Screening for colorectal cancer: Strategies in patients at average risk

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INTRODUCTION

Colorectal cancer (CRC) is a common and lethal cancer worldwide and one of the leading causes of cancer death in the United States.

This topic addresses CRC screening in the general population at average risk for CRC. Screening is intended for patients without signs or symptoms of possible CRC. Multiple expert groups endorse screening average-risk adults for CRC [1-8].

CRC epidemiology, including incidence, mortality rates, and variability by sex, age, and portion of the colon, is described in detail separately. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Epidemiology'.)

Recommendations for patients at increased risk are described in detail separately:

- (See "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp".)
- (See "Familial adenomatous polyposis: Screening and management of patients and families".)
- (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Cancer screening and management", section on 'Colorectal cancer'.)
- (See "Juvenile polyposis syndrome", section on 'Screening and management'.)

- (See "Medical management of low-risk adult patients with mild to moderate ulcerative colitis", section on 'Other therapies'.)
- (See "Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults".)
- (See "Peutz-Jeghers syndrome: Clinical manifestations, diagnosis, and management", section on 'Gastrointestinal cancer'.)
- (See "*MUTYH*-associated polyposis", section on 'Colorectal cancer surveillance'.)
- (Related Pathway(s): Colorectal cancer (CRC) screening: Asymptomatic patients with no history of colon polyps.)
- (Related Pathway(s): Colon polyps: Surveillance after colon polyp resection.)

For patients with colon polyps that require follow-up surveillance for CRC, recommendations are described separately. (See "Overview of colon polyps".)

SCREENING RATIONALE

Natural history of colorectal cancer and colon polyps — Most colorectal cancers (CRC) arise from adenomatous colon polyps that progress from small (<8 mm) to large (≥8 mm) polyps, then to dysplasia and carcinoma. Adenomatous polyps occur in about 30 percent of men and about 20 percent of women. A colon polyp must be biopsied to determine its pathology, because gross appearance does not reliably distinguish adenomatous polyps from hyperplastic polyps, which are typically not precancerous.

Progression from adenoma to carcinoma is believed to take an average of at least 10 years [9]. This estimate is imprecise and may not apply to all types of polyps. The clinical presentation and natural history of colon polyps are described in detail separately. (See "Overview of colon polyps".)

Benefits of screening — We recommend that average-risk patients over the age 45 years be screened for CRC. CRC incidence and mortality rates have been declining in the United States, likely due to increasing uptake of screening [10-12]. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Epidemiology'.)

Screening tests for CRC can improve disease prognosis by identifying early-stage CRC that is easier to treat and has a lower mortality rate than CRC detected after symptoms develop. In addition, screening can prevent CRC by detecting and removing premalignant polyps before they progress to CRC.

Across the multiple strategies that are recommended for screening by major guidelines, the numbers of CRC deaths averted appear to be relatively similar, although sensitivity and

specificity for detection of polyps and of CRC vary, as shown in a figure (figure 1). A mortality benefit has been demonstrated in randomized clinical trials for guaiac-based fecal occult blood testing (gFOBT) and sigmoidoscopy and is inferred for other screening tests based on observational studies and indirect comparison with studies of other screening strategies that have undergone randomized controlled trials. The types of evidence supporting efficacy of each CRC screening strategy are summarized in a table and are discussed in detail separately. (See "Tests for screening for colorectal cancer".)

Harms associated with screening — Most of the harms of screening for CRC are related to the risks from colonoscopy, including perforation. Any abnormal results of initial screening tests other than colonoscopy (eg, stool test, virtual colonoscopy) necessitate a colonoscopy to evaluate the abnormality; thus, all screening modalities are associated with the potential for colonoscopy-associated complications [5,13]. In a meta-analysis of over 335,000 individuals screened initially by either FOBT or sigmoidoscopy with positive results followed up with colonoscopy, a major complication was recorded in 0.08 percent of participants, including 0.03 percent who initiated screening with FOBT [14]. In older adults, colonoscopy carries increased risk of complications. Complications of colonoscopy are described in detail separately. (See "Overview of colonoscopy in adults", section on 'Complications'.)

Cost and cost effectiveness — The cost of the various screening tests for CRC varies over a wide range, from a few US dollars for gFOBT to USD $1000 or more for colonoscopy. Models regarding the cost-effectiveness (cost per year of life saved) of CRC screening come to somewhat different conclusions because they make different assumptions. The cost per year of life saved is within the generally accepted range in the United States (USD $50,000), relative to no screening, for all of the recommended CRC screening tests [15]. For example, in one analysis the cost per year of life saved was USD <$15,000 for all recommended tests, compared with no screening [16].

ASSESSING RISK FOR COLORECTAL CANCER

The first step in screening is identifying the patient's level of risk for colorectal cancer (CRC) because level of risk impacts screening and follow-up recommendations. For this purpose, patients are generally determined to be either at average risk or at increased risk.

We assess the risk for CRC at the initial visit for an adult who is age 20 years or older, unless a genetic risk is already known and documented, to identify high-risk patients who should begin CRC screening at an earlier age than those at average risk. Subsequent reassessment every three to five years identifies whether the patient or their biologic family members have

developed factors that raise the patient's level of risk for CRC. Although there are no published guidelines supporting this approach, one study from a United States national population-based cancer registry found that the number of patients who would meet criteria for high-risk screening based on family history significantly increased from age 30 (2.1 percent) to age 50 (7.1 percent), supporting the need to update the family history [17].

