KAISER PERMANENTE

Colorectal Cancer Screening Guideline

Last guideline approval: October 2022

Guidelines are systematically developed statements to assist patients and providers in choosing appropriate health care for specific clinical conditions. While guidelines are useful aids to assist providers in determining appropriate practices for many patients with specific clinical problems or prevention issues, guidelines are not meant to replace the clinical judgment of the individual provider or establish a standard of care. The recommendations contained in the guidelines may not be appropriate for use in all circumstances. The inclusion of a recommendation in a guideline does not imply coverage. A decision to adopt any particular recommendation must be made by the provider in light of the circumstances presented by the individual patient.

Changes as of October 2022

This updated 2022 guideline has only minor differences from the previous (2021) version. The evidence review included five new questions to the literature; while several newly published, high-quality studies were identified and reviewed, none led to a change in the guideline recommendations.

Background

Colorectal cancer (CRC) is the fourth most commonly diagnosed cancer and the second leading cause of cancer deaths in the United States. There is good evidence that CRC-related morbidity and mortality can be reduced through early detection and treatment of early-stage disease and through the identification and removal of adenomas, the precursor of colorectal cancers.

Screening

Colorectal cancer risk groups

Average risk: Patients aged 45 years or older with no personal history of CRC or adenomas, no inflammatory bowel disease, and with a negative first- and second-degree family history for CRC.

Increased risk: Patients with a personal or family history of CRC or related conditions. (See Table 4.)

CRC screening recommendations by age group

Table 1. Colorectal cancer screening recommendations by age group

Age	Recommendation
30 through 44 years	**Review family history** to identify patients at increased risk for CRC (Table 4) or at high risk for inherited cancer syndromes (see Referral to Genetics).
45 through 75 years	Provide routine screening for patients at average risk (Table 2) and at increased risk (Table 4).
76 through 85 years	Consider routine screening only for patients who have not been up to date with screening prior to age 76 years and/or who are healthy enough to undergo treatment if CRC is detected and have a life expectancy of 10 years or more.
86 years and older	Screening is not recommended.

Recommended screening tests at KPWA medical facilities

Fecal immunochemical test (FIT)

Average-risk patients: Annual FIT is a simple method for screening average-risk patients as its net benefit is similar to the more invasive and resource-intensive recommended techniques. FIT is a simple and rapidly performed test that does not require preparation, sedation, or a doctor appointment. Its cost is minimal and conserves colonoscopy resources for patients who are at higher risk and for those who test positive on stool-screening tests. However, screening with FIT is effective only when performed annually and is not suitable for patients unable to adhere to the annual testing cycle. FIT is not the appropriate test for patients at increased risk for CRC because of family or personal history of cancer or other high-risk conditions (e.g., ulcerative colitis). A positive FIT **must** be followed by a colonoscopy.

Colonoscopy

Average-risk patients: Colonoscopy at 10-year intervals is an acceptable screening method for patients who prefer this approach or those who may have difficulty with adhering to an annual FIT testing regimen. Patients should be informed of the differences in potential risks associated with colonoscopy compared with annual FIT testing. For questions about colonoscopy coverage, patients can contact Member Services.

Increased-risk patients: Colonoscopy is the only screening method recommended for patients with a personal or family history of CRC or related conditions. See Table 4 for recommended screening frequency and age at initial screening.

Other acceptable screening tests

The following additional screening tests are less-preferred options. However, an adult who has had one of these tests is considered screened. Follow-up screening using a preferred option is recommended.

Stool DNA test (FIT-DNA, Cologuard)

The stool DNA test incorporates multiple molecular biomarkers with FIT. It was approved by the U.S. Food and Drug Administration (FDA) in 2014 for screening men and women aged 50 or older with an average risk of CRC. The test is covered by Medicare at 3-year intervals, as it is considered an acceptable testing modality by USPSTF. Coverage criteria may vary among health plans, so members should check with Member Services to be certain about coverage.

The USPSTF reviewed the evidence on the stool DNA test in its 2021 recommendation and noted that it had a higher single-test sensitivity than FIT alone in detecting colorectal cancer. However, it has a lower specificity than FIT alone, which leads to increased false-positives and a higher risk of harms from follow-up colonoscopies. A more recent meta-analysis (Dolatkhah 2022) concluded that multi-target stool DNA (Mt-sDNA) had acceptable diagnostic accuracy for CRC diagnosis, but with lower sensitivity and specificity compared to colonoscopy. The meta-analysis also concluded that Mt-sDNA had a higher sensitivity for CRC diagnosis, with almost the same specificity rates as FIT. Both screening colonoscopy every 10 years and annual FIT are more effective and less costly than stool DNA.

