Medical Coverage Policy

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Colorectal Cancer Screening and Surveillance

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Related Coverage Resources

Genetic Testing for Hereditary Cancer Susceptibility Syndromes
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Overview

This Coverage Policy addresses screening and surveillance testing regimens for colorectal cancer.

Coverage Policy

In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

For an average-risk individual age 45 years and older, the following colorectal cancer (CRC) screening testing regimens are considered medically necessary:

- annual fecal occult blood test (FOBT) or fecal immunochemical test (FIT)
- flexible sigmoidoscopy every five years
- double-contrast barium enema (DCBE) every five years
- colonoscopy every 10 years
- computed tomographic colonography (CTC)/virtual colonoscopy every five years
- stool-based deoxyribonucleic acid (DNA) (i.e., Cologuard) testing every one to three years

For an increased- or high-risk individual who fits into any of the categories listed below, more intensive colorectal cancer screening, surveillance or monitoring is considered medically necessary:

- personal history of adenoma or adenomatous polyps found on colonoscopy
- familial history of adenoma or adenomatous polyp found at colonoscopy in a first-degree relative
- personal or family history of colorectal cancer
- personal history of inflammatory bowel disease (e.g., ulcerative colitis, Crohn's disease)
- personal or inherited risk of a colorectal cancer (e.g., familial adenomatous polyposis [FAP], attenuated FAP, hereditary nonpolyposis colorectal cancer [HNPCC], MYH polyposis)

Chromoendoscopy with or without optical technologies such as narrow band imaging is considered medically necessary for colorectal cancer surveillance for patients at increased risk based on personal history of inflammatory bowel disease (IBD).

The following are considered experimental, investigational, or unproven for any indication including, but not limited to, the screening, diagnosis, or surveillance of colorectal cancer:

- chromoendoscopy for any other indication
- fiberoptic polyp analysis
- urine-based test for detection of adenomatous polyps (e.g., PolypDX)

General Background

Colorectal cancer (CRC) is the third most diagnosed cancer and the third most common cause of cancer-related death in both men and women in the United States. More than half of all CRCs are attributable to modifiable risk factors, such as smoking, an unhealthy diet, high alcohol consumption, physical inactivity, and excess body weight. In addition, a large proportion of CRC incidence and mortality is preventable through the receipt of regular screening, surveillance, and treatment.

- In 2023, there will be an estimated 153,020 new cases of colorectal cancer (CRC) diagnosed in the US and 52,550 people will die from the disease, including 19,550 diagnoses and 3,750 deaths in individuals younger than age 50.
- 20% (1 in 5) of CRCs in 2019 were in people 54 years or younger, up from 11% (1 in 10) in 1995.
- CRC death rates increased by 1% annually in people younger than 50 years of age since about 2005.
- Incidence rates for advanced disease have increased by about 3% annually in people younger 50 years of age and 0.5%-2% annually in people 50-64 years of age since around 2010.
- CRC incidence in the US is highest in people who are Alaska Native (88.5 per 100,000), American Indian (46.0), or Black (41.7) versus White (35.7); racial and ethnic disparities are similar for mortality (35.9, 17.5, and 17.6 per 100,000, respectively, versus 13.1).
- Five-year relative survival for CRC ranges from 60% in Black people to 65% in White people and 67% in Asian American and Pacific Islander people (American Cancer Society [ACS] Colorectal Cancer Facts & Figures 2023-2025).

RISK STRATIFICATION/COLORECTAL CANCER RISK FACTORS

In the US, more than half (55%) of all CRCs are attributable to lifestyle factors, such as an unhealthy diet, insufficient physical activity, high alcohol consumption, and smoking. However, the strongest risk factor is a family history of the disease; people with a first-degree relative (parent, sibling, or child) who has been diagnosed with CRC have 2 to 4 times the risk of developing the disease compared to people without this family history, with a higher risk when diagnosis is before age 50 and when multiple relatives are affected. Up to 30% of people diagnosed with CRC have a family history of the disease, which is why these individuals should begin screening early; young people with a family history should have a conversation with their health care provider about when to start screening (ACS Colorectal Cancer Facts & Figures 2023-2025).

Source	Risk Factor Definitions
American Cancer Society	For screening, people are considered to be at average risk if they do not have: • A personal history of colorectal cancer or certain types of polyps • A family history of colorectal cancer • A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease) • A confirmed or suspected hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP) or Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC) • A personal history of getting radiation to the abdomen or pelvic area to treat a prior cancer People at increased or high risk of colorectal cancer includes people with:

<table>
<tr><th>Source</th><th>Risk Factor Definitions</th></tr>
<tr><td></td><td>

A strong family history of colorectal cancer or certain types of polyps
A personal history of colorectal cancer or certain types of polyps
A personal history of inflammatory bowel disease (ulcerative colitis or Crohn’s disease)
A known family history of a hereditary colorectal cancer syndrome such as familial adenomatous polyposis (FAP) or Lynch syndrome (also known as hereditary non-polyposis colon cancer or HNPCC)
A personal history of radiation to the abdomen or pelvic area to treat a prior cancer

(https://www.cancer.org/cancer/types/colon-rectal-cancer/detection-diagnosis-staging/acs-recommendations.html, last revised Nov 17, 2020)
</td></tr>
<tr><td>American Gastroenterological Association (AGA)</td><td>
<table>
<tr><th>Risk category</th><th>Level of CRC risk, %</th><th>Risk factors</th></tr>
<tr><td>Very high</td><td>>20</td><td>• Personal or family history of a hereditary CRC syndrome (eg, adenomatous polyposis syndromes, Lynch syndrome, and hamartomatous polyposis syndromes)
• Serrated polyposis syndrome</td></tr>
<tr><td>High</td><td>10-20</td><td>• Family history of 1 or more first-degree relative with CRC younger than 60 years or 2 first-degree relatives at any age
• Personal history of AA or advanced serrated polyp
• Inflammatory bowel disease</td></tr>
<tr><td>Average</td><td>4</td><td>• No symptoms and no factor above</td></tr>
</table>
(Burke et al. AGA Clinical Practice Update on Approach to the Use of Noninvasive Colorectal Cancer Screening Options: Commentary. Gastroenterology. 2022 Mar;162(3):952-956)
</td></tr>
<tr><td>National Comprehensive Cancer Network® (NCCN®)</td><td>
<u>Average risk</u>

Age ≥45 years[a]
No personal history of adenoma or sessile serrated polyp/sessile serrated lesion (SSP/SSL)[b] or CRC
No personal history of inflammatory bowel disease (IBD)
No personal history of high-risk CRC genetic syndromes
No personal history of cystic fibrosis
No personal history of childhood cancer
Negative family history for confirmed advanced adenoma (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology) or an advanced SSP/SSLb,[c] (≥1 cm, any dysplasia) in first-degree relatives.
Negative family history for CRC in first-, second-, or third-degree relatives[d]

<u>Increased risk</u>
</td></tr>
</table>

Source	Risk Factor Definitions

	• Personal history
	  ➢ Adenoma or SSP/SSL[b]
	  ➢ CRC
	  ➢ IBD (ulcerative colitis, Crohn's colitis)
	• Positive family history
	• Personal history of childhood, adolescent, and young adult cancer (including individuals who meet criteria for therapy-associated polyposis)
	
	For individuals at average risk, the choice of a particular screening modality should include a conversation with the patient concerning their preference and availability. For individuals at increased risk, colonoscopy is the preferred method.
	
	<u>High-risk genetic syndromes with predisposition to CRC</u>
	• Lynch syndrome (LS; hereditary nonpolyposis CRC [HNPCC])
	• Polyposis syndromes
	  ➢ Classical familial adenomatous polyposis
	  ➢ Attenuated familial adenomatous polyposis
	  ➢ *MUTYH*-associated polyposis
	  ➢ Peutz-Jeghers syndrome
	  ➢ Juvenile polyposis syndrome
	  ➢ Serrated polyposis syndrome (rarely inherited)
	• Cowden syndrome/PTEN hamartoma tumor syndrome
	• Li-Fraumeni syndrome
	
	a The panel has reviewed existing data for beginning screening of individuals at age <50 years who are of average risk. Based on their assessment, the panel agrees that the data are stronger to support beginning screening at 50 years, but acknowledges that lower-level evidence supports a benefit for screening earlier. When initiating screening for all eligible individuals, the panel recommends a discussion of potential harms/risks and benefits, and the consideration of all recommended CRC screening options.
	
	b The terms sessile serrated polyp, sessile serrated lesion, (SSP/SSL), and sessile serrated adenoma are synonymous; SSPs/SSLs are a type of serrated polyp that
	are not dysplastic but they can develop foci of dysplasia and are then termed SSP/SSL with dysplasia (SSP/SSL-d). These guidelines will use "SSP/SSL" for SSPs/ SSLs without dysplasia and "SSP/SSL-d" for SSPs/SSLs with dysplasia.
	
	c Advanced SSPs/SSLs are generally considered to have a comparable cancer risk and are managed similarly to advanced adenomas, rather than high-risk adenomas, a definition which includes multiplicity.
	
	d While current risk estimates for a family history of CRC in only second- and third-degree relatives may not be sufficiently elevated to recommend increased screening, there are some data showing that having a second- and, to a lesser degree, a third-degree relative with early-onset (<50 years old) CRC increases risk of both CRC and early-onset CRC. Some

Source	Risk Factor Definitions
	combinations of affected first-, second-, and third-degree relatives may increase risk sufficiently to alter screening guidelines. If there are multiple distant relatives affected, consider evaluation for an inherited colorectal syndrome in the family. (NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Colorectal Cancer Screening. Version 1.2023 — May 17, 2023)
US Preventive Services Task Force (USPSTF)	Average risk • no prior diagnosis of colorectal cancer, adenomatous polyps, or inflammatory bowel disease • no personal diagnosis or family history of known genetic disorders that predispose them to a high lifetime risk of colorectal cancer [such as Lynch syndrome or familial adenomatous polyposis] (Colorectal cancer: Screening. USPSTF recommendation statement. May 18, 2021)

TESTS AND PROCEDURES FOR CRC SCREENING/SURVEILLANCE/MONITORING

The objective of cancer screening is to reduce mortality through a reduction in incidence of advanced disease. It is thought that CRC screening can reach this goal through the detection of early-stage adenocarcinomas and with the detection and removal of adenomatous polyps. There are CRC screening options for average-risk and higher-risk individuals. The choices fall into general categories such as structural exams (these may also include in vivo analysis of colorectal polyps), stool-based tests, blood (serum)-based tests, and urine-based tests. Each category and specific test has benefits and risks as well as target population. The NCCN (v.1.2023) notes that the choice of modality for individuals at average risk should include consideration of patient preference and availability. Please see the Professional Society recommendations included below for specific test recommendations.

