair genes result in a phenomenon known as MSI instability. Microsatellites are repeated sequence of DNA that are a defined length for each individual. Because of the accumulation of errors, these sequences can become abnormally longer or shorter; this is referred to as MSI.[15] An MSI high phenotype is reported in 85% to 92% of HNPCC colon cancers and approximately 15% of sporadic cancers.[12] MSI testing is also an appropriate strategy for Amsterdam-negative families who are positive by the Bethesda criteria.

Familial Adenomatous Polyposis (FAP), an autosomal dominant trait, is characterized by numerous (usually > 100) adenomatous colon polyps and accounts for about 1% of all cases of CRC.[10] The FAP gene is nearly 100% penetrant, so if a person is not treated they will develop CRC because of the sheer number of polyps. The mean age of cancer onset is 39; although as many as 75% will have developed adenomas by age 20.[17,18] A less severe form of FAP called "attenuated familial adenomatous polyposis" (AFAP) is characterized by less than 100 polyps (usually about 20) at presentation and later onset of CRC. There are over 800 mutations in the APC gene associated with FAP.[12] Deleterious mutations in this tumor suppressor gene result in the premature truncation of the APC protein.[18,19] There is also an autosomal recessive gene on chromosome

TABLE 2.
Key Indicators of Hereditary Colon Cancer Syndromes

HNPCC
- Personal history of CRC diagnosed before age 50
- Personal history of endometrial cancer diagnosed before age 50
- First-degree relative with CRC before age 50
- Two or more relatives with CRC or an HNPCC-associated cancer (including endometrial, ovarian, gastric, hepatobiliary, small bowel, renal pelvis or ureter cancer). One relative must be a first-degree relative of another
- CRC occurring in two or more generations on the same side of the family
- A personal history of CRC and a first-degree relative with adenomas diagnosed before age 40
- An affected relative with a known HNPCC mutation

FAP
- Patient has a clinical diagnosis of FAP (100 or more polyps)
- Patient has suspected FAP or AFAP (15 to 99 polyps)
- Patient is a first-degree relative of FAP or AFAP patient
- Patient has an affected relative with a known FAP or MYH mutation
- Patient with any number of adenomas in a family with FAP

Abbreviations: CRC, colorectal cancer; HNPCC, hereditary non-polyposis colorectal cancer; FAP, familial adenomatous polyposis.
NOTE. The presence of one or more of these factors in an individual or family history is suggestive of hereditary risk for CRC and warrants further evaluation.
Data from Lynch and de la Chapelle,[10] Vasen et al,[16] Balmana et al,[17] Calvert and Frucht,[18] and Jeter et al.[19]

TABLE 3.
Comparison of the Amsterdam and Bethesda Criteria Used in Assessment of Risk for Hereditary Colon Cancer

Amsterdam Criteria	Bethesda Criteria
At least 1 person was diagnosed before age 50	CRC diagnosed in a patient who is less than 50 years of age
There are at least 3 relatives with an HNPCC-related cancer (large bowel, endometrium, ureter or renal pelvis); does not include stomach, ovary brain, bladder, or skin	Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors, regardless of age. These tumors would include colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain
FAP has been excluded	CRC with the MSI-High pathology diagnosed in a patient who is <60 years of age
At least two successive generations are affected	CRC diagnosed in 1 or more first-degree relatives with an HNPCC-related tumor, with 1 of the cancers being diagnosed under age 50 years

Abbreviations: HNPCC, hereditary non-polyposis colorectal cancer; FAP, familial adenomatous polyposis.
Data from Umar et al[15] and Vasen et al.[16]

1, MYH, that is associated with polyposis.[20] Approximately 25% of individuals with FAP have a "de novo mutation," which means they are the first person in their family with the hereditary mutation for FAP.[18] Subsequent generations are at risk for inheriting the mutation.

Preventive Measures

Prevention of CRC focuses on two areas. The first deals with the modification of risk factors when possible. The second area addresses potential chemoprevention strategies.

Maintaining a Healthy Body Weight

The percentage of Americans who are overweight or obese has increased over the past 25 years. Nearly two thirds (64%) of US adults 20 years or older met the criteria for overweight or obesity in 2000, while 30.5% qualified as obese.[21] The percentage of overweight children and adolescents has also increased since the late 1980s.