CT colonography/virtual colonoscopy

Virtual colonoscopy is not preferred for primary screening. It may be considered for patients who have relative contraindications to colonoscopy or who have attempted a colonoscopy that was unsuccessful. See Clinical Review Criteria for Virtual Colonoscopy or CT Colonography. The USPSTF recommendation concludes that sensitivity to detect adenomas was similar between CT colonography with bowel prep and colonoscopy for both adenomas 10 mm or larger (sensitivity 0.89 versus 0.89–0.95) and for adenomas 6 mm or larger (sensitivity 0.86 versus 0.75–0.93). However, CT colonography may pose harms from low-dose ionizing radiation and from the follow-up colonoscopy that may be required when extracolonic findings are detected (USPSTF 2021). In addition, there is no direct evidence evaluating whether screening with CT colonography reduces colon cancer mortality. These recommendations will be revisited when more evidence becomes available.

Screening recommendations for patients at AVERAGE risk

Table 2. Colorectal cancer screening for patients at AVERAGE risk
"Average risk" is defined as aged 45 years or older with no personal history of CRC or adenomas, no inflammatory bowel disease, and with a negative first- and second-degree family history for CRC.

Test	Age at initial screening	Frequency
Fecal immunochemical test (FIT)	45 years	Annually through age 75
Colonoscopy	45 years	Every 10 years through age 75

Shared decision-making

Due to the lack of head-to-head trials comparing the net benefits of the different tests, efforts to reduce CRC deaths should focus on implementing strategies that maximize the number of patients who get screening of some type. The different CRC screening options are variably acceptable to patients; eliciting patient preferences is one step in improving adherence. Ideally, shared decision-making between clinicians and patients incorporates information on local test availability and accuracy, as well as patient preference (USPSTF 2021).

Table 3. Shared decision-making about CRC screening options—patients at AVERAGE risk

Advantages/benefits	Disadvantages/risks
FIT (fecal immunochemical test) – KPWA preferred option	
• Can be done at home. • Quick. • Noninvasive. No risk of bowel tears or infections. • Does not require a doctor appointment or sedation. • Requires no advance preparation, dietary modification, or loss of time from work. • Minimal handling of stool. • There is direct evidence that stool screening test (followed by colonoscopy when positive) decreases CRC mortality. • Single specimen required.	• Some patients have discomfort with the thought of handling stool. • Colonoscopy is required if FIT is positive. • Must be done annually to be an effective screening method—adherence is important to the effectiveness of the program. • Cannot visually identify polyps.
Colonoscopy – KPWA preferred option	
• Views entire colon. Direct visualization techniques offer greater sensitivity for detection of adenomas of all sizes. • Requires testing only every 10 years (presuming no polyps or other abnormalities). • Only screening method with the potential to prevent CRC, as it allows not only for the detection but also the removal of polyps and precancerous lesions.	• Requires full bowel prep. Effectiveness of colonoscopy diminished if bowel prep is incomplete. • Sedation needed. • May require loss of time from work. • May be associated with a potential risk of bowel tears. • The evidence on the benefit of colonoscopy is indirect.
Stool DNA test (FIT-DNA, Cologuard) – non-preferred	
• Has same benefits as FIT test: non-invasive, no dietary change needed, and done at home. • Sensitivity may be higher than FIT.	• Specificity is lower than FIT, resulting in more false-positives and more follow-up colonoscopies, which increases the risk of harms. • FIT-DNA sensitivity was compared to the sensitivity of a single FIT test, rather than to 3 annual FIT tests (e.g., the recommended FIT screening frequency), so it is unknown whether the increase in sensitivity holds true in standard clinical practice. • No direct evidence evaluating the effect on CRC mortality.

Screening recommendations for patients at INCREASED risk

Table 4. Colorectal cancer screening for patients at INCREASED risk
"Increased risk" is defined as a personal or family history of CRC or related conditions.
Recommendations are based on 2017 U.S. Multi-Society Task Force on Colorectal Cancer Screening (Rex 2017).

Eligible population	Test	Age at initial screening	Frequency if colonoscopy negative
Personal history			
CRC or adenomatous polyps [1]	Colonoscopy	Consult with Gastroenterology.	Consult with Gastroenterology.
Inflammatory bowel disease (Crohn's disease, ulcerative colitis)	Colonoscopy	Consult with Gastroenterology.	Every 1–2 years
Family history			
1 first-degree relative [2] with CRC or advanced adenoma [3] diagnosed at age < 60 years **or** 2 first-degree relatives [2] with CRC or advanced adenoma [3] diagnosed at any age	Colonoscopy	**Whichever comes first:** Age 40 **or** 10 years prior to earliest age of diagnosis	Repeat per colonoscopy findings.
1 first-degree relative [2] with CRC or advanced adenoma [3] diagnosed at age ≥ 60 years	Colonoscopy	Age 40	Repeat per colonoscopy findings.
1 first-degree relative [2] with advanced serrated adenoma [4] or advanced adenoma [3] diagnosed at any age	Colonoscopy	**Whichever comes first:** Age 40 **or** Age of diagnosis	Repeat per colonoscopy findings.