Factors important to determine increased CRC risk can be assessed by asking several questions. A "no" response to all of these questions generally indicates average risk.

- **Have you ever had CRC or an adenomatous polyp?** A personal history of CRC increases the risk of another primary (metachronous) cancer. Surveillance following CRC is discussed separately. (See "Post-treatment surveillance after colorectal cancer treatment", section on 'Diagnosing second cancers and polyps'.)

  A personal history of adenomatous colorectal polyps increases the risk of CRC [18]. The number and types of polyp lesions guide the determination of the appropriate interval for surveillance. Recommendations for follow-up are described separately. (See "Overview of colon polyps", section on 'Surveillance'.)

  If there is uncertainty about the patient's personal polyp history, records should be obtained to determine if the patient had an adenomatous polyp. If records cannot be obtained, the patient may recall being told a polyp was found and advised to have a follow-up colonoscopy in five years or sooner, suggesting the polyp was adenomatous.

- **Have any biologic family members had CRC or a documented advanced polyp?** An advanced polyp is defined as an advanced adenoma (adenoma ≥1 cm, or with high-grade dysplasia, or adenoma with tubulovillous or villous histology [19]) or advanced serrated lesion (sessile serrated polyp [SSP] ≥1 cm, or traditional serrated adenoma ≥1 cm, or SSP with cytologic dysplasia).

  If so, how many biologic family members, were they first-degree relatives (parent, sibling, or child), and at what age was the cancer or polyp first diagnosed? Enhanced screening is warranted for a patient with increased risk of CRC due to a family history of CRC or documented advanced polyp and is described in detail separately. (See "Screening for colorectal cancer in patients with a family history of colorectal cancer or advanced polyp".)

  If a biologic family member is reported to have had a polyp but there is lack of available documentation about the type of polyp, the patient is typically screened as if a family member did not have an advanced polyp. (See "Screening for colorectal cancer in patients

with a family history of colorectal cancer or advanced polyp", section on 'Assessing risk due to family history'.)

If the patient cannot obtain any family history whatsoever related to colorectal cancer or polyps, some experts suggest screening the patient as average risk, although there are no data that evaluate that approach.

- **Do you have biologic family members with any of the known genetic syndromes that can cause CRC?** Patients with a family history of a known genetic syndrome for CRC may require enhanced screening plus genetic counseling. These syndromes and associated screening recommendations are discussed in detail separately:
  - (See "Familial adenomatous polyposis: Screening and management of patients and families".)
  - (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Cancer screening and management", section on 'Colorectal cancer'.)
  - (See "Juvenile polyposis syndrome", section on 'Screening and management'.)
  - (See "Peutz-Jeghers syndrome: Clinical manifestations, diagnosis, and management", section on 'Gastrointestinal cancers'.)
  - (See "*MUTYH*-associated polyposis", section on 'Colorectal cancer surveillance'.)
- **Do you have inflammatory bowel disease (ulcerative colitis or Crohn disease)?** Patients with inflammatory bowel disease (IBD) of the colon (ulcerative colitis or Crohn disease) have an increased risk of CRC. The approach to surveillance for CRC in patients with IBD is discussed separately. (See "Surveillance and management of dysplasia in patients with inflammatory bowel disease", section on 'Our approach to surveillance'.)
- **Did you receive abdominal radiation for childhood cancer?** Adults who received abdominal radiation in childhood for malignancy are at increased risk of CRC. Enhanced screening recommendations are described separately. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Abdominopelvic radiation'.)

Other risk factors that may influence screening advice include:

- **HIV infection in men** – For male patients who are living with HIV, the risk for cancer in the colon seems to be similar to the general population risk, so screening strategies for CRC should be based on other risk factors the patient has [20].

  Male patients with HIV have an increased risk for anal neoplasia (though not for colon cancer) compared with the general population. Specific screening recommendations for anal cancer are described separately. (See "Anal squamous intraepithelial lesions:

Epidemiology, clinical presentation, diagnosis, screening, prevention, and treatment", section on 'Screening for anal SIL'.)

- Additional risk factors for CRC, including lifestyle matters (eg, dietary factors, obesity, alcohol use, smoking) that may impact CRC risk, are discussed in detail separately. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Factors that may influence screening recommendations'.)

A detailed discussion of risk factors for CRC is presented separately. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors".)

SOCIAL FACTORS AND HEALTH EQUITY

In the United States, incidence rates and mortality for colorectal cancer (CRC) are higher among Native American/Alaskan Native, Native Hawaiian, other Pacific Islander, and Black people, particularly Black males, than among those in other racial or ethnic groups [21]. CRC incidence is also disproportionately high in geographic locations such as the Mississippi Delta region area that is correlated with socioeconomic disadvantage [22,23]. Disparities in incidence and mortality among Black people are apparent even prior to the age recommended for initiating screening in people at average risk for CRC.

