Intended Use of SimpleScreen CRC

The SimpleScreen™ CRC test is a qualitative, in vitro diagnostic test intended to detect molecular signals associated with colorectal cancer. SimpleScreen CRC utilizes circulating cell-free DNA from plasma of peripheral whole blood collected in the SimpleScreen CRC blood collection kit.

SimpleScreen CRC is indicated for colorectal cancer screening in adults aged 45 years and older who are at average risk for CRC. Patients with a positive result should be followed by colonoscopy. SimpleScreen CRC is not a replacement for diagnostic colonoscopy or for surveillance colonoscopy in high-risk individuals.

Precaution

Based on data from clinical studies, SimpleScreen CRC has limited detection (57%) of Stage I colorectal cancer (64% when U.S. 2020 Census age-sex adjusted) and does not detect 87% of advanced precancerous lesions (86% when U.S. 2020 Census age-sex adjusted). One out of 10 patients with a negative SimpleScreen CRC result may have a precancer that would have been detected by a screening colonoscopy.

Is SimpleScreen CRC test right for you?

SimpleScreen CRC is a blood based colorectal cancer (CRC) screening test for people at average risk of colorectal cancer. It is NOT indicated for use for individuals that have the following:

- Personal history of colorectal cancer, advanced precancerous lesions, or other related cancers
- Family history of colorectal cancer, defined as having one or more first-degree relatives (parent, sibling, or child) diagnosed with colorectal cancer at any age
- Positive result on another colorectal cancer screening method within the last six months, or:
  - A fecal occult blood test (FOBT) or fecal immunochemical test (FIT) within the last 12 months
  - A FIT-DNA test within the last 36 months
- Personal history of any of the following high-risk conditions for CRC:
  - Inflammatory bowel disease (IBD), including chronic ulcerative colitis (CUC) and Crohn's disease
  - Relevant hereditary cancer syndromes including but not limited to: hereditary non-polyposis colorectal cancer syndrome (HNPCC) or Lynch syndrome, familial adenomatous polyposis (FAP or Gardner's), Familial Hyperplastic Polyposis, Peutz-Jeghers syndrome, MUTYH-associated polyposis (MAP), Cowden's syndrome, Juvenile polyposis syndrome, serrated polyposis syndrome, Turcot's/Crail's syndrome, Cronkhite-Canada syndrome, or Neurofibromatosis.

SimpleScreen CRC is not a replacement for diagnostic colonoscopy or for surveillance colonoscopy in high-risk individuals.

1. What is cancer screening?

Checking for the presence of cancer in people without signs or symptoms of the disease is known as cancer screening. Several cancers can be found before any symptoms are present, so cancer screening can be recommended by providers even if people have no symptoms of disease. Screening for cancer may find cancers at an earlier stage, when they are more treatable.

2. Why get screened for colorectal cancer?

Colorectal cancer, which develops in the colon or rectum,[1] is the second leading cause of cancer-related deaths in the United States.[2] When colorectal cancer is found as an early, localized disease, the 5-year survival rate is 91%, but this rate falls to 13% when cancer has spread.[2]

Colorectal cancer is a disease that grows slowly, often starting from small groups of cells in the body called precancer that gradually change and become cancerous. One type of precancer, advanced precancerous lesions, is a specific type of polyp or growth in the colon or rectum that has a higher risk of becoming colorectal cancer if left untreated.

The goal of colorectal cancer screening is to identify colorectal cancer and precancers at an early stage, when they are the easiest to treat. National guidelines, including those from the American Cancer Society and the United States Preventive Services Task Force, recommend that adults aged 45 years and older with an average risk of colorectal cancer undergo regular screening.[3,4]

3. What is the SimpleScreen colorectal cancer screening blood test?

SimpleScreen CRC is a blood test that identifies unique aspects of DNA signals released from colorectal cancer into the blood of people at average risk for colorectal cancer. Average risk for colorectal cancer means not having a specific personal or family medical history that increases the likelihood to develop the disease.