[1] Adenomatous polyps (also called adenomas) are growths with malignant potential and are the most common type of colorectal polyp.
[2] First-degree relative = parent, sibling, or child.
[3] Advanced adenomas meet any of these criteria: high-grade dysplasia, ≥ 10 mm, any villous component.
[4] Advanced serrated adenomas have diffuse and often mild cytological dysplasia, and are predominantly located in the distal colon. They have high malignant potential.

Referral to Genetics

Refer patients with any of the following to Genetics for further risk evaluation/assessment for high-risk cancer syndromes:

- Personal history of CRC before age 50
- Personal history of CRC and endometrial cancer at any age
- Personal history of CRC and ovarian cancer at any age
- Personal history of CRC and two first-degree relatives with history of colorectal, endometrial, or ovarian cancer at any age
- Family history of inherited syndromes such as hereditary nonpolyposis colon cancer (Lynch syndrome or HNPCC), familial adenomatous polyposis (FAP), or familial diffuse gastric cancer (include immune histochemistry or microsatellite instability changes detected on tumor testing)

- Personal history of 10 or more adenomatous polyps
- Personal history of multiple primary colon cancers at any age

Follow-up

Table 5. Follow-up of screening test results
Recommendations are consistent with 2020 U.S. Multi-Society Task Force Recommendations for Follow-up After Colonoscopy and Polypectomy (Gupta 2020).

Test	Result	Follow-up testing
FIT	Negative	**Screen again in 1 year** with one of the options for average-risk patients (Table 2).
	Positive	Refer for **colonoscopy.**
FIT-DNA	Negative	**Screen again in 3 years** with one of the options for average-risk patients (Table 2).
	Positive	Refer for **colonoscopy.**
Colonoscopy [1]	Normal or ≤ 20 HPs [2] < 10 mm	**Screen again in 10 years** with one of the options for average-risk patients (Table 2).
	Abnormal	**Repeat colonoscopy at**
	1–2 adenomas < 10 mm	7–10 years
	1–2 SSPs [3] < 10 mm	5–10 years
	3–4 adenomas < 10 mm; 3–4 SSPs [3] < 10 mm; HP [2] ≥ 10 mm	3–5 years
	5–10 adenomas < 10 mm; 5–10 SSPs [3] < 10 mm; adenoma or SSP ≥ 10 mm; adenoma w/villous or tubulovillous histology; adenoma w/high-grade dysplasia; SSP w/dysplasia; traditional serrated adenoma	3 years
	> 10 adenomas	1 year
	Piecemeal resection of SSP or adenoma ≥ 20 mm	6 months

1 Colonoscopy must be of high quality, defined as: complete to cecum, adequate bowel prep to detect polyps > 5 mm, adequate colonoscopist adenoma detection rate, and complete polyp resection
2 Hyperplastic polyps (HP) are the most common type of polyp, usually small in size (< 5 mm), and predominantly located in the distal colon. They have low malignant potential.
3 Sessile serrated polyps (SSP) are typically seen in the proximal colon. SSPs with cytological dysplasia have very high malignant potential.

Evidence Summary

The Colorectal Cancer Screening Guideline was developed using an evidence-based process, including systematic literature search, critical appraisal, and evidence synthesis.

As part of our improvement process, the Kaiser Permanente Washington guideline team is working towards developing new clinical guidelines and updating the current guidelines every 2–3 years. To achieve this goal, we are adapting evidence-based recommendations from high-quality national and international external guidelines, if available and appropriate. The external guidelines should meet several quality standards to be considered for adaptation. They must: be developed by a multidisciplinary team with no or minimal conflicts of interest; be evidence-based; address a population that is reasonably similar to our population; and be transparent about the frequency of updates and the date the current version was completed.

In addition to identifying the recently published guidelines that meet the above standards, a literature search was conducted to identify studies relevant to the key questions that are not addressed by the external guidelines.