Several factors have been shown to contribute to disparities, including disproportionate rates of exposure to risk factors, historical social injustices, and barriers to access to screening and other preventive services. Disparities have also been documented in the quality of screening and care received, such as delays in initiation of treatment. A report by the US Preventive Services Task Force (USPSTF) found an extensive body of literature on implementation strategies for delivering preventive care services, including CRC screening [24,25]. The USPSTF encouraged development of delivery services to ensure equitable access to high-quality care from screening through treatment, particularly for people from groups that experience disproportionate incidence, late-stage diagnosis, and death from CRC. Studies in the state of Delaware and in Kaiser Permanente, Northern California have shown that system-based coordinated strategies for equitable delivery of screening and follow-up care while addressing structural barriers, including patient navigation and reminder systems, can reduce or even eliminate disparities [26,27]. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Race and sex'.)

AGE TO INITIATE SCREENING

We initiate screening at age 45 years in adults at average risk consistent with US Preventive Services Task Force (USPSTF) recommendations. Colorectal cancer (CRC) incidence is generally higher with increasing age (figure 2). Although most cases of CRC occur over age 50 years, initiating screening at age 45 years balances the benefits of detection and prevention with the burden on the patient and the risk of harms from screening [8]. (See 'Benefits of screening' above.)

- The USPSTF recommends initiating screening at age 45 (Grade B) while maintaining its strongest recommendation (Grade A) for initiating at age 50 [8].
- The American College of Gastroenterology (ACG) 2021 guidelines also recommend initiating screening at age 45 in all adults at average risk [28].
- Initiating screening at age 45 years is a “qualified” recommendation from the American Cancer Society (ACS); this accompanies its strong recommendation to screen at age 50 or older [5,6]. The ACS noted that data to support starting at age 45 years are limited; the rationale is supported from some but not all modeling analyses [29].
- Initiating screening at age 50 years for average-risk adults is recommended by the Canadian Task Force on Preventive Health Care (CTFPHC), the European Council, the American Academy of Family Physicians (AAFP), and the American College of Physicians (ACP) [1-4].

DISCONTINUING SCREENING

The decision about when to discontinue screening should be individualized based on shared decision-making, taking into account the patient’s risk for colorectal cancer (CRC), prior screening history, personal values, and whether the patient's comorbid conditions and life expectancy justify the risks of continued screening [30-33].

We continue to screen for CRC through age 75 years for average-risk patients, as long as their life expectancy is 10 years or greater. Screening at least until age 75 years for patients at average risk for CRC is recommended by most guidelines [1-5,8,34]. This is based on the increasing frequency of CRC with age and the time course of progression from polyp to CRC.

For older adults who have never been screened, results of a modeling study suggest that one-time screening appears to be cost-effective up to an age that varies depending on the patient’s life expectancy, comorbidities, and the test used for screening [35]. As an example, for patients at average risk for CRC and without any comorbidities, in the simulation study, assuming a

willingness to pay USD $100,000 per quality-adjusted life-year gained, colonoscopy was cost-effective to age 83 years, sigmoidoscopy to 84 years, and fecal immunochemistry testing (FIT) to 86 years. In that study, colonoscopy was the most effective, due to its overall effectiveness for both CRC and adenomas, and was also the most expensive strategy for one-time screening.

For patients aged 76 to 85 years who have been screened before, we individualize the decision about whether to continue screening, based on factors including the patient's preferences, prior testing results, and comorbidities. Some guidelines recommend not continuing screening, whereas others recommend that the decision to screen adults 76 to 85 years be individualized, taking into account the patient's overall health and prior screening history [1,5,8,34,36,37]. Data supporting continued screening are limited; trials have included too few older patients to provide reliable evidence-based guidance about the balance of benefits and harms of screening beyond age 75 years. A prospective observational study of Medicare beneficiaries found that undergoing colonoscopy modestly decreased the risk of developing CRC over an eight-year period for those aged 70 to 74 years (2.2 versus 2.6 percent in the no-screening group), with a non-significant decrease in risk for those 75 to 79 years. In a modeling study of adults aged 65 years at average risk for CRC with average life expectancy and negative colonoscopy at age 55, extending screening beyond age 75 resulted in net harm (loss of quality-adjusted life-years) due to complications from colonoscopy.

> Shortened life expectancy modifies these age guidelines. Patients with a life expectancy less than 10 years (some would say five years) would not be expected to benefit from colorectal screening, since studies indicate benefit from screening in a population starts to accrue after about five years. For example, in a meta-analysis of screening with sigmoidoscopy, an absolute risk reduction of one CRC-related death for every 5000 sigmoidoscopies was observed at 4.3 years, and an absolute risk reduction of one CRC-related death for every 1000 sigmoidoscopies occurred by 9.4 years [38]. In one modeling study, screening patients ages 67 to 69 with three or more comorbidities would save fewer lives than screening older patients (ages 75 to 79) with no comorbidity (81 versus 459 lives saved per 100,000) [39]. Some guidelines recommend stopping screening for CRC when the patient's life expectancy is less than 10 years [34].

CHOOSING A SCREENING TEST

Recommended tests are either based on stool testing or visualization of the colon endoscopically or radiographically. Characteristics and effectiveness of tests available as options for colorectal cancer (CRC) screening are discussed in more detail separately. (See "Tests for screening for colorectal cancer".)

A 2019 guidance statement from the American College of Physicians provides a summary and an appraisal of various guidelines on colorectal cancer screening as well as information on recommended screening tests [40].