Is SimpleScreen CRC accurate and effective in finding colorectal cancer?

In the largest clinical study of its kind (more than 27,000 participants evaluated),[5] SimpleScreen CRC accurately detected colorectal cancer in 57 out of 72 individuals, which means it has a sensitivity for colorectal cancer of 79.2%, and can accurately identify colorectal cancer in 8 out of 10 patients with the disease (Figure 1).

SimpleScreen CRC has a specificity of 91.5% for those without colorectal cancer or advanced precancerous lesions. If 10 people do not have colorectal cancer or advanced precancerous lesions, this test will accurately identify 9 of them as not having the disease (Figure 1).

SimpleScreen CRC has varying sensitivity for stage I, II, III and IV colorectal cancer (Table 1). It does a better job of identifying Stage II, III, and IV colorectal cancer than Stage I (Figure 1)

SimpleScreen CRC has limited ability to detect advanced precancerous lesions (i.e., pre-cancerous lesions that have the potential to develop into colorectal cancer called advanced precancerous lesions). This impacts the opportunity to prevent the development of colorectal cancer.

In the same clinical study, SimpleScreen CRC accurately detected 321 of 2567 people with advanced precancerous lesions. This means SimpleScreen CRC has an advanced precancerous lesion sensitivity of 12.5% (Figure 1).

Only a colonoscopy can confirm the presence of colorectal cancer or advanced precancerous lesions and prevent colorectal cancer development.