Educating individuals about ways to achieve a healthy body weight is an important nursing responsibility. Many individuals know this is important, but need encouragement and support from a healthcare provider to actually implement effective interventions. Excess body fat can be reduced by decreasing caloric intake and increasing physical activity. For most adults a reduction of 50 to 100 calories per day may prevent gradual weight gain, whereas a reduction of 500 calories or more per day is a common initial goal in weight loss programs.[22,23] Research suggests that up to 60 minutes of moderate to vigorous intensity physical activity per day may be needed to prevent weight gain, but as much as 60 to 90 minutes of moderate intensity physical activity per day may help to sustain weight loss for previously overweight people. In terms of CRC prevention, physical activity causes food to move more quickly through the intestine, reducing the length of time that the bowel lining is exposed to potential carcinogens.[21] Therefore, regular physical activity and a healthy diet can help decrease the risk of CRC.[22] This reduction in risk is intended not only for healthy persons, but also for persons who have been diagnosed with colorectal ancer. Increased physical activity and a healthy diet may reduce the risk of a second primary cancer, including CRCs.[24]

Eating a Healthy Diet

A diet rich in fruits and vegetables appears to be important for cancer risk reduction. Research suggests that the body uses certain nutrients in vegetables and fruits to protect the body against damage to tissues that occurs constantly as a result of normal metabolism. Because such damage is associated with increased cancer risk, the antioxidant nutrients are thought to protect against cancer.[22] Antioxidants include vitamin C, vitamin E, carotenoids, and many other phytochemicals.

The amount of fat and fiber in the diet has been examined extensively as risk factors associated with CRC. A diet high in fiber and low in fat, which for adults is 20 to 35 grams of fiber per day and about 30% or less of their total daily calories from fat, along with limited consumption of red meat, helps reduce the risk of

CRC.[8] It also is recommended that men and women regularly eat fruits and cruciferous vegetables, and consume calcium to decrease the risk of CRC.[23,24]

Many questions remain concerning nutrition and cancer. Epidemiologic studies have shown that populations whose diets are high in vegetables and fruits and low in animal fat, meat, and/or calories have a reduced risk of some of the most common types of cancer.[22] Until more is known about the specific components of diet that influence cancer risk, current recommendations are to consume a mostly plant-based diet that includes at least five servings of vegetables and fruits each day, to choose whole-grain carbohydrate sources over refined sources, and to limit saturated fat, alcohol, and excess calories.[8]

Avoidance of Tobacco and Alcohol Products

Evidence shows that 12% of CRC deaths are attributed to smoking.[25] The carcinogens found in tobacco increase cancer growth in the colon and rectum, and increase the risk of being diagnosed with this cancer.

Alcohol consumption is also a factor in the diagnosis of CRC, especially at a younger age. Increased alcohol intake is also associated with increased risk of cancer in the distal colon. Regular consumption of alcohol doubles the risk of developing CRC; thus limiting alcohol intake is recommended.[25]

Chemopreventive Measures

CRC chemoprevention has been an active area of research; focusing on NSAIDs, aspirin, and COX-1 and COX-2 inhibitors. Results have been variable. Aspirin, an inhibitor of COX-1 and COX-2, has been studied in several randomized studies, but the effect on CRC prevention is unclear. The US Physician's Health Study (n = 22,071) showed that aspirin had no effect on the incidence of polyps or colon cancer.[26] A different study of aspirin combined with folate (n = 1,121) showed that the 81-mg dose of aspirin prevented recurrence of colorectal adenomas (19% reduction).[27] This study also reported a relative-risk reduction of 40% in the 81-mg aspirin group for advanced lesions. Analysis of the folate intervention is ongoing. This data suggests that aspirin may be a potential chemopreventative agent for CRC.[28]

The benefit of NSAIDs in chemoprevention has been reported in certain high-risk groups. Sulindac reduces MSI in HNPCC cell lines carrying MLH1, hMSH2, and MSH6 mutations and in persons with FAP.[29-31] Individuals with these mutations, should be counseled regarding the potential benefits of these agents in reducing polyp formation.

The use of COX-2 inhibitors and NSAIDs in the primary prevention of sporadic CRC is being studied.[31,32] To date, none of these agents is recommended for prevention in the general population. The United States Prevention Services Task Force (USPSTF) currently recommends against the routine use of NSAIDs and aspirin for the prevention of CRC in persons of average risk.[33,34] This is based on the premise that these agents do not have an effect on the number of deaths due to CRC and are associated with potential harms, especially in terms of GI bleeding.

Screening Tests for Detection of CRC

Screening remains the single most important means to reduce the morbidity and mortality associated with CRC. The most recent guidelines change emphasis from a focus on detection to one that includes both early detection and prevention. In addition, they introduce new recommendations including the incorporation of stool DNA testing (sDNA) and virtual colonoscopy. This is a major shift from previous guidelines for the early detection of CRC. There are many screening test options and intervals. For some of the detection strategies, the interval guideline is fairly clear and for others more research is needed. It also places a tremendous amount of responsibility in the hands of the healthcare provider to give patients enough education so they can make an informed choice about CRC screening. The number of choices will undoubtedly be a source of confusion for some healthcare providers and much of the public. Screening for CRC has been categorized into tests that are likely to detect CRC and tests that are likely to detect polyps and/or cancers.[7] Table 4 provides a summary of the strengths and limitations of screening tests for CRC.