Advising patients about screening — After determining a patient is at average risk for CRC, we use motivational interviewing to assess patient preferences and recommend screening. (See 'Assessing risk for colorectal cancer' above.)

During shared decision-making about CRC screening, individual patient preferences, values, and risk, as well as test effectiveness, resource availability, test safety, convenience, comfort, and cost, are factors in determining which screening test among those recommended by guidelines groups is preferred by a specific patient. Characteristics and effectiveness of tests available as options for CRC screening are summarized in a table and are discussed in more detail separately. (See "Tests for screening for colorectal cancer".)

The best screening test is one that the patient is willing to complete according to the test instructions [41]. The US Preventive Services Task Force (USPSTF) and the American Cancer Society (ACS) note that being screened with a test acceptable to the patient is preferable to having the patient decline screening because of not being given options of screening tests [5,41].

Patient preferences among screening tests were evaluated in randomized trials that found participation rates for patients assigned to screening with FIT were greater than with stool guaiac, sigmoidoscopy, or colonoscopy [42,43], suggesting greater preference for convenient tests that do not require dietary restrictions or multiple stool samples (fecal immunochemistry testing [FIT]), as is recommended for guaiac-based tests, and for ease of testing without bowel preparation or a post-sedation recovery period (stool testing compared with more invasive procedures). However, findings from these studies represent the average preference for groups of patients and should not be applied without assessing individual preferences.

Noninvasive screening tests such as FIT and multitarget stool deoxyribonucleic acid testing (MT-sDNA) can be mailed directly to patients to be completed in the comfort of their homes. This approach makes it possible to provide screening directly to patients as a primary approach or when a face-to-face visit is not possible or safe to do, such as during the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic.

Preferred tests — In our practice, we prioritize the following screening tests (as noted, other authorities and guidelines may make somewhat different recommendations):

- **Colonoscopy** – We advise colonoscopy every 10 years for most patients at average risk for CRC who are willing to undergo this procedure. Screening with colonoscopy is associated with reduced incidence and mortality from CRC. Among screening tests, colonoscopy has the highest sensitivity for CRC and adenomatous polyps (figure 1) and allows lesion removal anywhere in the colon during just one procedure with the potential to detect as well as prevent cancer by removing adenomatous polyps prior to malignant transformation. (See "Tests for screening for colorectal cancer", section on 'Colonoscopy'.)

  The frequency of follow-up for patients with findings on a colonoscopy is described separately. (See "Overview of colon polyps", section on 'Surveillance'.)

  When an adequate screening colonoscopy is accomplished, intercurrent stool tests (ie, between colonoscopy examinations) are not necessary. In addition, for patients who have had a negative colonoscopy and have been recommended to have routine screening in 10 years, screening with FIT or other screening tests is not indicated prior to the end of the 10-year period.

  Colonoscopy is recommended as a screening option by many expert groups, including the USPSTF, ACS, American College of Physicians (ACP), National Comprehensive Cancer Network (NCCN), and American Academy of Family Physicians (AAFP), and is in the most highly recommended tier of tests according to the US Multisociety Task Force on Colorectal Cancer (MSTF) [3-5,7,44-46]. It is a suggested alternative in the American Society of Clinical Oncology (ASCO) guideline [47,48]. However, the Canadian Task Force on Preventive Health Care (CTFPHC) does **not** recommend using colonoscopy as a screening test [1].

- **Fecal immunochemical testing** – We advise screening by FIT for occult blood annually on a single sample for patients unable or unwilling to have a colonoscopy as initial screening, or when access to colonoscopy is limited, with the understanding that if the FIT result is positive, colonoscopy needs to be performed promptly. Compared with colonoscopy, FIT has similar detection rates for CRC but lower detection rates for advanced adenomas. However, compared with fecal occult blood testing (FOBT), FIT has greater sensitivity without loss of specificity as well as better detection of advanced adenomas [45,49-51]. (See "Tests for screening for colorectal cancer", section on 'Fecal immunochemical test (FIT) for blood'.)

  FIT is recommended as a screening option according to many expert groups. Annual testing with FIT is one of several options recommended by the USPSTF, which does not endorse test preferences [45]. A European consensus panel recommended use of a quantitative FIT with automated high throughput analysis as the fecal test of choice for

CRC screening [52]. In the United States, the MSTF recommends FIT as one of the first-tier (most highly recommended) choices [7]. ACP, ACS, AAFP, and ASCO include FIT as a screening option [3-5,47,48] and NCCN suggests it as an alternative test [44].

- **Multitarget stool DNA testing** – MT-sDNA, also known as FIT-DNA and multitarget fecal DNA, combines fecal markers for hemoglobin and DNA mutation and methylation. It is available as Cologuard in the United States. The test is performed every three years on one stool collection sample, but the USPSTF recommends use of MT-sDNA every one to three years. (See "Tests for screening for colorectal cancer", section on 'Multitarget stool DNA tests with fecal immunochemical testing'.)

  MT-sDNA testing has a higher single-application sensitivity and a lower specificity than FIT for CRC and advanced precancerous lesions [53], and it is more expensive than FIT.

  MT-sDNA testing is included as a second-tier choice by MSTF and is also recommended by the ACS, NCCN, and USPSTF [5,7,54].