Structural exams

These exams can reach the dual goals of detecting adenocarcinoma as well as identifying adenomatous polyps. Testing options in this group include:

- Colonoscopy: Colonoscopy is considered the current gold standard for assessing the sensitivity of detecting neoplasia for other screening modalities. Colonoscopy allows direct mucosal inspection of the entire colon along with same session biopsy sampling or polypectomy in case of pre-cancerous polyps and some early-stage cancers. Preparation involves adopting a liquid diet one or more days before the examination, followed by either ingestion of oral lavage solutions or saline laxatives to stimulate bowel movements. Patients generally receive a mild sedative prior to procedure. Colonoscopy involves greater risk and inconvenience to the patient than other screening tests, and not all examinations visualize the entire colon. Significant risks include postpolypectomy bleeding and perforation of the colon.

- Flexible Sigmoidoscopy: Flexible sigmoidoscopy is an endoscopic procedure that examines the lower half of the colon lumen. Positive test findings will need to be followed up with a colonoscopy. Compared to colonoscopy, sigmoidoscopy requires no sedation and less bowel preparation, but is limited to examination of the distal colon.

- Double-contrast Barium Enema (DCBE): DCBE, also referred to as air-contrast barium enema, examines the colon in its entirety by coating the mucosal surface with high-density barium and distending the colon with air introduced through a flexible catheter that is inserted into the

rectum. In general, DCBE is included as a screening option because it offers an alternative means to examine the entire colon.

- Computed Tomographic Colonography (CTC): Computed tomographic colonography (CTC) uses data from computed tomography (CT) to generate two- and three-dimensional images of the colon and rectum. This procedure is also referred to as virtual colonoscopy. It is a minimally invasive procedure that requires no intravenous administration of sedatives or analgesics. The day before the procedure, bowel cleansing is performed, similar to requirements for a colonoscopy. Colonic perforation is extremely low with this test since it is minimally invasive.

Stool-Based Tests

These tests are appropriate for the detection of cancer, although they may deliver positive findings for some advanced adenomas. Stool-based tests screening tests for CRC do not require fasting or bowel preparation and can be performed at home. Testing options in this group include:

- guaiac-based Fecal Occult Blood test (gFOBT): uses the chemical guaiac to detect blood in the stool. With a test kit ordered by a heathcare provider, an individual at home obtains a small amount of stool. The test kit is returned to the doctor or a lab, where the stool samples are checked for the presence of blood. Individuals may be recommended to avoid use of anticoagulants, non-steroidal anti-inflammatory drugs (NSAIDs), red meat (such as rare beef or lamb), vitamin C and iron prior to testing.

- Fecal Immunochemical test (FIT): uses antibodies to detect blood in the stool. It is done in the same way as a gFOBT. FIT can be obtained from a clinic, pharmacy or via mail, and requires collection of a small stool sample in a container that should be mailed within 24 hours of collection to prevent degradation of hemoglobin. Examples of these include, but are not limited to InSure™ (Enterix Inc., Edison, NJ) and Instant-View™ Fecal Occult Blood Rapid Test (Alpha Scientific Designs, Inc., Poway, CA).

- Multi-target Stool DNA (mt-sDNA, MTsDNA, sDNA-FIT, FIT-DNA): Known as Cologuard®, evaluates 11 biomarkers—7 point mutations in the *KRAS* gene, 2 methylation markers of the *NDRG4* and *BMP3* genes, β-actin as a control for human DNA quantity, and human hemoglobin using an FIT. Cologuard® (Exact Sciences Corp., Madison, WI) is approved only in average-risk adults aged 45–85 years. s-DNA-FIT is reported as positive if either the FIT or DNA biomarker component is abnormal. In the prospective study that resulted in FDA approval for the FIT plus multitargeted stool DNA (FIT-DNA) test (Cologuard), the sensitivity of FIT-DNA for colorectal cancer and advanced adenomas was 92% and 42%, respectively (Imperiale, et al., 2014). Meta-analysis has shown that 13.5% of s-DNA-FIT tests are positive compared to 6.4% of FIT, (Pickhardt, et al., 2021) and 45% of patients with a positive s-DNA-FIT have no significant findings on colonoscopy (Imperiale, et al., 2014) (Carethers JM, 2023).

  The impact of race and ethnicity on MTsDNA performance has been assessed. In a sub-analysis of Black participants within a comparative study of MTsDNA and FIT, overall sensitivity and specificity for CRC and advanced adenoma was 43% and 91% for MTsDNA vs 32% and 97% for FIT, respectively, and did not differ between Black and White participants (AGA/Burke 2022; Cooper, et al., 2018).

Blood (serum)-Based Tests

- For the Septin 9 blood (serum) genetic test, known as Epi proColon (Epigenomics), see Medical Coverage Policy 0520 titled Molecular and Proteomic Diagnostic Testing for Hematology and Oncology Indications. It may be accessed from the Related Coverage Resources section located at the top of this policy document.

Urine-based Tests

- A urine-based lab test that tests for metabolites using liquid chromatography–mass spectrometry (LC-MS) technology is called PolypDx™ (Metabolomic Technologies Inc, Edmonton, AB, Canada). It is proposed as a test for the detection of colon polyps for colorectal cancer screening. It is not FDA-approved at this time.
  The accuracy of PolypDx was assessed in 867 patients from Canada and validated in 661 Chinese participants undergoing colonoscopy (Wang, et al., 2014; Deng, et al., 2017). In an unblinded training set followed by a blinded set, adenomas were identified with 89% and 83% sensitivity and 50% and 51% specificity, respectively (Wang, et al., 2014). In the Chinese study, the sensitivity was 83% and specificity was 42.4% (Deng, et al., 2017). This product is not FDA-approved or currently available commercially (American Gastroenterological Association Clinical Practice Update/Burke, et al., 2022).

In Vivo Analysis of Colorectal Polyps

- Chromoendoscopy: The NCCN defines chromoendoscopy as an "image-enhanced endoscopic procedure using dye or optical technologies (Buchner, 2017)". Buchner (2017) notes that chromoendoscopy is an image-enhanced endoscopic technique achieved either through dye-based chromoendoscopy or electronic chromoendoscopy, which includes optical technologies such as narrow-band imaging (NBI, Olympus), flexible spectral imaging color enhancement (FICE, Fujinon), and i-scan (Pentax). Chromoendoscopy provides detailed contrast enhancement of the surface of gastrointestinal mucosa.
  The use of chromoendoscopy - using dye or optical technologies - in inflammatory bowel diseases is supported by the NCCN (Colorectal Cancer Screening. V.1.2023 — May 17, 2023) and the American Gastroenterological Association (AGA) (Murthy, et al., 2021). Published studies support its use in patients with a personal history of inflammatory bowel disease (Alexandersson, et al., 2020; Resende, et al., 2020; Iannone, et al., 2017; Brown, et al., 2016).
  The use of chromoendoscopy in other diagnosis is not currently supported. The NCCN does not make a specific recommendation in Lynch syndrome, noting that it may be considered in patients with Lynch syndrome, but larger prospective randomized trials are needed to better understand its role in Lynch syndrome. A meta-analysis including four randomized studies showed that adenoma detection rate in patients with Lynch syndrome was not significantly improved with chromoendoscopy compared to white light endoscopy, though quality of evidence was low (NCCN Guidelines® Genetic/Familial High-Risk Assessment: Colorectal (v.1.2023 — May 30, 2023; Houwen, 2021).

- Fiberoptic analysis: Fiberoptic polyp analysis has been proposed to assist the physician in determining if potential cancerous changes are present within the colon. Positive findings would be suggestive of the need for potential biopsy of the area.
  The SpectraScience™ Optical Biopsy™ System received premarket approval (PMA) as a Class III device from the FDA in November 2000. In 2001 the name was changed to WavStat™ Optical Biopsy System. It is indicated for use as an adjunct to lower gastrointestinal (GI) endoscopy. The device is intended for the evaluation of polyps less than 1 cm in diameter that the physician has not already elected to remove. The device is only to be used in deciding whether such polyps should be removed (which includes submission for histological examination).
  The laser energy is delivered to the target polyp through the optical fiber at a pre-defined intensity and energy level. The energy is absorbed by the target polyp, which then emits autofluorescence back through the optical fiber. The autofluorescence is recorded and measured by the system software. By comparing the received spectral information to the spectra of adenomatous and hyperplastic tissue, the device determines whether the tissue is "suspicious" (adenomatous) or "not suspicious" (hyperplastic).

There is a lack of both professional society recommendation and well-designed, published scientific literature supporting the use of this technology.