Fecal Occult Blood Tests

Stool blood tests or fecal occult blood tests (FOBT) are one of the more common tools used in the detection of CRC. There are two types of FOBTs depending on the analysis process. These can be guaiac based (gFOBT) or a fecal immunochemical test (FIT). The premise of using the FOBT is that occult blood, although a nonspecific

finding, may be due to bleeding from a large polyp.[7] Blood in the stool is a nonspecific finding but may originate from CRC or larger (>1 to 2 cm) polyps. Because small adenomatous polyps do not tend to bleed and bleeding from cancers or large polyps may be intermittent or simply not always detectable in a single sample of stool, the proper use of stool blood tests requires annual testing that consists of collecting multiple specimens from consecutive bowel movements while following a specific dietary regimen.[35]

A significant difference in FOBTs is in the processing. FITs are usually processed in a clinical laboratory, whereas gFOBT can be processed either in the physician's office or in a clinical laboratory. A positive gFOBT or FIT requires a diagnostic workup with colonoscopy to examine the entire colon to rule out the presence of cancer or advanced neoplasia.

The gFOBT are the most common FOBT in use for CRC screening and the only CRC screening test for which there is evidence of efficacy from prospective, randomized controlled trials.[7] Three large, prospective, randomized controlled trials with gFOBT have shown that screened patients have cancers detected at an early and more curable stage than unscreened patients, with reductions in CRC mortality of 15% to 33%.[37-39] Usual gFOBT protocol consists of collecting two samples from each of three consecutive bowel movements at home. Collection of all three samples is important because test sensitivity improves with each additional stool sample.[35,36] The sensitivity and specificity of a gFOBT has been shown to be highly variable depending on the brand of the test, specimen collection technique, number of samples collected per test, whether or not the stool specimen is rehydrated, and variations in interpretation, screening interval, and other factors.[40-42]

A significant limitation of the potential of testing with gFOBT is that it is commonly performed in the doctor's office as a single-panel test following a digital rectal exam. It has been demonstrated that sensitivity is only 4.9% for advanced neoplasia and only 9% for cancer.[42] The accuracy of this method is so low that it cannot be considered an acceptable measure for CRC screening.[7]

The concept of applying an immunochemical method to testing stool for occult blood was first proposed in the 1970s and commercialization of the technology began in the 1980s.[7] A limitation is that FIT is more expensive than gFOBT. A significant advantage of FIT is that it detects human globin, a protein that along with heme constitutes human hemoglobin. Thus, FIT is more specific for human blood than guaiac-based tests, which rely on detection of peroxidase in human blood and also react to the peroxidase that is present in dietary constituents such as rare red meat, cruciferous vegetables, and some fruits. Finally, the sample collection for some variants of FIT are less demanding of patients than gFOBT, requiring fewer samples or less direct handling of stool. Despite the physiologic evidence that FIT is possibly a better test, it has never been tested in a randomized trial where the outcome of interest is CRC mortality.[7,43]

Genetic Testing of Stool

Adenoma and carcinoma cells that contain altered DNA are continuously shed into the colon and passed out of the body through feces. Because DNA is stable in stool, it can be isolated from bacterial DNA found in the feces.[44] A limitation of this testing is that no single gene mutation is present in cells shed by every adenoma or cancer.[45] Thus, a multitarget DNA stool assay is required to achieve adequate sensitivity; the commercial availability of this test is limited. The primary benefit of sDNA is that this methodology has acceptable sensitivity for CRC and is built upon the concept of detecting molecular markers associated with advanced colorectal neoplasia. It is not dependent on the detection of occult bleeding, which is intermittent and nonspecific, and it requires only a single stool collection.[46]

Flexible Sigmoidoscopy

Flexible sigmoidoscopy (FSIG) directly examines the lumen of the lower half of the colon. The endoscope is passed to the transverse colon (~ 60 cm). FSIG is performed without sedation and with a limited bowel preparation. It is an attractive screening tool because it can be performed in the office setting by a variety of healthcare professionals, including nurses with specialized training.[47,48]

FSIG has been studied extensively and promoted extensively. It is documented to have a 60% to 80% reduction in CRC mortality for the area of the colon that can be examined.[7] For persons at higher risk, it is not a sufficient examination because a significant portion of the colon is not evaluated. The effectiveness of sigmoidoscopy