- **Computed tomography colonography** – We advise computed tomography colonography (CTC, formerly referred to as “virtual colonoscopy”) as another option. CTC is performed every five years. CTC is more sensitive than any test other than colonoscopy to detect adenomatous polyps, although data are limited on other outcomes. Patients should understand that if CTC findings suggest polyps or CRC, colonoscopy is required promptly for evaluation. (See "Tests for screening for colorectal cancer", section on 'Computed tomography colonography'.)

  For older patients with comorbidities (eg, cardiopulmonary disease, diabetes mellitus, or history of stroke), CTC might be preferred over colonoscopy, because the risks of colonoscopy increase with age [55]. However, patients with abnormal findings on CTC should undergo colonoscopy. Therefore, patients who choose CTC should also be candidates for colonoscopy.

  CTC requires either a bowel preparation or oral ingestion of a preparation to tag stool so it can be electronically “removed” from CTC radiographic images, exposes the patient to some abdominal radiation, and may identify incidental abdominal findings that need follow-up to determine if they are of clinical significance. Detection of incidental extra-colonic findings also rises with increasing age, which can lead to testing and procedures that carry risks. The preparation, technique, and risks of CTC are described separately. (See "Overview of computed tomographic colonography".)

CTC is recommended as a second-tier option by MSTF, a suggested alternative by ASCO, and recommended by ACS [5,7,47,48]. NCCN did not come to consensus about CTC for screening [44].

Other tests used — Other testing strategies appropriate for average risk patients include the following:

- **Sigmoidoscopy combined with FIT (or sensitive gFOBT)** – The combination of sigmoidoscopy with FIT or guaiac-based FOBT (gFOBT) theoretically enhances lesion detection by offering direct visualization up to 60 cm as well as by detecting colon lesions beyond the reach of a sigmoidoscope by testing for occult blood. FIT is preferred over sensitive gFOBT. (See "Tests for screening for colorectal cancer", section on 'Sigmoidoscopy plus FIT or gFOBT'.)

  The recommended frequencies of each test vary among expert guidelines. USPSTF recommends sigmoidoscopy every 10 years with annual FIT, which is also an option in ASCO guidelines [8,47,48]. NCCN includes an option for sigmoidoscopy every five years with annual FOBT [44]. ACP includes sigmoidoscopy every five years plus combined FOBT or FIT every three years [4].

- **Sigmoidoscopy alone** – If the option of adding a stool-based test is not available or practical for a patient to do in conjunction with sigmoidoscopy, then screening with sigmoidoscopy alone every 5 to 10 years may be offered.

  Sigmoidoscopy can be performed with minimal patient preparation and does not require sedation. However, a sigmoidoscopy can only identify lesions up to the distal 60 cm of the bowel. This may be problematic in women and older patients because they have a higher frequency of more proximal lesions. (See "Colorectal cancer: Epidemiology, risk factors, and protective factors", section on 'Incidence' and "Tests for screening for colorectal cancer", section on 'Sigmoidoscopy'.)

  Recommendations for how often to perform screening with sigmoidoscopy alone vary among guidelines. Sigmoidoscopy every five years is a screening option recommended by the USPSTF and other groups [4,5,8,47,48]. MSTF includes it as an option to be performed every 5 to 10 years, and CTFPHC includes sigmoidoscopy every 10 years [1,7].

- **Guaiac-based fecal occult blood test** – If this method is chosen, the sensitive gFOBT (eg, Hemoccult SENSA) should be used. gFOBT is done annually on three samples as a take-home test that the patient mails back, rather than on stool obtained during a digital rectal examination (DRE). Stool obtained by DRE is not sensitive for CRC screening.

Some clinicians advise dietary restrictions during testing, though these restrictions may limit patient adherence to testing and thus some clinicians no longer restrict diet during testing. It typically takes at least three days to complete the testing due to the number of samples needed; however, bowel preparation and sedation are not needed.

Stool guaiac tests (gFOBT) have low sensitivity for polyps and relatively low specificity for clinically important disease. Additionally, gFOBT needs to be repeated annually if negative. (See "Tests for screening for colorectal cancer", section on 'Guaiac-based fecal occult blood test (gFOBT)'.)

gFOBT is included by the ACP, ACS, ASCO, and NCCN as an option to be done yearly, and by the CTHPHC to be done every two years; it was the only screening test recommended by the European Council in 2012 [1,2,4,5,44,47,48].

- **Capsule colonoscopy** – Capsule colonoscopy every five years is included in the MSTF guideline as a third-tier option, although it is not among the tests included in some screening guidelines [7]. In this test, the patient swallows a capsule containing tiny video cameras. A stool preparation is needed; however, sedation is not needed. In the United States, this test is not approved by the Food and Drug Administration (FDA) as a standalone screening method for CRC, but it is approved as an option for patients who had an incomplete colonoscopy. (See "Tests for screening for colorectal cancer", section on 'Colon capsule endoscopy' and "Wireless video capsule endoscopy", section on 'Colon capsule endoscopy'.)

Tests that are less effective or lack sufficient evidence on effectiveness — Certain tests, including some used previously, are not suggested for screening because they have lower accuracy than those that are recommended.