PROFESSIONAL SOCIETY RECOMMENDATIONS

Source	Recommendation
American Cancer Society	Wolf et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. CA Cancer J Clin. 2018 Jul;68(4):250-281. • Adults aged 45 years and older with an average risk of CRC undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability. As a part of the screening process, all positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy. ➢ The recommendation to begin screening at age 45 years is a qualified recommendation**. ➢ The recommendation for regular screening in adults aged 50 years and older is a strong recommendation*. • Average-risk adults in good health with a life expectancy of greater than 10 years continue CRC screening through the age of 75 years (qualified recommendation**). • Clinicians individualize CRC screening decisions for individuals aged 76 through 85 years based on patient preferences, life expectancy, health status, and prior screening history (qualified recommendation**). • Clinicians discourage individuals over age 85 years from continuing CRC screening (qualified recommendation**). The options for testing include: Stool-based tests: • Highly sensitive fecal immunochemical test (FIT) every year • Highly sensitive guaiac-based fecal occult blood test (gFOBT) every year • Multi-targeted stool DNA test (MT-sDNA) every three years Visual (structural) exams of the colon and rectum: • Colonoscopy every 10 years • CT colonography every five years • Flexible sigmoidoscopy (FSIG) every five years The guidelines note that for screening, people are considered to be at average risk if they do not have: • A personal history of colorectal cancer or certain types of polyps • A family history of colorectal cancer • A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease) • A confirmed or suspected hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP) or Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC)

Source	Recommendation
	• A personal history of getting radiation to the abdomen or pelvic area to treat a prior cancer *A strong recommendation conveys the consensus that the benefits of adherence to that intervention outweigh the undesirable effects that may result from screening. **Qualified recommendations indicate there is clear evidence of benefit (or harm) of screening but less certainty about the balance of benefits and harms or about patients' values and preferences, which could lead to different decisions about screening.
American College of Gastroenterology (ACG)	Shaukat et al. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol. 2021 Mar 1;116(3):458-479. • CRC screening in average-risk individuals between ages 50 and 75 years to reduce incidence of advanced adenoma, CRC, and mortality from CRC. (Strong recommendation; moderate-quality evidence) • CRC screening in average-risk individuals between ages 45 and 49 years to reduce incidence of advanced adenoma, CRC, and mortality from CRC. (Conditional recommendation; very low-quality evidence) • A decision to continue screening beyond age 75 years be individualized. (Conditional recommendation; very low-quality evidence) • Colonoscopy and FIT as the primary screening modalities for CRC screening. (Strong recommendation; low-quality evidence) • Consideration of the following screening tests for individuals unable or unwilling to undergo colonoscopy or FIT: flexible sigmoidoscopy, multitarget stool DNA test, CT colonography or colon capsule. (Conditional recommendation; very low-quality evidence) • Against Septin 9 for CRC screening. (Conditional recommendation, very low-quality of evidence) • The following intervals should be followed for screening modalities: FIT every one year, colonoscopy every 10 years (Strong recommendation; low-quality evidence) • The following intervals should be followed for screening modalities: multitarget stool DNA test every three years, flexible sigmoidoscopy every five to ten years, CTC every five years, CC every five years (Conditional recommendation; very low-quality evidence) • Initiating CRC screening with a colonoscopy at age 40 or 10 years before the youngest affected relative, whichever is earlier, for individuals with CRC or advanced polyp in one first degree relative (FDR) at age <60 years or CRC or advanced polyp in ≥ two FDR at any age. ACG suggests interval colonoscopy every five years. (Conditional recommendation; very low-quality evidence) • Consideration of genetic evaluation with higher familial CRC burden (higher number and/or younger age of affected relatives). (Conditional recommendation; very low-quality evidence) • Initiating CRC screening at age 40 or 10 years before the youngest affected relative and then resuming average-risk screening

Source	Recommendation
	recommendations for individuals with CRC or advanced polyp in one FDR at age ≥60 years. (Conditional recommendation; very low-quality evidence) • In individuals with one second-degree relative (SDR) with CRC or advanced polyp, follow average-risk CRC screening recommendations. (Conditional recommendation; low-quality evidence)
American College of Gastroenterology (ACG)	Rubin et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. 2019 Mar;114(3):384-413. Colorectal cancer prevention in ulcerative colitis: 47. We suggest colonoscopic screening and surveillance to identify neoplasia in patients with UC of any extent beyond the rectum (conditional recommendation, very low quality of evidence). 48. When using standard-definition colonoscopes in patients with UC undergoing surveillance, we recommend dye spray chromoendoscopy with methylene blue or indigo carmine to identify dysplasia (strong recommendation, low quality of evidence). 49. When using high-definition colonoscopes in patients with UC undergoing surveillance, we suggest white-light endoscopy with narrow-band imaging or dye spray chromoendoscopy with methylene blue or indigo carmine to identify dysplasia (conditional recommendation, low quality of evidence).
American College of Physicians (ACP)	Qaseem A, Harrod CS, Crandall CJ, Wilt TJ; Clinical Guidelines Committee of the American College of Physicians; et al. Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement From the American College of Physicians (Version 2). Ann Intern Med. 2023 Aug;176(8):1092-1100. • Guidance Statement 1: Clinicians should start screening for colorectal cancer in asymptomatic average-risk adults at age 50 years. • Guidance Statement 2: Clinicians should consider not screening asymptomatic average-risk adults between the ages of 45 to 49 years. Clinicians should discuss the uncertainty around benefitsand harms of screening in this population. • Guidance Statement 3: Clinicians should stop screening for colorectal cancer in asymptomatic average-risk adults older than 75 years or in asymptomatic average-risk adults with a life expectancy of 10 years or less. • Guidance Statement 4a: Clinicians should select a screening test for colorectal cancer in consultation with their patient based on a discussion of benefits, harms, costs, availability, frequency, and patient values and preferences. • Guidance Statement 4b: Clinicians should select among a fecal immunochemical or high-sensitivity guaiac fecal occult blood test every 2 years, colonoscopy every 10 years, or flexible sigmoidoscopy every 10 years plus a fecal immunochemical test every 2 years as a screening test for colorectal cancer.

Source	Recommendation
	• Guidance Statement 4c: Clinicians should not use stool DNA, computed tomography colonography, capsule endoscopy, urine, or serum screening tests for colorectal cancer.
American Gastroenterological Association (AGA)	Lieberman et al. Reducing the Burden of Colorectal Cancer: AGA Position Statements. Gastroenterology. 2022 Aug;163(2):520-526 Some of the statements include: • Statement #1: The AGA supports the development of a national approach to CRC screening to ensure accessibility to all individuals in the United States with the goal to eliminate suffering and death from CRC. • Statement #2: There is strong evidence from randomized controlled trials, observational clinical studies, and modeling studies that increasing CRC screening rates will reduce CRC incidence and mortality. • Statement #3: A screening program should include both colonoscopy and noninvasive screening options, patient education, outreach, and navigation support.
American Gastroenterological Association (AGA)	Murthy et al. AGA Clinical Practice Update on Endoscopic Surveillance and Management of Colorectal Dysplasia in Inflammatory Bowel Diseases: Expert Review. Gastroenterology. 2021 Sep;161(3):1043-1051.e4. The Best Practice Advice regarding endoscopic surveillance and management of colorectal dysplasia in inflammatory bowel diseases includes: 1. Precancerous colorectal lesions in inflammatory bowel disease should be described as either polypoid (≥2.5 mm tall), nonpolypoid (<2.5 mm), or invisible (detected on nontargeted biopsy), using a modified Paris Classification. The older terms dysplasia-associated lesion or mass, adenoma-like mass, and flat dysplasia (when referring to dysplasia detected in nontargeted biopsies) should be abandoned 2. Visible precancerous lesions should be described based on size, morphology, clarity of borders, presence of ulceration, location, presence within an area of past or current colitis, perceived completeness of resection, and whether any special techniques were used for visualization. 3. Initial colonoscopy screening for dysplasia should be performed at 8–10 years after disease diagnosis in all people with colonic inflammatory bowel disease, and immediately on diagnosis of primary sclerosing cholangitis. Staging biopsies should be taken from multiple colonic segments to assess histologic disease activity and extent and to help guide future surveillance intervals. 4. Conditions and practices for dysplasia detection should be optimized, including control of inflammation, use of high-definition endoscopes, bowel preparation, careful washing and inspection of all colorectal mucosa, and targeted sampling of any suspicious mucosal irregularities.

Source	Recommendation
	5. Targeted biopsies should be performed where mucosal findings are suspicious for dysplasia or are inexplicably different from the surrounding mucosa. Endoscopic resection is preferred to biopsies when lesions are clearly demarcated without stigmata of invasive cancer or submucosal fibrosis. Mucosal biopsies surrounding a resected lesion are not required unless there are concerns about resection completeness. 6. Dye spray chromoendoscopy, performed by appropriately trained endoscopists, should be considered in all persons with colonic inflammatory bowel disease undergoing surveillance colonoscopy, particularly if a standard definition endoscope is used or if there is a history of dysplasia. 7. Virtual chromoendoscopy is a suitable alternative to dye spray chromoendoscopy for dysplasia detection in persons with colonic inflammatory bowel disease when using high definition endoscopy. 8. Extensive nontargeted biopsies (roughly 4 adequately spaced biopsies every 10 cm) should be taken from flat colorectal mucosa in areas previously affected by colitis when white light endoscopy is used without dye spray chromoendoscopy or virtual chromoendoscopy. Additional biopsies should be taken from areas of prior dysplasia or poor mucosal visibility. Nontargeted biopsies are not routinely required if dye spray chromoendoscopy or virtual chromoendoscopy is performed using a high definition endoscope, but should be considered if there is a history of dysplasia or primary sclerosing cholangitis. 9. All clearly delineated dysplastic-appearing lesions without stigmata of invasive cancer or significant submucosal fibrosis should be considered for endoscopic resection. If the resectability of a lesion is in question, referral to a specialized endoscopist or inflammatory bowel disease center is suggested. 10. A finding of invisible dysplasia should prompt repeat examination by an experienced endoscopist using high-definition dye spray chromoendoscopy under optimized viewing conditions, with extensive nontargeted biopsies in the area of prior dysplasia if no lesion is seen. A finding of unresectable visible dysplasia or of invisible multifocal or high-grade dysplasia on histology should prompt colectomy. For visible lesions that can be resected or if histologic dysplasia is not confirmed on a high-quality dye spray chromoendoscopy examination, continued endoscopic surveillance at frequent intervals is appropriate. 11. After a negative screening colonoscopy, surveillance colonoscopy should be performed every 1–5 years based on risk factors for colorectal cancer, considering current and prior burden of colonic inflammation, family history of colorectal cancer, primary sclerosing cholangitis, history of colorectal dysplasia, and frequency and quality of prior surveillance examinations. 12. Pouch surveillance should be performed at least annually in those at high risk for developing colorectal dysplasia (prior colorectal cancer or dysplasia, primary sclerosing cholangitis), as well as in those with persistent moderate to severe pouchitis and/or pre-