TABLE 4.
Strengths and Limitations of Screening Tests for Colorectal Cancer

Test	Recommendations	Preparation	Accuracy	Risks	Patient Teaching
FSIG	ACS – every 5 years NCCN – every 5 years ACG – every 5 years USPSTF – every 5 years	Partial bowel prep with laxatives and enemas Sedation usually not used	45%-50% sensitivity	Potential discomfort	Evaluates lower third of colon A positive screen requires follow-up with colonosocopy May be some discomfort Very small risk of bleeding, infection, or perforation
Colonoscopy	ACS – every 10 years NCCN – every 10 years ACG – every 10 years USPSTF – every 10 years	Complete bowel prep	Up to 95% sensitivity Can usually view entire colon Can biopsy and remove polyps Can diagnose other diseases	Requires conscious sedation Perforation and bleeding; risk is increased with polypectomy	Will need to miss a day of work Will need someone to take them to and from appointment
DCBE	ACS – every 5 years NCCN – every 5 years ACG – every 5 years USPSTF – every 5 years	Complete bowel prep No sedation needed	Sensitivity of 48% to 73%	Rare cases of perforation	Cannot biopsy polyps A positive screen requires follow-up with colonoscopy
CTC	ACS – every 5 years NCCN – no recommendation ACG – no recommendation USPSTF – no recommendation	Complete bowel prep No sedation	Sensitivity of 55% to 59% for large polyps	Rare cases of perforation Costly – may not be covered by insurance	A positive screen necessitates the need for colonoscopy; if not available same day a second prep will be required May detect other problems outside of the colon that need evaluation
gFOBT	ACS – annually NCCN – annually USPSTF – annually ACG – annually	Requires collection of at least 2 – 3 samples No risk of bowel injury Done in privacy of home Relatively Inexpensive	Sensitivity ranges from 37% to 79%		Foods to avoid 48 hours prior to and during collection include aspirin, NSAIDs, vitamin C, red meat, poultry, fish, raw vegetables A positive screen requires further evaluation with colonoscopy
FIT	ACS – Annually NCCN – No recommendation ACG – no recommendation USPSTF – no recommendation	No risk of injury to bowel Done in privacy of home	Senisitivity ranges from 29% to 94%		One time testing is likely to be ineffective A positive screen requires follow-up with colonoscopy Requires specific instructions on tranports to lab
sDNA	ACS – no recommended interval NCCN – no recommendation ACG – no recommendation USPSTF – no recommendation	No risk of injury to bowel No dietary restrictions Done in privacy of home	Sesnitivity ranges from 52% to 91% Specificity ranges from 93% to 97%		Requires collection of an adequate sample and proper preservation and shipping to laboratory A positive screen requires follow-up with colonoscopy

Abbreviations: FSIG, flexible sigmoidoscopy; ACS, American Cancer Society; NCCN, National Comprehensive Cancer Network; ACG, American College of Gastroenterology; USPSTF, United States Preventive Services Task Force.
Data from Bernardet al,[7] American Cancer Society,[8] Levin et al,[9] Winawaer et al,[35] and Pigone et al.[36]

depends on the completion of a high-quality exam. Studies have reported variable adenoma detection rates at screening sigmoidoscopy that are attributed to exam quality and completeness.[49] The American Cancer Society (ACS), USPSTF, and American Gastroenterology Society (AGS) recommend that if sigmoidoscopy is performed for CRC screening, insertion to 40 cm or beyond is required.[7,34-36]

The success of FSIG depends not only on exam quality, but on good decision-making in the management of polyps and adequate follow-up. An underlying assumption is that if a polyp is detected in the sigmoid colon or rectum, the patient will be referred for total colonoscopy. Patients should fully understand that in most circumstances colonoscopy will be recommended if an adenoma is detected during FSIG and that if they are unwilling to accept referral to colonoscopy, they should have a different form of screening.

Colonoscopy

In the United States, FSIG has decreased in populatrity in the past 10 years and colonoscopy has increased in use (see Fig. 2A and B). Much of this shift is attributed to Medicare coverage for colonoscopy, which began in 1998.[50] Colonoscopy has increased in popularity not only because of a shift in insurance coverage, but because it not only detects polyps but makes it possible to remove polyps in one procedure. Adenomatous polyps (a known precursor lesion to CRC) are common in adults over age 50 years. The majority of polyps will not develop into adenocarcinoma, but the removal of such polyps is considered a true form of primary cancer prevention.[51]

With proper technique using a colonoscope, it is possible to examine the lumen of the entire bowel ending at the cecum. Preparation includes a clear liquid diet at least 24 hours prior to the exam followed by oral lavage solutions or saline laxatives, resulting in multiple bowel movements until the colon is clear. Adequate bowel preparation is critical to having a complete exam, making colonoscopy a reasonable procedure from a cost-effectiveness standpoint.[7]

Despite its widespread use and recommendations, there has never been a prospective, randomized, controlled trial evaluating colonoscopy as a means to reduce the incidence and mortaity from CRC.[7,34-36] Several case control studies have shown that when colonoscopy with polypectomy is combined with other screening modalities there is evidence that it decreases mortality.[34,52,53] The ACS concluded that these data support the conclusion that colonoscopy reduces CRC incidence by polypectomy and, theoretically, if incidence is decreased, so is mortality.[7,35]

There are several important patient education points related to colonoscopy. A primary benefit of colonoscopy is that it allows for a full examination of the lumen of the colon and rectum in a single examination and for the detection of colorectal polyps and cancers with simultaneous biopsy or polypectomy. All other forms of screening, if positive, require colonoscopy as a second procedure. Limitations of colonoscopy include dietary restrictions and bowel preparation, the need for someone to transport the patient because of sedation, and at least 1 lost day in terms of work productivity. The procedure is only effective if the preparation is complete.