An assay (Epi proColon 2.0) to detect septin 9 DNA, which is hypermethylated in CRC but not in normal colon tissue, is approved by the FDA as an aid for CRC detection in average-risk patients who refuse screening by more sensitive guideline-recommended method, but it is not currently recommended by the USPSTF. Its sensitivity for CRC (75 percent) in people who selected based on their disease status and a lack of evidence on effectiveness on mortality outcomes make it inadequate as a primary screening strategy. (See "Tests for screening for colorectal cancer", section on 'Blood-based markers'.)

Tests no longer recommended include DRE, office-based gFOBT after DRE, and barium enema (single- or double-contrast [DCBE]) [56].

Carcinoembryonic antigen (CEA), a tumor marker that may be used for surveillance of patients with CRC, is not a useful screening test for CRC. (See "Clinical presentation, diagnosis, and staging of colorectal cancer", section on 'Tumor markers'.)

Various technologies such as plasma-based assay of circulating cell-free DNA from tumors are being developed with the goal of detecting multiple types of cancers using a single test (aka multicancer early detection). However, these tests have not been studied in unselected populations and are not recommended by the USPSTF [57].

Resource-limited settings — An ASCO guideline, developed by a multinational panel, stratifies recommended and alternative CRC screening tests for average-risk patients aged 50 to 75 according to availability of clinical resources in the patient's setting [47,48].

- In a basic setting, highly sensitive gFOBT is recommended every one (preferred) to two years, with FIT as a suggested alternative every one (preferred) to two years.
- In a limited setting with more resources, recommended tests include highly sensitive gFOBT yearly or sigmoidoscopy every five years with suggested alternatives of FIT yearly or sigmoidoscopy every 10 years plus yearly FIT (preferred) or yearly FOBT.

FOLLOW-UP OF ABNORMAL RESULTS

Screening should be supported by a program that assures prompt follow-up of abnormal findings as well as ongoing screening. Patients with an incomplete screening test that did not demonstrate an abnormal finding should have the screening test repeated; this is described separately. (See "Tests for screening for colorectal cancer", section on 'Follow-up of inadequate testing'.)

A patient with any positive (ie, abnormal) screening test for colorectal cancer (CRC) other than colonoscopy itself requires a timely colonoscopy to evaluate for colon polyps and CRC [5,13]. If a stool-based test (fecal immunochemistry test [FIT], guaiac-based fecal occult blood test [gFOBT], or FIT-DNA multitarget stool DNA testing [MT-sDNA]) is positive, a second stool test should **not** be done instead of a diagnostic colonoscopy, because a subsequent negative stool test result does not mean that the first result was a false positive. Additionally, if the patient has gastrointestinal symptoms or signs (eg, iron deficiency anemia, upper gastrointestinal symptoms), a diagnostic evaluation of the entire colon is indicated, even if a noninvasive test is negative. (See "Evaluation of occult gastrointestinal bleeding", section on 'Evaluation of a positive fecal occult blood test'.)

Performing the colonoscopy promptly and within three months is advised. Prompt follow-up colonoscopy minimizes the potential for progression of a preclinical lesion to a less curable stage due to a delay in diagnostic testing [58,59]. In a retrospective cohort of >70,000 patients aged 50 to 70 who had a positive FIT between 2010 and 2014, rates of detection of any CRC or advanced CRC increased with increasing intervals between FIT and colonoscopy [60]. We therefore do not recommend screening patients if there is no access to colonoscopy if the test is positive.

The further evaluation and management of patients with colonoscopy-detected CRC and polyps are described separately. (See "Clinical presentation, diagnosis, and staging of colorectal cancer" and "Overview of colon polyps".)

When a screening FIT, gFOBT, or MT-sDNA stool test is positive, and colonoscopy is both complete (to the cecum with adequate bowel preparation) and without abnormality, patients should return to the routine screening schedule.

While some clinicians may be concerned that a positive MT-sDNA test in the setting of a normal colonoscopy may represent a true rather than a false positive, the available data suggest that such patients do not have a higher risk of cancer than the general population [61]. While this suggests that returning to the routine screening schedule is reasonable for patients with an apparent false-positive MT-sDNA test, larger studies with longer follow-up are needed to confirm these findings.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Screening for colorectal cancer".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading

level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Colon and rectal cancer screening (The Basics)")
- Beyond the Basics topics (see "Patient education: Screening for colorectal cancer (Beyond the Basics)" and "Patient education: Colonoscopy (Beyond the Basics)" and "Patient education: Flexible sigmoidoscopy (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Screening rationale** – Screening for colorectal cancer (CRC) can identify premalignant lesions and detect asymptomatic early-stage malignancy that have greater chance of being cured. Screening has been shown to decrease mortality from CRC, and organized screening has been shown to reduce disparities; most of the risks of CRC screening are due to the risks of colonoscopy. (See 'Natural history of colorectal cancer and colon polyps' above and 'Benefits of screening' above and 'Harms associated with screening' above.)
- **Assessing risk** – We do an initial risk assessment to determine if a patient is at increased risk for CRC at a first office visit and update the information at a minimum of every five years. Patients at sufficiently increased risk to change screening recommendations (eg, start screening at an earlier age and/or perform screening more frequently) include those with a personal or family history of CRC or advanced adenomatous polyp and other risk factors. (See 'Assessing risk for colorectal cancer' above.)
- **Age to initiate and discontinue screening** – We recommend that average-risk patients age ≥ 45 years be screened for CRC (**Grade 1A**).
  - We initiate screening at age 45 years in most average-risk adults to balance the benefits of detection and prevention with the burden on the patient and the risk of harms from screening. (See 'Age to initiate screening' above.)
  - We continue to screen for CRC through age 75 years for average-risk patients, as long as their life expectancy is 10 years or greater. Screening at least until age 75 years for patients at average risk for CRC is recommended by most guidelines. Screening decisions should be individualized and based on shared decision-making for those aged

76 to 85 years. Screening until age 86 may be reasonable for patients who have never been screened, depending on their comorbidities. (See 'Discontinuing screening' above.)