Source	Recommendation
	pouch ileitis (to assess for treatment response). Surveillance intervals in those at lower risk should be individualized. 13. Targeted biopsies of representative or concerning pseudopolyps is appropriate during colonoscopy. Removal and sampling of all lesions is neither required nor practical. Surgery should be a last resort to manage colorectal cancer risk in the setting of severe pseudopolyposis. Dye spray chromoendoscopy should not be used to detect flat or subtle lesions within a field of pseudopolyps. 14. Optimal disease control with medical therapy is imperative to minimizing an individual's lifetime risk of developing colorectal cancer. There is uncertainty regarding the independent chemotherapeutic benefit of mesalamine therapy in people with colonic inflammatory bowel disease.
American Society of Clinical Oncology (ASCO)	Lopes et al. Early Detection for Colorectal Cancer: ASCO Resource-Stratified Guideline. J Glob Oncol. 2019;5:1-22. Screening: asymptomatic, average-risk population, high-incidence areas, age 50 to 75 years: • Basic setting options include the following: should receive highly sensitive guaiac fecal occult blood test (gFOBT) every one (preferred) to two years if resources are available (Evidence quality: high; Strength of recommendation: strong) or may receive fecal immunochemical testing (FIT), if available, every one (preferred) to two years (Evidence quality: intermediate; Strength of recommendation: moderate) • Limited setting options include the following: should receive highly sensitive gFOBT annually (Evidence quality: high; Strength of recommendation: strong) or may receive FIT annually (Evidence quality: intermediate; Strength of recommendation: moderate) or should receive flexible sigmoidoscopy every five years (Evidence quality: high; Strength of recommendation: strong) or may receive flexible sigmoidoscopy every 10 years plus FIT (or, if FIT not available, then FOBT) every year (Evidence quality: intermediate; Strength of recommendation: strong) • Enhanced setting options include the following: should receive highly sensitive gFOBT annually (Evidence quality: high; Strength of recommendation: strong) or may receive FIT annually (Evidence quality: intermediate; Strength of recommendation: moderate) or should receive flexible sigmoidoscopy every five years (Evidence quality: high; Strength of recommendation: strong) or may receive flexible sigmoidoscopy every 10 years plus FIT every year (Evidence quality: intermediate; Strength of recommendation: strong) or may receive colonoscopy every 10 years (Evidence quality: low; Strength of recommendation: weak) • Maximal setting options include the following: should receive highly sensitive gFOBT annually (Evidence quality: high; Strength of recommendation: strong) or may receive FIT annually (Evidence quality: intermediate; Strength of recommendation: moderate) or

Source	Recommendation
	should receive flexible sigmoidoscopy every five years (Evidence quality: high; Strength of recommendation: strong) or may receive Flexible sigmoidoscopy every 10 years plus FIT every year (Evidence quality: intermediate; Strength of recommendation: strong) or may receive colonoscopy every 10 years (Evidence quality: low; Strength of recommendation: weak) or may receive computed tomography (CT) colonography (Evidence quality: low; Strength of recommendation: weak) or may receive FIT DNA (Evidence quality: low; Strength of recommendation: weak) Reflex testing: If patients have a positive result from colorectal cancer screening: • Basic/limited: then clinicians should refer patients to colonoscopy (first choice) or sigmoidoscopy (second choice and the only option for basic) if available; however, since endoscopy is not available in most basic settings, clinicians should perform or refer patients to reflex testing with double contrast barium enema. If a patient's barium enema results are positive, refer to colonoscopy, if available; otherwise, refer the patient to surgery (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: strong) • Enhanced/maximal: If patients have a positive result from a noncolonoscopy colorectal cancer screening, then clinicians should perform or refer patients to a colonoscopy. (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: strong) For people with positive premalignant polyps or other abnormal screening results—pedunculated, enhanced/maximal, overarching—refer patients to endoscopy if available and feasible; otherwise, refer to surgery: • Colonoscopy should be performed always with therapeutic intent (Evidence quality: insufficient; Strength of recommendation: strong), and it should be performed by endoscopist with training in polypectomy (Evidence quality: low; Strength of recommendation: strong) • Lesions should be removed with polypectomy (Evidence quality: intermediate; Strength of recommendation: strong) • Patients with large premalignant lesions not suitable for endoscopic resection should be referred for surgical resection (Evidence quality: insufficient; Strength of recommendation: strong) • If lesion cannot be removed or if large lesion has a high likelihood of malignancy (Type: informal consensus), mucosal tattooing may be performed (Evidence quality: insufficient; Strength of recommendation: weak) • Removed lesions should be retrieved for histologic exam; confirm negative borders of resection (Evidence quality: insufficient; Strength of recommendation: strong) • Referral to surgery: Only patients with lesions that cannot be removed endoscopically should be referred to surgery (Evidence quality: insufficient; Strength of recommendation: strong)

Source	Recommendation
	For nonpedunculated, enhanced/maximal (term used to define sessile and flat colonic lesions): • Colonoscopy should be performed by endoscopists with training in large complex polyps (Evidence quality: low; Strength of recommendation: weak) always with therapeutic intent; endoscopic resection is first-line therapy for large nonpedunculated colorectal polyps with no suspicion of malignancy (Intent, Evidence quality: insufficient; Strength of recommendation: strong; Resection, Evidence quality: intermediate; Strength of recommendation: strong) • Lesions should be removed with polypectomy; removal of lesions is dependent on the low likelihood of malignancy (Evidence quality: intermediate, Strength of recommendation: strong) • Endoscopic assessment of lesion using enhanced endoscopy methods (if available, may include chromoendoscopy); clinicians should follow the British Society of Gastroenterology/Association of Coloproctologists of Great Britain and Ireland (BSGACGB) guideline (Evidence quality: insufficient; Strength of recommendation: strong) • If lesion cannot be removed (in BSGACGB guideline) or if large lesion has a high likelihood of malignancy, mucosal tattooing should be performed. For patients with polyps that are completely removed, clinicians may perform tattooing for surveillance purposes (Evidence quality: insufficient; Strength of recommendation: strong) • Removed lesions should be retrieved for histologic exam; confirm negative borders of resection (Evidence quality: insufficient; Strength of recommendation: strong) • Referral to surgery: Only patients with lesions that cannot be removed endoscopically should be referred to surgery (Evidence quality: insufficient; Strength of recommendation: strong) Optimal strategy for workup/diagnosis for those with symptoms: • Basic/limited: physical exam with digital rectal examination (DRE; Type: informal consensus; Evidence quality: insufficient), Double contrast barium enema (Type: informal consensus; Evidence quality: insufficient); colonoscopy with biopsy if no contraindications and available. If contraindications to colonoscopy, then flexible sigmoidoscopy with biopsy barium enema (Evidence quality: low; Strength of recommendation: weak) • Limited: see basic/limited recommendations. Also, if incomplete colonoscopy, barium enema (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: strong) • Enhanced: colonoscopy with biopsy if no contraindications;if contraindications to colonoscopy, flexible sigmoidoscopy with biopsy, if no contraindication, with full visualization of the colon (barium enema or CT colonography; Evidence quality: low; Strength of recommendation: weak); CT colonography if contraindications to both of the endoscopy options or double contrast enhanced barium enema (Evidence quality: high, Strength of recommendation: moderate)

<table>
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If incomplete colonoscopy, a double contrast enhanced barium enema or CT colonography (for colonography, if the local radiology service can demonstrate competency in this technique) (Evidence quality: intermediate; Strength of recommendation: strong)
Maximal: physical exam with DRE (Type: informal consensus; Evidence quality: insufficient); colonoscopy with biopsy if no contraindications and available; flexible sigmoidoscopy with biopsy, if no contraindication, with full visualization of the colon (barium enema or CT colonography; Evidence quality: low; Strength of recommendation: weak); CT colonography if contraindications to both of the endoscopy options or double contrast enhanced barium enema (Evidence quality: high; Strength of recommendation: moderate)
Repeat colonoscopy: If not feasible, the next tier would be one of the two following options: CT colonography (if the local radiology service can demonstrate competency in this technique) or barium enema (Evidence quality: intermediate, Strength of recommendation: strong)

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<tr><td>American Society of Colon and Rectal Surgeons (ASCRS)</td><td>Steele et al. Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. Practice Guideline for the Surveillance of Patients After Curative Treatment of Colon and Rectal Cancer. Dis Colon Rectum. 2015 Aug;58(8):713-25.

Surveillance colonoscopy is recommended at one year after curative resection for patients with surgically treated stage I to IV colorectal cancer. Subsequent colonoscopies should be performed every three to five years depending on the findings at the first postoperative examination. In cases of incomplete colon evaluation before surgery, the initial colonoscopy should be performed within three to six months or upon the completion of adjuvant therapy. Grade of Recommendation: Strong recommendation based on moderate-quality evidence, 1B.

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<tr><td>National Comprehensive Cancer Network® (NCCN®)</td><td>NCCN® Colorectal Cancer Screening Clinical Practice Guidelines™ (V.1.2023 — May 17, 2023)

<table>
<tr><th>Screening test*</th><th>Recommended Testing Interval**</th></tr>
<tr><td>Colonoscopy</td><td>Every 10 years</td></tr>
<tr><td>Flexible sigmoidoscopy***</td><td>Every 5–10 years</td></tr>
<tr><td>CT colonography</td><td>Every 5 years</td></tr>
<tr><td>High-sensitivity guaiac-based test</td><td>Annually</td></tr>
<tr><td>Quantitative FIT (using OC-Sensor)</td><td>Annually</td></tr>
<tr><td>Quantitative FIT (using OC-light)</td><td>Annually</td></tr>
<tr><td>mt-sDNA test****</td><td>Every 3 years</td></tr>
</table>
Note: All recommendations are category 2A unless otherwise indicated.