In addition, there are technical concerns about the effectiveness of the endoscopist. The lack of formal quality assurance programs for endoscopists and the current reimbursement system does not reward the endoscopist for a thorough examination; it may encourage very rapid and less than thorough examinantions.[50,54]

Another significant, but often overlooked issue is that polypectomy is not universally effective in completely removing polyps, which has been attributed to an etiologic factor in approximately 25% of the CRCs that develop between screening examinations.[55-58] A summary of the ACS recommendations about management of polyps is shown in Table 5. When using these recommendations, the endoscopist needs to consider the preparation, the patient's risk factors, and the quality of the examination, and modify appropriately.

Double Contrast Barium Enema

The double contrast barium enema (DCBE) is a radiographic technique that evaluates the entire colon by coating the mucosal lumen with barium and distending it with air through a flexible catheter placed in the rectum. Multiple radiographs are obtained. Similar to colonoscopy, a DCBE requires a bowel preparation to clean the colon. Any positive finding must be evaluated with colonoscopy, which will require an additional bowel preparation. Like colonoscopy, there have not been any randomized controlled trials to evaluate its ability to decrease the morbidity, incidence, and mortality associated with CRC. A benefit of

DCBE is that it evaluates the entire colon in almost all cases and can detect most cancers and the majority of significant polyps. DCBE also provides an opportunity for a full structural examination for individuals for whom colonoscopy has either failed or cannot be performed for other medical reasons.[7] DCBE is considered a relatively safe procedure with a lower perforation rate when compared with colonoscopy (1 of 25,000 vs 1 of 1,000 to 2,000).[59]

Virtual Colonoscopy

A CT of the colon (CTC) is commonly referred to as virtual colonoscopy. It has recently been added to the recommendations from the ACS for the detection of CRC.[7] CTC is considered a minimally invasive means to evaluate the colon and rectum. The CTC is an imaging procedure that has been studied extensively and refined greatly since first being introduced in the 1990s.[59] Newer technology can make 1- to 2-mm slices in 2- and 3-dimensional views throughout the intestine.[60]

A CTC also requires a bowel preparation similar to colonoscopy. During the examination, the colon is expanded with air or carbon dioxide to improve visualization. Some patients find this uncomfortable. The procedure is very quick; taking only about 10 minutes. It can be accomplished without sedation, so recovery is very quick and there is no need to arrange for transportation. If an abnormality or polyp is detected, it is desirable to have access to immediate colonoscopy, so the patient does not have to repeat the bowel preparation.

The sensitivity for detecting large polyps (>10 mm) is 85% to 93% and the specifity is 97%. The overall sensivity for CRC is 96%.[61] Because CTC provides a time-efficient procedure with good accuracy and minimal invasiveness, the ACS now considers it a reasonable option for screening for CRC.[7] More research is needed to determine if CTC will reduce the incidence and mortality of CRC. Institutions that offer this technology need radiologists who are trained in the procedure; access is limited in many geographic areas.[62] CTC is a minimally invasive test and the risk for colonic perforation during screening is extremely low (< .06%).[63] Another potential benefit is the possiblity of finding extracolonic pathology because CTC produces an image of the colon as well as the upper and lower abdomen. Preliminary research demonstrates that significant extracolonic pathology or findings may occur in 4.5% to 11% of all CTCs performed.[64] Of concern are the false-positive extracolonic findings that are of limited clinical signficance, but result in additional evaluation, costs, and anxiety. The exact incidence of these insignificant findings in CTC is not fully understood.[65]

The management of CTC findings is controversial and there is a need for more defined guidelines.[66-69] At this time the recommendation is that all patients with $\geq$ 1 polyps 10 mm or $\geq$ 3 polyps 6 mm should be referred for colonoscopy.[67,68] The management of patients with $\leq$ 3 polyps in which the largest polyp is 6 to 9 mm remains controversial. These polyps are typically removed during colonoscopy because it is relatively easy to accomplish and decreases the risk of developing CRC. The actual risk of such polyps developing into CRC is not fully understood and has implications for CTC.

Patient and Family Education

There are a number of patient and family education issues that nurses need to consider when promoting the early detection of CRC. These center around clarification of why there are different guidelines, the role of risk assessment in CRC, and general information regarding the strengths, limitations, and risks associated with screening. Nurses need to structure such education to remove barriers to CRC screening.

Education Regarding Guidelines

There are several agencies with recommendations for CRC screening (Table 3). There are also various choices in CRC screening.[7,8,69] These recommendations are continually being updated. Nurses can compare these updated guidelines at www.guidelines.gov. Unless the nurse is familiar with the continual updates, it is impossible to provide current education.