- **Discussing screening tests with patients** – After determining that a patient is at average risk for CRC, we use a motivational interviewing and shared decision-making process to discuss specific CRC screening test protocols. Individual patient preferences, values, and risk, as well as test effectiveness, resource availability, test safety, convenience, comfort, and cost, are factors in determining which screening test among those recommended by guidelines groups is preferred by a specific patient. (See 'Advising patients about screening' above.)

- **Our approach** – A variety of tests are endorsed for screening by major guidelines. The numbers of CRC deaths averted appear to be relatively similar across modalities that are recommended by guidelines, although the frequency of testing and the sensitivity and specificity for detection of polyps and of CRC vary, as shown in the figure (figure 1).

  - We advise colonoscopy every 10 years for most patients at average risk for CRC who are willing to undergo this procedure. We advise screening by FIT for occult blood annually on a single sample, by multitarget stool DNA (MT-sDNA) testing every one to three years, or by computed tomography colonography (CTC) every five years for patients unable or unwilling to have a colonoscopy as initial screening, or when access to colonoscopy is limited, with the understanding that if the other test result is positive, colonoscopy needs to be performed promptly. (See 'Preferred tests' above.)

  - Other tests available for CRC screening include sigmoidoscopy with FIT or with gFOBT, sigmoidoscopy alone, gFOBT alone, and capsule colonoscopy. (See 'Other tests used' above.)

  - Colorectal cancer screening should **not** be based on an office-based gFOBT performed following a digital rectal examination (DRE). Barium enema tests are no longer recommended for screening because other tests are more effective. (See 'Tests that are less effective or lack sufficient evidence on effectiveness' above.)

- **Follow-up of abnormal results** – Every positive CRC screening test other than colonoscopy should be followed expeditiously by a colonoscopy to visualize the entire colon, evaluate lesions, and remove polyps. (See 'Follow-up of abnormal results' above.)

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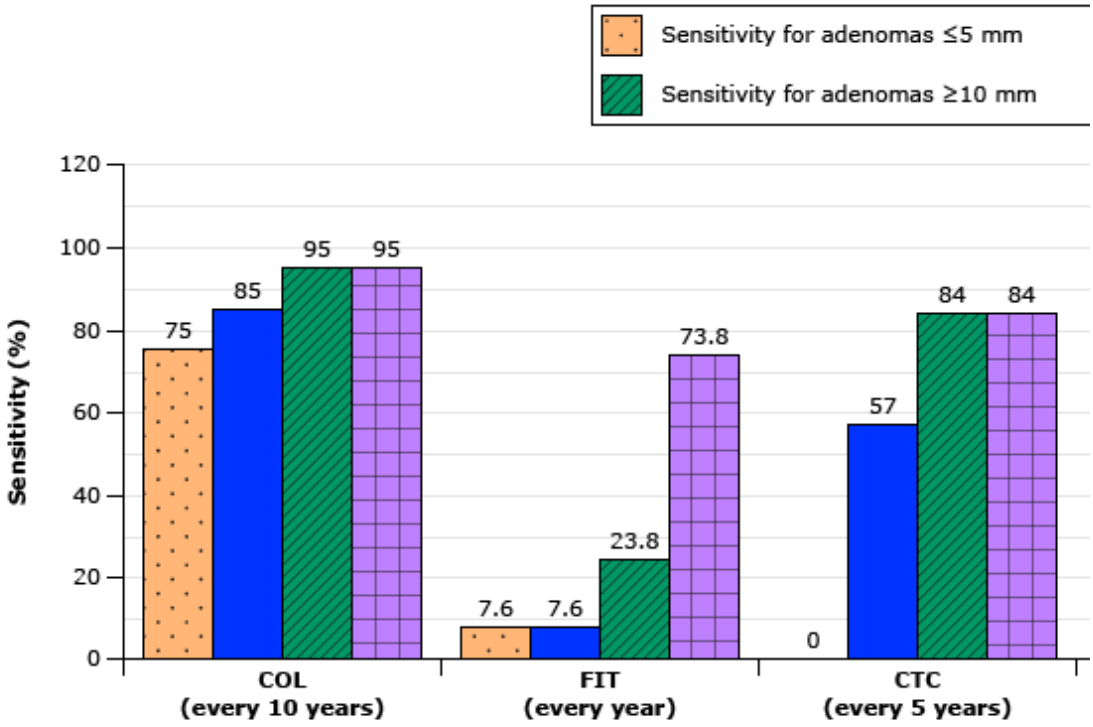
Topic 7565 Version 122.0

GRAPHICS

Estimated sensitivity, specificity, and cancer-specific deaths averted for each co



Test specificity	86	96.4	88
Colorectal cancer deaths averted per 1000 40-year-olds (n)*	22 to 24	20 to 23	16 to 24

Sensitivity, specificity, and cancer-specific deaths averted for each screening strategy.