*A blood test that detects circulating methylated SEPT9 DNA has been FDA-approved for CRC screening for those who refuse other screening</td></tr>
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Source	Recommendation
	modalities. Based on current data, the panel concludes that the interval for repeating testing is unknown/unclear. The panel will continue to review this strategy and monitor data as they emerge. **Frequency based upon normal (negative) results. ***Data for the sensitivity and specificity of flexible sigmoidoscopy are for the entire colon and are based on the completion of colonoscopy for those found to have a distal colon lesion on flexible sigmoidoscopy. ****Optimal FIT thresholds will vary across screening programs, taking into consideration available colonoscopy resources to investigate abnormal results, including false-positive tests (page CSCR-A, 2 OF 6). Colonoscopy: In the United States, colonoscopy is the most commonly employed CRC screening test for populations at average and high risk. There are multiple options; however, the choice of modality for individuals at average risk should include consideration of patient preference and availability (page CSCR-A, 3 OF 6). Stool-based screening: This modality should only be employed for screening in individuals of average risk unless colonoscopy cannot be safely employed. If colonoscopy is used as the screening modality in a patient at average risk, then additional interval stool-based testing is not indicated. If a stool-based screening test is positive, colonoscopy should be recommended (CSCR-A, 4 OF 6) FIT/mt stool DNA-based testing: This modality is only FDA approved for individuals of average risk. Non-randomized studies have demonstrated that FIT is more sensitive than guaiac-based testing and also reduces mortality (CSCR-A, 5 OF 6). mSEPT9 blood test A blood test that detects circulating methylated SEPT9 DNA has been FDA approved for CRC screening for those who refuse other screening modalities. Based on current data, the panel concludes that the interval for repeating testing is unknown/unclear. The panel will continue to review this strategy and monitor data as they emerge (CSCR-A, 6 OF 6). <u>Screening of Individuals at Increased Risk / Personal History of Polyps Found at Colonoscopy</u> • Individuals with adenomatous polyps, SSPs, TSAs, or large hyperplastic polyps (≥1 cm) are at increased risk for recurrent polyps and CRC. To minimize the risk of developing CRC, a surveillance program is recommended for these patients following colonoscopy and complete polypectomy. • The panel recommends surveillance colonoscopy in adults with a history of adenomas aged 45 to 75 years, who may have a life expectancy of 10 or more years.

Source	Recommendation
	• Surveillance of individuals between ages 76 and 85 years should be individualized and include a discussion of risks and benefits of continued colonoscopy based on comorbidity status, estimated life expectancy, and finding on the last or most recent colonoscopy. • For patients with completely resected adenomatous polyps, the surveillance schedule depends on the risk of recurrence, which in turn is related to the number, size, and histology of adenomatous polyps. • Furthermore, when there is uncertainty about the completeness of removal in large and/or sessile polyps and when the colonic preparation was suboptimal, shorter surveillance intervals may be necessary. • Individuals with high-risk polyps (advanced or multiple polyps) should have a repeat colonoscopy in 3 years, although some data suggest that intervals of 5 years may be appropriate. If the examination is normal, subsequent surveillance colonoscopies are recommended in 5 years (MS-18, MS-19) <u>Management of Large Colorectal Polyps</u> • The management of large polyps is challenging and may require surgical resection. one major limitation of endoscopic resection is its association with a high rate of recurrence, attributed to the presence of residual adenoma tissue at the time of resection. Frequent surveillance with colonoscopy is appropriate in this setting. • For patients with no high-risk features receiving complete resection, a follow-up colonoscopy is recommended in 1 to 3 years if no invasive cancer and no unfavorable risk factors for recurrence were found. Consider follow-up within 3 years when polyp(s) is greater than 2 cm or confidence of complete en bloc resection is low. • Surveillance should be maintained in 3 years if no recurrence is found at the first surveillance colonoscopy. • If risk factors (LSL size ≥40 mm, intraprocedural bleeding requiring endoscopic control, high-risk dysplasia, or macroscopic tissue ablation performed) for recurrence are associated with complete resection or a piecemeal resection is performed, follow-up with colonoscopy within 6 months is recommended. • After complete resection and appropriate follow-up, if there is no disease recurrence, surveillance with colonoscopy within 1 year and subsequently in 3 years is appropriate. • For individuals with pedunculated polyps, follow-up with colonoscopy in 3 years is recommended if there is no disease recurrence (MS-20). <u>Individuals with a personal history of CRC</u> • Individuals with a personal history of CRC should be followed according to the surveillance recommendations in the NCCN Guidelines for Colon Cancer and the NCCN Guidelines for Rectal Cancer.

Source	Recommendation
	• These NCCN guidelines recommend a complete colonoscopy preoperatively as well as at 1 year following surgery. If this examination is normal, colonoscopy should be repeated in 3 years, then every 5 years. Shorter intervals (1 year) are recommended if adenomatous polyps or SSPs are found. Subsequent colonoscopic intervals are individualized and generally should not exceed 5 years (MS-21). <u>Personal History of Inflammatory Bowel Disease</u> • The NCCN Panel recommends colorectal surveillance by colonoscopy, initiated 8 years after the onset of symptoms in patients with a personal history of IBD involving the colon. • If primary sclerosing cholangitis (PSC) is present, annual surveillance colonoscopies should be started independent of the individual's time since symptom onset or colonoscopic findings and instead should be initiated at the time of PSC diagnosis. Family history of CRC is another important risk factor for developing CRC in patients with IBD, and such individuals may benefit from earlier initiation of colonoscopic surveillance • Colonoscopic surveillance in patients with IBD should be performed during quiescent disease. Colonoscopic surveillance may be performed by chromoendoscopy (dye spray or high-definition virtual) with targeted biopsy. Colonoscopic surveillance in IBD may also be performed with high-definition white light endoscopy (HD-WLE) (CSCR-8, MS-22). <u>Increased Risk Based on Personal History of Cystic Fibrosis</u> • The NCCN Panel recommends that, in patients with a history of solid organ transplant, surveillance should be initiated at ≥30 years of age or within 2 years of the transplantation. • In patients with no history of solid organ transplant, initiation of surveillance should begin at ≥40 years of age. • Surveillance methodology involves colonoscopies with intensive bowel preparation specific for patients with CF, because standard colonoscopy bowel preparation is often inadequate. If the colonoscopy returns no findings, a colonoscopy should be repeated every 5 years. If the colonoscopy reports adenomatous polyps, a coloscopy should be repeated every 3 years (MS-24). <u>Increased Risk Based on Positive Family History</u> • Patients not meeting criteria for consideration of a hereditary cancer syndrome or if appropriate testing for a hereditary cancer syndrome rules it out or is not done should have their individualized risk based on family history. • For patients with at least one affected first-degree relative with CRC at any age, colonoscopy is recommended every 5 years, beginning 10 years prior to the earliest diagnosis in the family, or by age 40 years at the latest. If colonoscopy is positive, follow-up colonoscopy should be based on findings. • Individuals with second- or third-degree relatives with CRC at any age are recommended to undergo colonoscopy every 10 years,

Source	Recommendation
	beginning by age 45. If colonoscopy is positive, follow-up should be based on colonoscopy findings. • Individuals with a first-degree relative with a confirmed history of advanced adenoma(s) (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology, TSA) or advanced SSPs (ie, ≥1 cm, any dysplasia) at any age should undergo colonoscopy at the relative's age of onset of adenoma or by age 40 years (whichever is earliest) with repeat colonoscopy every 5 to 10 years or based on findings. • Multiple (≥2) negative colonoscopies may support stepwise lengthening of the colonoscopy interval in these individuals (MS-25, MS-25). <u>Increased Risk Based on Personal History of Childhood, Adolescent, and Young Adult Cancer</u> • For patients with a history of chemotherapy only, a colonoscopy starting at 35 years of age or 10 years after chemotherapy (whichever occurs first) is recommended. • For patients that have a history of RT that included the abdominopelvic field or total body irradiation with or without chemotherapy, a colonoscopy starting at 30 years of age or 5 years after treatment (whichever occurs last) and repeating every 5 years is recommended. • For patients who have no history of chemotherapy or RT that included the abdominopelvic field, it is recommended to follow the average-risk screening guidelines, which entail receiving a colonoscopy starting at age 45 years and repeating every 10 years (MS-26).
National Comprehensive Cancer Network® (NCCN®)	NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Genetic/Familial High-Risk Assessment: Colorectal (Version 1.2023 — May 30, 2023) <u>Lynch Syndrome Management (LS-B, LS-C, LS-D, LS-E)</u> • If Lynch syndrome is confirmed, a high-quality colonoscopy is advised. The age to start CRC screening will depend on the P/LP variant. For MLH1 and MSH2/EPCAM variant carriers, a high-quality colonoscopy should start between the ages of 20 to 25 or 2 to 5 years younger than the youngest diagnosis age in the family, whichever comes first, and should be repeated every 1 to 2 years. • For MSH6 and PMS2 P/LP variant carriers, consider a later age of onset for colonoscopy initiation, such as at age 30 to 35 years or 2 to 5 years younger than age of any relative with CRC if diagnosed before age 30, repeating every 1 to 3 years. • Some patients may benefit from a shorter 1-year versus a longer 2-year screening interval.Factors that may favor a 1-year interval may include: being male, age >40 years, having MLH1/MSH2 pathogenic variants, or having a history of CRC or adenomas (MS-10). • <u>Chromoendoscopy</u> may also be used during colonoscopy in which dye spray is used to enhance visualization. Chromoendoscopy may be considered in patients with Lynch syndrome, but larger

Source	Recommendation
	prospective randomized trials are needed to better understand its role in Lynch syndrome (MS-11). <u>Lynch Syndrome Colonoscopy Surveillance Findings and Follow-up (LS-F)</u> • If there are no pathologic findings, continued surveillance every 1 to 3 years is recommended. Some patients may benefit from a shorter 1-year versus a longer 2-year screening interval. Factors that may favor a 1- year interval may include: being male, age >40 years, harboring MLH1/MSH2 P/LP variants, or having a history of CRC or adenomas (MS-14). • For patients with adenomatous polyps, recommendations include endoscopic polypectomy with a follow-up colonoscopy every 1 to 2 years (MS-15). <u>Familial Adenomatous Polyposis (FAP/AFAP-1)</u> Preoperative Surveillance for Individuals with a Family History of Classical FAP (FAP-2) Surveillance for at-risk individuals with a family history of FAP depends on genetic testing results, as described below. • Negative genetic testing: If an individual at risk is found not to carry the APC P/LP variant responsible for familial polyposis in the family, screening as an average-risk individual is recommended. • Positive genetic testing: If an APC P/LP variant is found, high-quality colonoscopy every 12 months, beginning at 10 to 15 years of age, is recommended (MS-18) Preoperative Surveillance for Individuals with a Personal History of AFAP (AFAP-1) • Treating patients with a personal history consistent with AFAP varies depending on the patient's age and adenoma burden. For patients with a small adenoma burden (defined somewhat arbitrarily as <20 adenomas, all <1 cm in diameter and none with advanced histology) that can be handled endoscopically, high-quality colonoscopy and polypectomy are recommended every 1 to 2 years with surgical evaluation and counseling if appropriate (MS-20). Preoperative Surveillance for Individuals with a Family History of AFAP (AFAP-2) • Negative genetic testing: If an individual at risk is found not to carry the APC P/LP variant responsible for polyposis in the family, screening as an average-risk individual is recommended, with modification based on their personal history of polyps and cancer. • Positive genetic testing, no genetic testing, or no familial pathogenic variant found: In an individual at risk who is found to carry the APC P/LP variant, colonoscopy surveillance should begin in the late teens, withrepeat examinations every 1 to 2 years (MS-20). <u>MUTYH-Associated Polyposis (MAP-1)</u> • Given conflicting evidence regarding CRC risk associated with having a monoallelic MUTYH pathogenic variant, the NCCN Panel recommends specialized screening for CRC mainly based on family