Much of the controversy about CRC screening stems from the multiple choices for screening. The first CRC screening recommendations for persons of average risk were issued in 1980 by the ACS.[68,69] These recommendations have been revised periodically. In 1997, the ACS stratified risk categories and differentiated between persons of average and high risk.[70] Although this differentiation is targeted at trying to use resources wisely, the risk stratification is sometimes confusing to both healthcare providers and consumers. Most recently, the guidelines have been modified to address management of

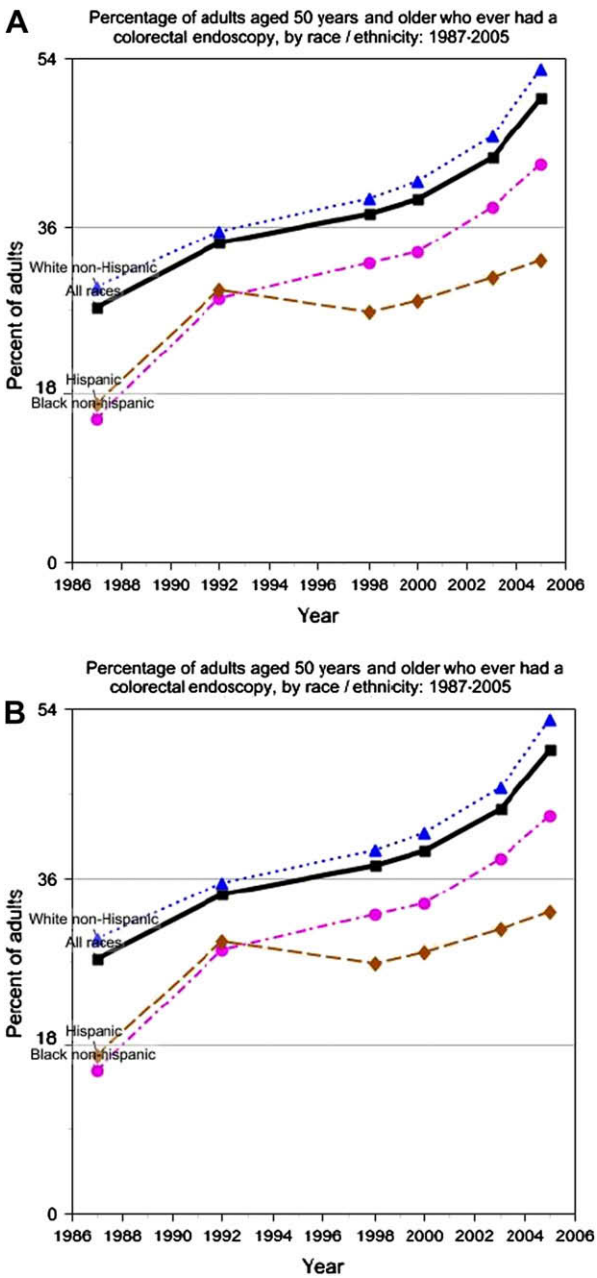

FIGURE 2. **(A) Trends in endoscopy for the early detection of colorectal cancer. (B) Trends in fecal occult blood testing utilization. Data are age-adjusted to the 2000 standard using age groups: 50-64, 65+. Analysis uses the 2000 Standard Population as defined by NCHS (http://www.cdc.gov/nchs/data/statnt/statnt20.pdf). (Source: Centers for Disease Control and Prevention, National Center for Health Statistics. National Health Interview Survey.)**

polyps as well.[7,58] Similar changes in guidelines have been issued by other organizations. Because of these continual changes and improvements in the guidelines, continual patient education is imperative.

The modification of the guidelines over time has been a source of confusion, but improvements in the technology for CRC screening have resulted in some decrease in the incidence and mortality of CRC.[71] In the last decade, there has been an increase in the number of options available for CRC screening, including the more mainstream use of colonoscopy (due in part to improved reimbursement), and more recently CTC.[69,71] Stool tests have been modified to increase sensitivity. With these changes in availability, there has recently been a decrease in FSIG utilization, some decrease in the use of stool tests, and a substantial decrease in the use of DCBE (see Fig. 2B).[7] Clearly the role of the nurse in educating about the guidelines and why guidelines change is an important one.

Risk Assessment and Management in CRC

Without risk assessment it is impossible to appropriately apply guidelines for the early detection of CRC. Nurses need to assess and stratify risk among average, high, and genetic risk. Such stratification may require referral to a genetics health professional when hereditary risk is suspected. When a person is identified with a mutation that places them at substantial risk for developing CRC and other cancers, a carefully implemented plan for prevention and early detection is the primary means to decrease the morbidity and mortality associated with the mutation and subsequent development of cancer. Individuals who test positive for an MSH2 or MLH1 mutation need a plan for screening and prevention of colorectal and gynecologic cancers. HNPCC is associated with an accelerated carcinogenesis in which polyps can develop into carcinomas in 2 to 3 years, instead of the typical 8 to 10 years seen in the general population.[10] Because of this potentially rapid development of malignancy, colonoscopy is recommended on an annual basis at age 20 to 25 years.[9] Research clearly shows that regular colonoscopy decreases the overall mortality rate by approximately 65%.[10]