External guidelines eligible for adapting

2021 American College of Gastroenterology Clinical Guidelines: Colorectal Cancer Screening (Shaukat 2021)

2021 Canadian Colorectal Cancer Screening Guidelines: Do They Need an Update Given Changing Incidence and Global Practice Patterns? (Kalyta 2021)

2021 Recommendation Statement: Colorectal Cancer: Screening. U.S. Preventive Services Task Force. (USPSTF 2021)

2020 Recommendations for Follow-Up After Colonoscopy and Polypectomy: A Consensus Update by the U.S. Multi-Society Task Force on Colorectal Cancer (Gupta 2020)

2019 Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement from the American College of Physicians (Qaseem 2019)

2017 Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer (Rex 2017)

Key questions addressed in the KPWA guideline

1. **In average-risk individuals undergoing CRC screening, what are the comparative effectiveness and harms of annual versus biennial CRC screening with FIT in reducing the incidence of advanced neoplasia, CRC, and CRC mortality?**
    - The optimal interval for repeating the FIT test is unknown: to date, there are no published randomized controlled trials (RCTs) that compared various FIT screening intervals in reducing the incidence of advanced neoplasia, CRC, CRC mortality, or all-cause mortality. All guideline recommendations are based on the results of earlier studies that evaluated the effectiveness of CRC screening using gFOBT.
    - Ongoing RCTs comparing annual versus biennial FIT with colonoscopy for CRC incidence and mortality reduction may provide answers to this question.

2. **In average-risk patients offered CRC screening with either FIT or colonoscopy:**
    - **What is the difference between the two strategies in screening adherence rates?**
    - **Does the difference in adherence between the two strategies (if any) have an effect on the overall yield for advanced neoplasia/cancer in the screening population?**

    The overall pooled results of published studies suggest that CRC screening with endoscopy is associated with lower attendance rates but with a higher advanced neoplasia detection rate compared to one to three rounds of fecal tests. The analyses had their limitations, and the published

studies mainly compared the outcome of endoscopy to one round of FIT, which might not be the appropriate comparison.

3. **In average-risk individuals undergoing CRC screening, is there any new evidence on the comparative accuracy or efficacy of multi-target stool DNA (Mt-sDNA) (Cologuard) and FIT in detecting CRC and any other pre-cancerous lesions (advanced adenomas)?**

   There are no new published RCTs that would add to the evidence on the accuracy, efficacy, or safety of MT-sDNA in CRC screening.

4. **In average-risk individuals with a positive screening FIT, is the time to follow-up colonoscopy associated with any increased risk of colorectal cancer outcomes?**

   - Despite the retrospective design and limitations in the published studies, the consistency and directness of the results from studies with large population sizes indicate that delays in receiving follow-up colonoscopy are associated with increased risk of advanced stage disease.
   - The delay in receiving a colonoscopy associated with increased risk, however, differed between the published studies, from ≥ 6 months in a large population study conducted in Taiwan (Lee 2019) to ≥ 10 months in a Kaiser Permanente study (Corley 2017).
   - Mutneja and colleagues' 2021 meta-analysis pooled the results of the five observational studies conducted in different countries using FIT for CRC screening and found that colonoscopy performed > 6 months after positive fecal tests was associated with higher odds of detecting colorectal cancer (advanced and overall) and high-risk/advanced adenoma, compared with colonoscopies performed within 6 months.
   - Forbes and colleagues' 2021 systematic review—which included the same five FIT screening studies but did not pool the results in a meta-analysis—reported that the two largest published studies (including 123,138 and 70,124 participants, respectively) show that patients with positive FIT have a higher risk of both incident CRC and advanced CRC when colonoscopy is delayed beyond 9 months from their initial screening test. However, the study recommended that, when possible, colonoscopy should not be delayed beyond 6 months of a positive stool test.
   - Meester and colleagues' 2016 modeling study estimated a 4% increase in CRC incidence and 16% increase in mortality among adults who delayed follow-up colonoscopy by 12 months versus those who received it within 2 weeks.

5. **In average-risk individuals eligible for CRC screening, what is the diagnostic accuracy of blood-based biomarkers including methylated septin 9 for the early detection of CRC compared with other screening tests?**

   The current evidence does not support the use of septin 9 for CRC screening. Further studies are needed to determine whether it is a reliable biomarker to screen for CRC.

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Guideline Development Process and Team

Development process

To develop the Colorectal Cancer Screening Guideline, the guideline team adapted recommendations from externally developed evidence-based guidelines and/or recommendations of organizations that establish community standards.

This edition of the guideline was approved for publication by the Guideline Oversight Group in October 2022.

Team

The Colorectal Cancer Screening Guideline development team included representatives from the following specialties: family medicine, gastroenterology, and population health.

Clinician lead: John Dunn, MD, MPH, Medical Director, Clinical Knowledge & Implementation
Guideline coordinator: Avra Cohen, MN, RN, Clinical Improvement & Prevention

Jamie Andrews, MHA, Director, Clinical Value Improvement
Maggie Chin, MD, Family Medicine, Cancer Screening Quality Champion
Nadia Salama, MD, MPH, PhD, Clinical Epidemiologist, Clinical Improvement & Prevention
Stanley Shyn, MD, Medical Director, Population Health
Ann Stedronsky, Clinical Publications, Clinical Improvement & Prevention
Ron Yeh, MD, Gastroenterology