Source	Recommendation
	history (GENE-9). Specifically, the panel recommends that monoallelic MUTYH carriers unaffected by CRC with a first-degree relative with CRC receive colonoscopy screening every 5 years beginning at age 40 or 10 years prior to first-degree relative's age at CRC diagnosis (MS-26). Preoperative and Surgical Management of MAP (MAP-2/-3) • Genetic counseling and testing is recommended for individuals with a family history of MAP and known MUTYH pathogenic variants (see Adenomatous Polyposis Testing Criteria, above). With positive genetic testing (biallelic MUTYH pathogenic variants) or no testing in such individuals, high-quality surveillance colonoscopy should begin no later than age 25 to 30 years and should be repeated every 1 to 2 years if negative. • Individuals <21 years of age with confirmed biallelic MUTYH pathogenic variants and small adenoma burden are followed with colonoscopy and complete polypectomy every 1 to 2 years, beginning no later than age 25 to 30; earlier colonoscopy may be indicated based on family history (MS-27). <u>Colonic Adenomatous Polyposis of Unknown Etiology (CPUE-1)</u> • If the patient has a history of 20 to <100 adenomas, and the adenoma burden is small and considered to be manageable by colonoscopy and polypectomy, the panel recommends high-quality colonoscopy and polypectomy every 1 to 2 years. • If the patient has a personal history of 10 to 19 adenomas, management should be based on clinical judgment. Frequency of surveillance may be modified based on factors such as age at which patient met cumulative adenoma threshold or total number of adenomas at most recent colonoscopy (MS-28). <u>Peutz-Jeghers Syndrome (PJS-1)</u> Management of Peutz-Jeghers Syndrome (PJS-2/3) • Individuals with PJS should receive a colonoscopy every 2 to 3 years, beginning at age 18 years (MS-29). <u>Juvenile Polyposis Syndrome (JPS-1)</u> • CRC screening via colonoscopy should begin around age 18 years, since the mean age of diagnosis for juvenile polyps is 18.6 years. High-quality colonoscopy should be repeated every 1 to 3 years for surveillance. Intervals should be based on polyp size, number, and pathology (MS-31). <u>Serrated Polyposis Syndrome (SPS-1)</u> • High-quality colonoscopy with polypectomy is recommended for all polyps ≥5 mm, every 1 to 3 years depending on size and number of polyps. • The panel considers it reasonable to screen first-degree relatives at the youngest age of onset of SPS diagnosis, 10 years earlier than earliest diagnosis with CRC in the family, or by age 40 years, whichever is earliest. Subsequent screening is per colonoscopic findings or every 5 years if no polyps are found (MS-32).

Source	Recommendation
	Multi-Gene Testing (GENE-1) APC *I1307K* Pathogenic Variant • For carriers of the APC I1307K pathogenic variant with CRC, the panel recommends high-quality colonoscopy surveillance based on the NCCN Guidelines for Colon Cancer and the NCCN Guidelines for Rectal Cancer. • For carriers of the APC I1307K pathogenic variant unaffected by CRC, the panel recommends colonoscopy surveillance every 5 years beginning at age 40 or 10 years prior to a first-degree relative's age at CRC diagnosis (MS-35). APC Promoter 1B • Colonoscopy to exclude colon polyposis may be considered. There are insufficient data to define CRC risk associated with APC promoter 1B, so CRC risk management should be based on family history (MS-35). AXIN2 P/LP Variants • For carriers of AXIN2 P/LP variants, the panel recommends initiation of high quality colonoscopic surveillance at ages 25 to 30 years and if no polyps are detected, to repeat colonoscopy every 2 to 3 years (MS-36). CHEK2 P/LP Variants • For carriers of CHEK2 P/LP variants, the panel recommends high-quality colonoscopy surveillance based on the NCCN Guidelines for Colon Cancer and the NCCN Guidelines for Rectal Cancer. For carriers of CHEK2 P/LP variants unaffected by CRC, the panel recommends colonoscopy surveillance every 5 years beginning at age 40 or 10 years prior to a first-degree relative's age at CRC diagnosis. Some patients may elect for less aggressive screening based on shared decision-making (MS-36). PTEN/PTEN Hamartoma Tumor Syndrome • Early-onset (<50 years of age) CRC has been reported in 13% of patients with PTEN P/LP variant-associated Cowden syndrome/PHTS, suggesting that routine colonoscopy may be warranted in this population (MS-38).
The Society for Post-Acute and Long-Term Care Medicine™ (commonly called AMDA)	Fifteen Things Physicians and Patients Should Question. Updated July 28, 2022. Available at URL address: https://paltc.org/choosing-wisely Don't recommend screening for breast, colorectal or prostate cancer if life expectancy is estimated to be less than 10 years.
U.S. Multi-Society Task Force (MSTF) on Colorectal Cancer	Patel et al. Updates on Age to Start and Stop Colorectal Cancer Screening. Am J Gastroenterol. 2022 Jan 1;117(1):57-69. Correction. Gastroenterology. 2022 Jul;163(1):339. Erratum for: Gastroenterology. 2022 Jan;162(1):285-299. And Rex et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients. Am J Gastroenterol. 2017 Jul;112(7):1016-1030. Updated CRC screening start age Recommendations (Patel, et al., 2022):

Source	Recommendation
	• We suggest that clinicians offer CRC screening to all average-risk individuals age 45-49 (weak recommendation; low-quality evidence). • For average-risk individuals who have not initiated screening before age 50, we recommend that clinicians offer CRC screening to all average-risk individuals beginning at age 50 (strong recommendation, high-quality evidence). Updated CRC screening CRC screening stop age Recommendations (Patel, et al., 2022): • We suggest that individuals who are up to date with screening and have negative prior screening tests, particularly high-quality colonoscopy, consider stopping screening at age 75 years or when life expectancy is less than 10 years (weak recommendation, low-quality evidence). • We suggest that persons without prior screening should be considered for screening up to age 85, depending on consideration of their age and comorbidities (weak recommendation, low-quality evidence). APPROACHES TO SCREENING (Rex, et al., 2017) Recommendations: 1. We recommend that clinicians offer CRC screening beginning at age 50 (strong recommendation, high quality evidence). (See below for adjustments in recommended age for onset of screening based on race and family history.) 2. We suggest that sequential offers of screening tests, offering multiple screening options, and risk-stratified screening are all reasonable approaches to offering screening (weak recommendation, low-quality evidence). PRACTICAL CONSIDERATIONS (Rex, et al., 2017) Recommendations: 1. We recommend colonoscopy every 10 years or annual FIT as first-tier options for screening the average-risk persons for colorectal neoplasia (strong recommendation; moderate-quality evidence). 2. We recommend that physicians performing screening colonoscopy measure quality, including the adenoma detection rate (strong recommendation, high-quality evidence). 3. We recommend that physicians performing FIT monitor quality (strong recommendation, low-quality evidence). The recommended quality measurements for FIT programs are detailed in a prior publication. 4. We recommend CT colonography every 5 years or FIT– fecal DNA every 3 years (strong recommendation, low quality evidence) or flexible sigmoidoscopy every 5 to 10 years (strong recommendation, high-quality evidence) in patients who refuse colonoscopy and FIT. 5. We suggest that capsule colonoscopy (if available) is an appropriate screening test when patients decline colonoscopy, FIT, FIT–fecal

Source	Recommendation
	DNA, CT colonography, and flexible sigmoidoscopy (weak recommendation, low quality evidence). 6. We suggest against Septin9 for CRC screening (weak recommendation, low-quality evidence). FAMILY HISTORY OF CRC AND POLYPS (Rex, et al., 2017) Recommendations: 1. We suggest that persons with 1 first-degree relative with CRC or a documented advanced adenoma diagnosed at age <60 years or with 2 first-degree relatives with CRC and/or documented advanced adenomas undergo colonoscopy every 5 years beginning 10 years younger than the age at which the youngest first-degree relative was diagnosed or age 40, whichever is earlier (weak recommendation, low-quality evidence). 2. We suggest that persons with 1 first-degree relative diagnosed with CRC or a documented advanced adenoma at age ≥60 years begin screening at age 40. The options for screening and the recommended intervals are the same as those for average-risk persons (weak recommendation, very-low-quality evidence). 3. We suggest that persons with 1 or more first-degree relatives with a documented advanced serrated lesion (SSP or traditional serrated adenoma ≥10 mm in size or an SSP with cytologic dysplasia) should be screened according to above recommendations for persons with a family history of a documented advanced adenoma (weak recommendation, very-low-quality evidence). 4. We recommend that persons with 1 or more first-degree relatives with CRC or documented advanced adenomas, for whom we recommend colonoscopy, should be offered annual FIT if they decline colonoscopy (strong recommendation, moderate-quality evidence). CONSIDERATIONS REGARDING AGE AND CRC RISK (Rex, et al., 2017) Recommendations: 1. We recommend that screening begin in non–African American average-risk persons at age 50 years (strong recommendation; moderate-quality evidence). 2. We suggest that screening begin in African Americans at age 45 years (weak recommendation, very-low-quality evidence). 3. We recommend that adults age <50 years with colorectal bleeding symptoms (hematochezia, unexplained iron deficiency anemia, melena with a negative upper endoscopy) undergo colonoscopy or an evaluation sufficient to determine a bleeding cause, initiate treatment, and complete follow-up to determine resolution of bleeding (strong recommendation, moderate-quality evidence). 4. We suggest that persons who are up to date with screening and have negative prior screening tests, particularly colonoscopy, consider stopping screening at age 75 years or when life expectancy is less than 10 years (weak recommendation, low-quality evidence). 5. We suggest that persons without prior screening should be considered for screening up to age 85, depending on consideration