Because HNPCC is also associated with increased risks to the endometrium and ovaries, females with the mutation need careful gynecologic surveillance and prophylaxis.[72] This usually includes annual or semi annual transvaginal ultrasound of the endometrium and ovaries, with concurrent endometrial aspiration for pathologic evaluation and CA-125 testing.[10] Although individuals with HNPCC may be at risk for other cancers,

TABLE 5.
American Cancer Society Recommendations for Follow-Up Screening Following Polypectomy

Finding	Screening Recommendation
Small hyperplastic rectal polyp	10 years
< 2 tubular adenomas (<1 cm) with low-grade dysplasia	5–10 years
3 to 10 low-grade adenomas or any adenoma with high-grade dysplasia	5 years
10 or more adenomas on one examination	< 3 years and referral for evaluation for hereditary cancer syndrome
Sessile adenomas removed in pieces	2–6 months to complete removal and when complete (both clinically and by pathology) at the descretion of the endoscopist
Persons with a known mutation for HNPCC or FAP	Annually
Persons with CRC	1 year after resection; if normal repeat in 3 years and then 5 years

Abbreviations: CRC, colorectal cancer; HNPCC, hereditary non-polyposis colorectal cancer; FAP, familial adenomatous polyposis.
Data from Bernard et al,[7] Winawer et al,[57] and Rex et al.[58]

there are no other standard screening recommendations at this time.[73] Many clinicians will also recommend upper endoscopy and gastroscopy, but there currently are no formal recommendations.[74]

Chemoprevention is another strategy sometimes considered in these families. The exact efficacy of NSAIDs and aspirin in decreasing GI cancers is not known.[9,73] Because oral contraceptives have been associated with decreased risk of developing ovarian and endometrial cancer, some women choose to consider this strategy.[73] Those persons considering chemoprevention strategies for colon or gynecologic cancers need a carefully balanced discussion of the potential benefits and risks associated with the proposed agent. These individuals may also want to consider enrolling in a research study. Similarly, there is minimal data available regarding the impact of a healthy diet and exercise in reducing risk of cancer development in persons with a mutation in HNPCC.[73] However, such behaviors may contribute to overall health and well-being and should be recommended.

Prophylactic colectomy in HNPCC is controversial and is not associated with a large increase in life expectancy over annual colonoscopy.[10] It is generally reserved for persons in whom colonoscopy is not technically possible or the individual refuses regular screening.[74]

Medical and surgical management of FAP syndromes is complex because the risk of developing CRC is virtually 100% and the age of onset can occur before age 20. In general, those with FAP usually receive a recommendation to begin screening with colonoscopy and often upper endoscopy at puberty and to undergo colectomy when symptomatic or the number of adenomas is considered worrisome or beyond the ability to manage with polypectomy.[10] Some patients will consider a total proctocolectomy with ileal pouch and anastomosis because the risks of developing rectal cancer are small and a permanent stoma is not necessary. This procedure is very complex, requires a temporary stoma, and carries a small risk for bladder and/or sexual dysfunction.[9] Other patients will choose a total abdominal colectomy with ileorectal anastomosis but will require regular endoscopy of the rectum because of the high risk of rectal cancer. These surgical procedures usually eliminate the need for a permanent stoma, which is often a deterrent to regular screening. Patients and families need much education and support when making decisions about colectomy.

Education Associated With Testing

Each CRC screening test has its own inherent strengths and weaknesses. For an individual to make an informed choice about what screening measure(s) to use, they need to not only understand their personal risk for developing CRC, but what limitations, benefits, and risks are associated with each test.

Most importantly, individuals need to understand that some tests, especially the stool tests, are probably only going to detect CRC, and not necessarily at an early stage. They may also result in false-positives, necessitating the need for more costly evaluation. The premise that polypectomy largely

TABLE 6.
Quality Assurance Considerations for Various Screening Strategies

gFOBT
- Follow dietary restrictions avoiding NSAIDs and aspirin for 7 days prior to testing and avoidance of vitamin C in excess of 250 mg, and red meats (beef, lamb, and liver) for 3 days before testing.
- Collect 3 consecutive specimens
- Although rehydration of gFOBT slides increases sensitivity, it is not recommended because it can adversely affect the readability of the test and also substantially increases the false-positive rate

sDNA
- Stool specimen must be packaged and shipped in a special collection kit with a specially designed ice pack.
- Patient must have access to a working freezer and allow the ice pack to freeze for at least 8 hours prior to use.
- If the specimen is returned without the ice pack or if there are delays in transport or processing, the specimen may be rejected for quality reasons

FSIG
- Endoscopist must have satisfactory training
- Examination must extend to at least 40 cm
- The endoscopist must have an expected adenoma detection rates based on age and gender
- The bowel preparation must be adequate to visualize the lumen
- If an adenoma is detected, the patient is referred for total colonoscopy