COL: colonoscopy; FIT: fecal immunochemical test; CTC: computed tomography colonography; SIG: sigmoidc multitargeted stool DNA test.

* Assumes screening from ages 50 to 75 years, including 100% adherence, complete follow-up without delay

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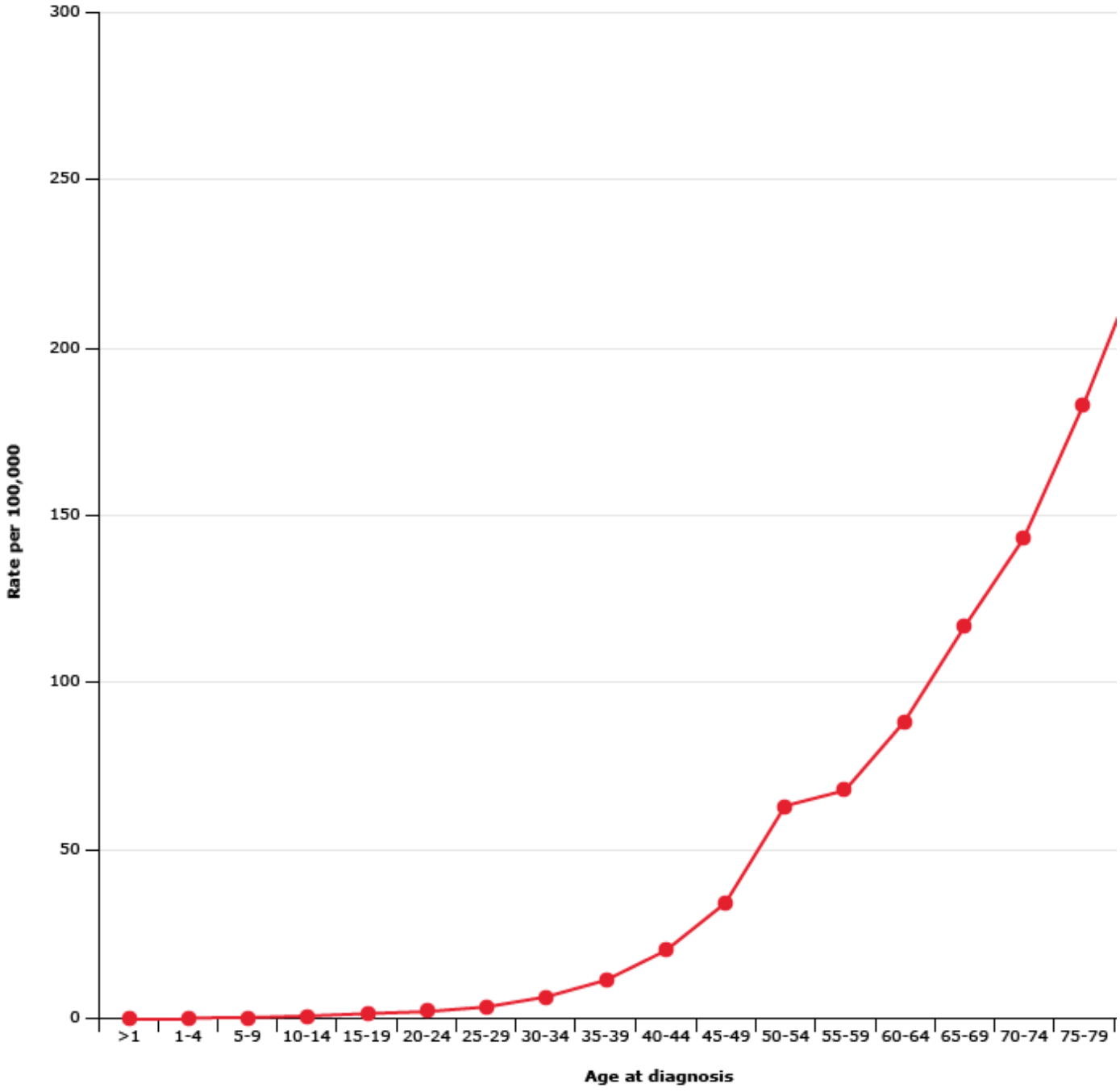
Data from:

1. *Zauber A, Knudsen A, Rutter CM, et al. Evaluating the Benefits and Harms of Colorectal Cancer Screening Strategies: A Collaborc for Healthcare Research and Quality; October 2015.*
2. *Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies: I*

Graphic 116366 Version 7.0

Increasing incidence of colorectal cancer in the United States with age, SEER 20



The age-specific incidence of colorectal cancer was measured between 2014 and 2018 in men and women of

SEER: Surveillance, Epidemiology, and End Results.

Data from: Surveillance, Epidemiology, and End Results (SEER) Program, 2014-2018. Available at: https://seer.cancer.gov/explorer/app site=20&data_type=1&graph_type=3&compareBy=sex&chk_sex_1=1&rate_type=2&race=1&advopt_precision=1&advopt_show_ci=on&a =2 (Accessed on July 13, 2021).

Graphic 111996 Version 3.0

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