Source	Recommendation
	of their age and comorbidities (weak recommendation, low-quality evidence). Rating of evidence: (Kahi, et al., 2016) • High quality: Further research is very unlikely to change our confidence in the estimate of effect • Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate • Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
U.S. Multi-Society Task Force (MSTF) on Colorectal Cancer	Kahi et al. Colonoscopy Surveillance After Colorectal Cancer Resection. Gastroenterology. 2016 Mar;150(3):758-768.e11. These guidelines include the following recommendations: • Patients with CRC undergo high-quality perioperative clearing with colonoscopy. The procedure should be performed preoperatively, or within a three to six-month interval after surgery in the case of obstructive CRC. The goals of perioperative clearing colonoscopy are detection of synchronous cancer and detection and complete resection of precancerous polyps. (Strong recommendation, low-quality evidence) • Patients who have undergone curative resection of either colon or rectal cancer receive their first surveillance colonoscopy one year after surgery (or one year after the clearing perioperative colonoscopy). (Strong recommendation, low-quality evidence) • After the one-year colonoscopy, the interval to the next colonoscopy should be three years (i.e., four years after surgery or perioperative colonoscopy) and then five years (i.e., nine years after surgery or perioperative colonoscopy). Subsequent colonoscopies should occur at five-year intervals until the benefit of continued surveillance is outweighed by diminishing life expectancy. If neoplastic polyps are detected, the intervals between colonoscopies should be in accordance with published guidelines for polyp surveillance intervals. These intervals do not apply to patients with Lynch syndrome. (Strong recommendation, low-quality evidence) • Patients with localized rectal cancer who have undergone surgery without total mesorectal excision, those who have undergone transanal local excision (i.e., transanal excision or transanal endoscopic microsurgery), or endoscopic submucosal dissection, and those with locally advanced rectal cancer who did not receive neoadjuvant chemoradiation and then surgery using total mesorectal excision techniques, are at increased risk for local recurrence. In these situations, suggest local surveillance with flexible sigmoidoscopy or EUS every three-six months for the first two-three years after surgery. These surveillance measures are in addition to recommended colonoscopic surveillance for

Source	Recommendation
	metachronous neoplasia. (Weak recommendation, low-quality evidence) Alternatives and adjuncts to colonoscopy: • In patients with obstructive CRC precluding complete colonoscopy, we recommend CTC as the best alternative to exclude synchronous neoplasms. Double-contrast barium enema is an acceptable alternative if CTC is not available. (Strong recommendation, moderate-quality evidence) • There is insufficient evidence to recommend routine use of FIT or fecal DNA for surveillance after CRC resection. Rating of evidence: • High quality: Further research is very unlikely to change our confidence in the estimate of effect • Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate • Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
U.S. Multi-Society Task Force (MSTF) on Colorectal Cancer	Robertson, et al. Recommendations on Fecal Immunochemical Testing to Screen for Colorectal Neoplasia. Gastroenterology. 2017 Apr;152(5):1217-1237.e3. Recommendations • With one-time application, FIT tests are approximately 80% sensitive for cancer detection and approximately 20%–30% sensitive for advanced neoplasia detection. To enhance advanced adenoma detection, repeated applications of FIT are required. Therefore, it is recommended repeated testing to maximize the effectiveness of cancer detection and prevention with this modality. Individuals choosing FIT should understand the need for recurring testing and for colonoscopy to evaluate a positive FIT result. Programs to track cycles of testing are encouraged to facilitate completion. (Strong recommendation; moderate-quality evidence) • Given the high positive predictive value of FIT for cancer detection, colonoscopy is recommended when the test is positive, not repeat FIT. (Strong recommendation; moderate-quality evidence) Rating of evidence: • Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
U.S. Multi-Society Task Force (MSTF) on Colorectal Cancer	Gupta et al. Recommendations for Follow-Up After Colonoscopy and Polypectomy. Gastrointest Endosc. 2020;91(3):463-485.e5. Risk for Incident and Fatal Colorectal Cancer After Normal Colonoscopy and After Polyp Removal

Source	Recommendation
	• Normal colonoscopy is associated with sustained reduced risk for incident and fatal CRC. (High quality of evidence) • Incremental effectiveness of repeat colonoscopy after baseline normal colonoscopy for further reducing CRC incidence and mortality is uncertain. (Insufficient evidence) • Risk for incident and fatal CRC after baseline adenoma removal is uncertain. (Low quality of evidence) • Surveillance colonoscopy after baseline removal of adenoma with high-risk features (e.g., size ≥10 mm) may reduce risk for incident CRC, but impact on fatal CRC is uncertain. (Low quality of evidence) • Incremental impact of surveillance colonoscopy after baseline removal of adenoma with low-risk features (such as 1–2 adenomas <10 mm) on risk for incident and fatal CRC is uncertain. (Low quality of evidence) • Risk for incident and fatal CRC among individuals with baseline SSP is uncertain. (Very low quality of evidence) Recommended Post-Colonoscopy Surveillance Strategies for Reducing Colorectal Cancer Risk • For patients with normal, high-quality colonoscopy, repeat CRC screening in 10 years. (Strong recommendation, high quality of evidence) • For patients with one to two tubular adenomas <10 mm in size completely removed at a high-quality examination, repeat colonoscopy seven to ten years. (Strong recommendation, moderate quality of evidence) • For patients with three to four tubular adenomas <10 mm in size completely removed at a high-quality examination, repeat colonoscopy in three to five years. (Weak recommendation, very low quality of evidence) • For patients with five to ten tubular adenomas <10 mm in size completely removed at a high-quality examination, repeat colonoscopy in three years. (Strong recommendation, moderate quality of evidence) • For patients with one or more adenomas ≥10 mm in size completely removed at high-quality examination, repeat colonoscopy in three years. (Strong recommendation, high quality of evidence) • For patients with adenoma containing villous histology completely removed at high-quality examination, repeat colonoscopy in three years. (Strong recommendation, moderate quality of evidence) • For patients with adenoma containing high-grade dysplasia completely removed at high-quality examination, repeat colonoscopy in three years. (Strong recommendation, moderate quality of evidence) • For patients with >10 adenomas completely removed at high-quality examination, repeat colonoscopy in one year. (Weak recommendation, very low quality of evidence) • For patients with ≤ 20 HPs <10 mm in size in the rectum or sigmoid colon removed at a high-quality examination, repeat CRC

Source	Recommendation
	screening in 10 years. (Strong recommendation, moderate quality of evidence) • For patients with ≤ 20 HPs <10 mm in size proximal to the sigmoid colon removed at a high-quality examination, repeat colonoscopy in 10 years. (Weak recommendation, very low quality of evidence) • For patients with one to two SSPs <10 mm in size completely removed at high-quality examination, repeat colonoscopy in five to ten years. (Weak recommendation, very low quality evidence) • For patients with TSA completely removed at a high-quality examination, repeat colonoscopy in three years. (Weak recommendation, very low quality of evidence) • For patients with three to four SSPs <10 mm at high-quality examination, repeat colonoscopy in three to five years. (Weak recommendation, very low quality of evidence) • For patients with any combination five to ten SSPs <10 mm at high-quality examination, repeat colonoscopy in three years. (Weak recommendation, very low quality of evidence) • For patients with SSP ≥10 mm at a high-quality examination, repeat colonoscopy in three years. (Weak recommendation, very low quality of evidence) • For patients with HP ≥10 mm, repeat colonoscopy three to five years. A three year follow-up interval is favored if concern about pathologist consistency in distinguishing SSPs from HPs, quality of bowel preparation, or complete polyp excision, whereas a five year interval is favored if low concerns for consistency in distinguishing between SSP and HP by the pathologist, adequate bowel preparation, and confident complete polyp excision. (Weak recommendations, very low quality of evidence) • For patients with SSP containing dysplasia at a high-quality examination, repeat colonoscopy in three years. (Weak recommendation, very low quality of evidence) • For patients with history of baseline adenoma removal and one subsequent colonoscopy, recommendations for subsequent surveillance should take into account findings at baseline and first surveillance. (Weak recommendation, low quality of evidence) • There is insufficient evidence to recommend use of currently published prediction models for polyp surveillance recommendations. (Weak recommendation, very low quality of evidence) • Evidence is insufficient to recommend differential management for patients with proximal adenoma. (Weak recommendation, very low quality of evidence) • For patients with piecemeal resection of adenoma or SSP >20 mm, repeat colonoscopy in six months. (Strong recommendation, moderate quality of evidence) Rating of evidence: • High quality: Further research is very unlikely to change our confidence in the estimate of effect

Source	Recommendation
	• Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate • Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate • Very low quality: Any estimate of effect is very uncertain
U.S. Multi-Society Task Force (MSTF) on Colorectal Cancer	Kaltenbach et al. Endoscopic Removal of Colorectal Lesions: Recommendations by the US Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol. 2020 Mar;115(3):435-464. Some Statements of Best Practice include: Statement 1: Lesion assessment and description • We suggest proficiency in the use of electronic- (eg, NBI, i-scan, Fuji Intelligent Chromoendoscopy, or blue light imaging) or dye (chromoendoscopy)-based image enhanced endoscopy techniques to apply optical diagnosis classifications for colorectal lesion histology. (Conditional recommendation, moderate-quality evidence) Statement 4: Surveillance • To assess for local recurrence, we suggest careful examination of the post mucosectomy scar site using enhanced imaging, such as dye-based (chromoendoscopy) or electronic-based methods, as well as obtaining targeted biopsies of the site. Post-resection scar sites that show both normal macroscopic and microscopic (biopsy) findings have the highest predictive value for long-term eradication. (Conditional recommendation, moderate-quality evidence)
U.S. Multi-Society Task Force (MSTF) on Colorectal Cancer	Durno et al. Recommendations on surveillance and management of biallelic mismatch repair deficiency (BMMRD) syndrome: a consensus statement by the US Multi-Society Task Force on Colorectal Cancer. Gastrointest Endosc. 2017 May;85(5):873-882. Recommendation 1 is the only recommendation that relates to colorectal cancer and states: "In patients with BMMRD, surveillance for CRC by colonoscopy is recommended annually beginning at age 6. Once polyps are identified, colonoscopy every 6 months is recommended. (Weak recommendation, low-quality evidence)
U.S. Preventive Services Task Force (USPSTF)	USPSTF Screening for Colorectal Cancer Final Recommendation Statement (May 2021) Recommendations • The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years. (A recommendation) • The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years. (B recommendation) • The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence

Source	Recommendation
	indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health, prior screening history, and preferences. (C recommendation) Grade definitions: • Grade A: The USPSTF recommends the service. There is high certainty that the net benefit is substantial. • Grade B: The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial. • Grade C: The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.