Colonoscopy
- Appropriate training and experience of the endoscopist
- Proper documentation of risk assessment
- Complete examination to the cecum with adequate mucosal visualization
- Adequate bowel preparation to visualize the mucosal surfaces
- Ability to detect and remove polyps safely
- Timely and appropriate management of any complications
- Appropriate follow-up of histopathology findings
- Appropriate recommendation for surveillance or repeat screening based on published guidelines

CTC
- Adequate training of the radiologist in interpreting images
- Adequate insufflation of the colon and appropriate use of CTC technique parameters when obtaining images
- Adequate preparation of the bowel to visualize all lumen surfaces
- Documentation of clinically significant colonic and extracolonic lesions for appropriate follow-up
- Availability of immediate colonoscopy if a adenoma is detected

DCBE
- Exam must evaluate the entire colon with adequate insufflation of the colon
- Adequate preparation of the bowel in preparation for the barium
- Patient must be able to be imaged in multiple positions including the prone and supine positions
- Adequate training of the radiologist to interpret the findings and refer appropriately when additioanl follow-up is needed

Abbreviations: gFOBT, guaiac-based fecal occult blood test; sDNA, stool DNA; FSIG, flexible sigmoidoscopy; CTC, CT of the colon; DCBE, double contrast barium enema.
Data from Bernard et al,[7] Lynch and Lynch,[11] Winawaer et al,[35] Smith et al,[42] Mysliwiec et al,[54] Zalis et al,[60] Rockey et al,[68] and Byers et al.[70]

prevents CRC influences the screening choice for some individuals. If that is the goal, one of the tests that detects polyps as well as CRC, such as colonoscopy or CTC, are probably most appropriate.

When counseling about screening choices, the individual must also understand what the expected course of action will be if a screening test is positive. In the case of stool tests (FSIG, DCBE, and CTC), a positive screen necessitates the need for colonoscopy to directly visualize the lumen of the bowel and biopsy and/or remove polyps or malignancy. For this reason, many will choose colonoscopy.

Bowel perforation is a possiblity with FSIG, DCBE, and colonoscopy. Incidence is low, even with colonoscopy (1 in 1,000), but when it occurs it can potentially result in significant morbidity.[59] Patients need to be informed about this potential risk. For some patients, sedation also carries significant risk, which must be considered when selecting a screening test.

Patients may find the bowel preparation distasteful and uncomfortable. Others find the screening examinations themselves uncomfortable and embarassing. An accurate presentation

of the potential benefits (including sensitivity and specificity) should be balanced with patient preferences when making an informed decision about CRC screening.

Increasing Participation in CRC Screening

Research suggests that despite improved reimbursement and refinements in screening modalties, the majority of US adults are not receiving regular age- and risk-appropriate screening or have never been screened at all.[8,69] A major nursing responsibility is to identify potential barriers and develop education and interventions that address and eliminate such barriers.

Documented barriers to CRC screening are lack of health insurance, lack of physician recommendation, and lack of awareness of the importance of CRC screening.[75] Theoretically, all adults should have access to comprehensive CRC risk assessment and all of options for CRC screening. In practice, especially in underserved and less affluent areas, all options may not be readily available. Most of the simpler, lower-cost options (gFOBT) are available in most settings, whereas other more costly options are not universally available (CTC and, in some cases, colonoscopy).[7,76] Nurses need to know what is available in their clinical practice area. Nurses also should be aware of reimbursement for CRC screening, which is now mandated by Medicare and offered through many private insurers. To discuss the multiple test options available can be time-consuming, and because patient education is often not reimbursible, it often receives a lower place in the priority issues of care.

When an individual chooses to participate in CRC screening, assurance should be provided that the test being used is of good quality. A summary of quality assurance considerations is provided in Table 6.

Motivating persons to engage in screening is important. Regular contact and trust in a healthcare provider who recommends screening may be the biggest factor in participation in a screening examination.[77,78] In addition to communication with the patients about the importance of screening, a regular system of office policies and reminder systems may help to assure that patients receive regular and appropriate recommendations for screening.[78] Once a healthcare provider determines the risk for developing CRC, an algorithm of the screening guidelines will help assure its proper implementation. Electronic medical records may be able to provide regular cues to discuss and recommend screening.

Conclusion

There is compelling research to support screening average-risk individuals over age 50 years for CRC. The latest guidelines are moving toward CRC prevention through the detection and removal of polyps. Epidemiologic evidence suggests that more individuals are engaging in screening and that incidence rates have dropped, but a large segement of persons still do not engage in any CRC screening. There have been technologic advances in the screening tools for polyps and CRC, but every test still has its own inherent strengths and weaknesses.[36] Individuals need a risk assessment and recommendation for appropriate screening based on risk and availability. The effectiveness of any single test or combination of tests depends on regular use of the test(s) with high-quality indicators. Nurses should not underestimate the role they play in risk assessment and education about screening. Appropriate CRC screening can ultimately decrease the morbidity and mortality associated with CRC and improve quality of life.

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