Characteristics of Colorectal Cancer Screening Strategies (USPSTF, 2021):

Screening Method[a]	Frequency[b]	Evidence of Efficacy	Other Considerations
Stool-Based Tests			
gFOBT	Every year	• Evidence from RCTs that gFOBT reduces colorectal cancer mortality • High-sensitivity versions (eg, Hemoccult SENSA) have superior test performance characteristics than older tests (eg, Hemoccult II), although there is still uncertainty about the precision of test sensitivity estimates. Given this uncertainty, it is unclear whether high-sensitivity gFOBT can detect as many cases of advanced adenomas and colorectal cancer as other stool-based tests	• Harms from screening with gFOBT arise from colonoscopy to follow up abnormal gFOBT results • Requires dietary restrictions and three stool samples • Requires good adherence over multiple rounds of testing • Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT	Every year	• Evidence from one large cohort study that screening with FIT	• Harms from screening with FIT arise from colonoscopy to follow up abnormal FIT results

Screening Method[a]	Frequency[b]	Evidence of Efficacy	Other Considerations
		reduces colorectal cancer mortality • Certain types of FIT have improved accuracy compared with gFOBT and HSgFOBT (20 µg hemoglobin per gram of feces threshold was used in the CISNET modeling)	• Can be done with a single stool sample • Requires good adherence over multiple rounds of testing • Does not require bowel preparation, anesthesia or sedation, or transportation to and from the screening examination (test is performed at home)
sDNA-FIT	Every one or three years [c]	• Improved sensitivity compared with FIT per one time application of screening test • Specificity is lower than that of FIT, resulting in more false-positive results, more follow-up colonoscopies, and more associated adverse events per sDNA-FIT screening test compared with per FIT test • Modeling suggests that screening every three years does not provide a favorable (ie, efficient) balance of benefits and harms compared with other stool-based screening options (ie, annual FIT or sDNA-FIT every one or two years) • Insufficient evidence about appropriate longitudinal followup of abnormal findings after a negative follow-up colonoscopy • No direct evidence evaluating the effect of sDNA-FIT on colorectal cancer mortality	• Harms from screening with sDNA-FIT arise from colonoscopy to follow up abnormal sDNA-FIT results • Can be done with a single stool sample but involves collecting an entire bowel movement • Requires good adherence over multiple rounds of testing • Does not require bowel preparation, anesthesia or sedation, or transportation to and from the screening examination (test is performed at home)
Direct Visualization Tests			

Screening Method[a]	Frequency[b]	Evidence of Efficacy	Other Considerations
Colonoscopy	Every 10 years	• Evidence from cohort studies that colonoscopy reduces colorectal cancer mortality • Harms from colonoscopy include bleeding and perforation, which both increase with age	• Screening and diagnostic follow-up of positive results can be performed during the same examination • Requires less frequent screening • Requires bowel preparation, anesthesia or sedation, and transportation to and from the screening examination
CT colonography	Every five years	• Evidence available that CT colonography has reasonable accuracy to detect colorectal cancer and adenomas • No direct evidence evaluating effect of CT colonography on colorectal cancer mortality • Limited evidence about the potential benefits or harms of possible evaluation and treatment of incidental extracolonic findings, which are common. Extracolonic findings detected in 1.3% to 11.4% of exams; <3% required medical or surgical treatment	• Additional harms from screening with CT colonography arise from colonoscopy to follow up abnormal CT colonography results • Requires bowel preparation • Does not require anesthesia or transportation to and from the screening examination
Flexible sigmoidoscopy	Every five years	• Evidence from RCTs that flexible sigmoidoscopy reduces colorectal cancer mortality • Risk of bleeding and perforation but less than risk with colonoscopy • Modeling suggests that it provides fewer life-years gained alone than when combined with FIT	• Additional harms may arise from colonoscopy to follow up abnormal flexible sigmoidoscopy results • Test availability has declined in the US but may be available in some communities where colonoscopy is less available

Screening Method[a]	Frequency[b]	Evidence of Efficacy	Other Considerations
		or in comparison to other strategies	
Flexible sigmoidoscopy with FIT	Flexible sigmoidoscopy every 10 years plus FIT every year	• Evidence from RCTs that flexible sigmoidoscopy + FIT reduces colorectal cancer mortality • Modeling suggests combination testing provides similar benefits to those of colonoscopy, with fewer complications • Risk of bleeding and perforation from flexible sigmoidoscopy but less than risk with colonoscopy	• Additional potential harms from colonoscopy to follow up abnormal flexible sigmoidoscopy or FIT results • Flexible sigmoidoscopy availability has declined in the US but may be available in some communities where colonoscopy is less available • Screening with FIT requires good adherence over multiple rounds of testing

Abbreviations: CISNET, Cancer Intervention and Surveillance Modeling Network; CT, computed tomography; FIT, fecal immunochemical test; gFOBT, guaiac fecal occult blood test; RCT, randomized clinical trial; sDNA-FIT, stool DNA test with fecal immunochemical test.

a To achieve the benefits of screening, abnormal results from stool-based tests, CT colonography, and flexible sigmoidoscopy should be followed up with colonoscopy.
b Applies to persons with negative findings (including hyperplastic polyps) and is not intended for persons in surveillance programs. Evidence of efficacy is not informative of screening frequency, with the exception of gFOBT and flexible sigmoidoscopy alone.
c As stated by the manufacturer (USPSTF, 2021).

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	National Coverage Determination (NCD) for Colorectal Cancer Screening Tests (210.3)	January 2021
LCD		Numerous	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Colorectal Cancer Screening, Surveillance, or Monitoring

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
45330	Sigmoidoscopy, flexible; diagnostic, including collection of specimen(s) by brushing or washing, when performed (separate procedure)
45331	Sigmoidoscopy, flexible; with biopsy, single or multiple
45333	Sigmoidoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps
45338	Sigmoidoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by snare technique
45346	Sigmoidoscopy, flexible; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
45378	Colonoscopy, flexible; diagnostic, including collection of specimen(s) by brushing or washing, when performed (separate procedure)
45380	Colonoscopy, flexible; with biopsy, single or multiple
45381	Colonoscopy, flexible; with directed submucosal injection(s), any substance
45384	Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by hot biopsy forceps
45385	Colonoscopy, flexible; with removal of tumor(s), polyp(s), or other lesion(s) by snare technique
45388	Colonoscopy, flexible; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre-and post-dilation and guide wire passage, when performed)
45390	Colonoscopy, flexible; with endoscopic mucosal resection
74263	Computed tomographic (CT) colonography, screening, including image postprocessing
74270	Radiologic examination, colon; contrast (eg, barium) enema, with or without KUB
74280	Radiologic examination, colon; air contrast with specific high density barium, with or without glucagon
81528	Oncology (colorectal) screening, quantitative real-time target and signal amplification of 10 DNA markers (KRAS mutations, promoter methylation of NDRG4 and BMP3) and fecal hemoglobin, utilizing stool, algorithm reported as a positive or negative result
82270	Blood, occult, by peroxidase activity (eg, guaiac), qualitative; feces, consecutive collected specimens with single determination, for colorectal neoplasm screening (ie, patient was provided 3 cards or single triple card for consecutive collection)
82274	Blood, occult, by fecal hemoglobin determination by immunoassay, qualitative, feces, 1-3 simultaneous determinations

HCPCS Codes	Description
G0104	Colorectal cancer screening; flexible sigmoidoscopy
G0105	Colorectal cancer screening; colonoscopy on individual at high risk
G0106	Colorectal cancer screening; alternative to G0104, screening sigmoidoscopy, barium enema
G0120	Colorectal cancer screening; alternative to G0105, screening colonoscopy, barium enema
G0121	Colorectal cancer screening; colonoscopy on individual not meeting criteria for high risk

HCPCS Codes	Description
G0122	Colorectal cancer screening; barium enema
G0328	Colorectal cancer screening; fecal-occult blood test, immunoassay, 1-3 simultaneous determinations
S0285	Colonoscopy consultation performed prior to a screening colonoscopy procedure

Considered Medically Necessary when used to report chromoendoscopy with or without optical technologies such as narrow band imaging for colorectal cancer surveillance for patients at increased risk based on personal history of inflammatory bowel disease (IBD):

CPT®* Codes	Description
44799	Unlisted procedure, intestine
45399	Unlisted procedure, colon
45999	Unlisted procedure, rectum

Considered Experimental/Investigational/Unproven:

CPT®* Codes	Description
0002U	Oncology (colorectal), quantitative assessment of three urine metabolites (ascorbic acid, succinic acid and carnitine) by liquid chromatography with tandem mass spectrometry (LC-MS/MS) using multiple reaction monitoring acquisition, algorithm reported as likelihood of adenomatous polyps

Considered Experimental/Investigational/Unproven when used to report in vivo analysis of colorectal polyps (e.g., chromoendoscopy, fiberoptic polyp analysis):

CPT®* Codes	Description
44799	Unlisted procedure, intestine
45399	Unlisted procedure, colon
45999	Unlisted procedure, rectum

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Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	• Removed narrow band imaging and confocal fluorescent endomicroscopy from the policy statement.	11/15/2023