Figure 1. SimpleScreen CRC Performance

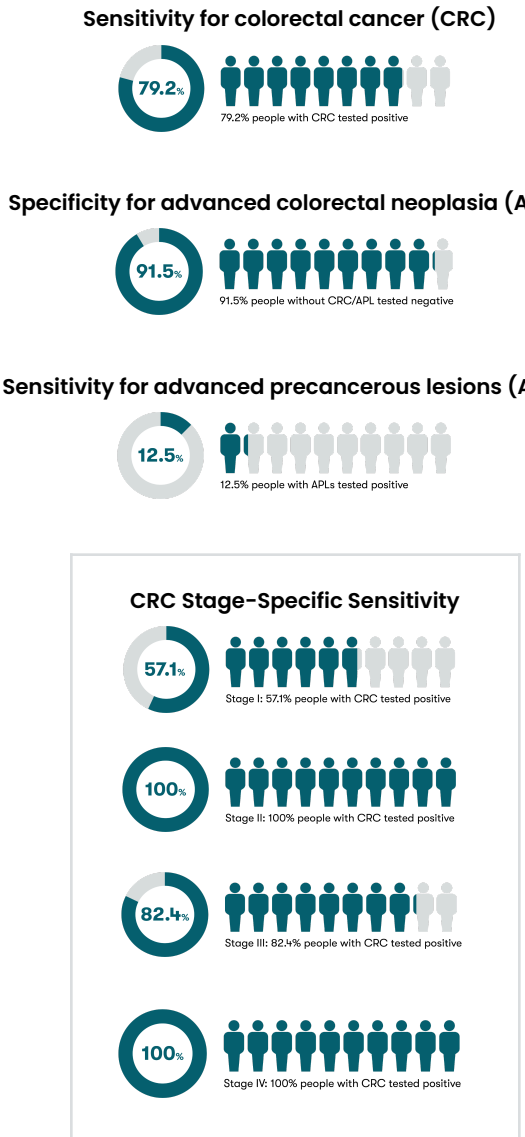

Table 1. SimpleScreen CRC Sensitivity

Observed CRC Sensitivity by Stage	Interpretation
CRC Sensitivity: 79.2%	Out of 100 people with CRC, SimpleScreen CRC detected approximately 79 people
Stage I: 57.1%	Out of 100 people with Stage I CRC, SimpleScreen CRC detected approximately 57 people
Stage II: 100%	Out of 100 people with Stage II CRC, SimpleScreen CRC detected approximately 100 people
Stage III: 82.4%	Out of 100 people with Stage III CRC, SimpleScreen CRC detected approximately 82 people
Stage IV: 100%	Out of 100 people with Stage IV CRC, SimpleScreen CRC detected approximately 100 people
APL Sensitivity: 12.5%	Out of 100 people with APLs, SimpleScreen CRC detected approximately 13 people
U.S. Census Adjusted CRC Sensitivity by Stage*	**Interpretation**
CRC Sensitivity: 81.1%	Out of 100 people with CRC, SimpleScreen CRC detected approximately 81 people
Stage I: 63.5%	Out of 100 people with Stage I CRC, SimpleScreen CRC detected approximately 64 people
Stage II: 100%	Out of 100 people with Stage II CRC, SimpleScreen CRC detected approximately 100 people
Stage III: 80.5%	Out of 100 people with Stage III CRC, SimpleScreen CRC detected approximately 81 people
Stage IV: 100%	Out of 100 people with Stage IV CRC, SimpleScreen CRC detected approximately 100 people
APL Sensitivity: 13.7%	Out of 100 people with APLs, SimpleScreen CRC detected approximately 14 people

*Census-adjusted values account for differences in age and sex between PREEMPT CRC participants and the 2020 U.S. population

4. SimpleScreen CRC is easy to use

SimpleScreen CRC can be ordered during a provider visit, on its own, or alongside other blood tests. There is no special preparation required before the blood draw. If SimpleScreen CRC is right for you, your healthcare provider will order the test. You will need to complete a blood draw. Your blood sample is sent to the Freenome Clinical Laboratory for testing. Your results will be available in about 2 weeks; and your healthcare provider will discuss your results with you.

5. Understanding your SimpleScreen CRC results

A positive result indicates a signal was detected that may suggest the presence of colorectal cancer or advanced precancerous lesions and should be followed by colonoscopy.

Your healthcare provider will discuss this result with you and will recommend a colonoscopy to determine if colorectal cancer is present.

SimpleScreen CRC has a false positive rate of approximately 10%. This means that out of 10 people who do not have colorectal cancer or advanced precancerous lesions, 1 of them will incorrectly receive a "Positive" test result.

A negative result indicates the test did not detect a signal associated with colorectal cancer or advanced precancerous lesions. A negative test result does not guarantee absence of colorectal cancer or advanced precancerous lesions. Healthcare providers should work with individuals to continue guideline-recommended CRC screening programs.

The SimpleScreen CRC has a false negative rate of 21% for colorectal cancer. This means that out of 100 people who have colorectal cancer, 21 of them will incorrectly receive a test result of "Negative."

SimpleScreen CRC has lower detection of Stage I colorectal cancer, and failed to detect 43% of Stage I CRC. It may also fail to detect as many as 87% of patients with advanced precancerous lesions which means that out of 100 people who have advanced precancerous lesions, 87 of them will incorrectly receive a negative SimpleScreen CRC result.

A no result test suggests an invalid test result. You may be required to complete a new blood draw.

6. Colorectal cancer screening tests

It is important to talk to your healthcare provider about which colorectal cancer screening test is right for you. There are several colorectal cancer screening tests available today. Considerations include:

- The ability of the test to find cancer, described by sensitivity and specificity
  - Sensitivity, which measures a test's ability to correctly identify people who have a particular disease
  - Specificity, which measures a test's ability to correctly identify people who do not have a particular disease
- How the test is performed
- How often the test needs to be taken
- Convenience of the test
- Potential harms of the test
- Follow-up care after the test

Colonoscopy should be discussed with all patients, given the test's ability to detect and potentially remove colorectal lesions.

It is important to evaluate your colorectal cancer screening options with your healthcare provider as part of a broader discussion of colorectal cancer screening.

7. Who can I contact if I have questions?

For any questions about the test, please contact Freenome Client Services at 833-990-6185 or email support@freenome.com.

8. References

1. American Cancer Society. *Colorectal Cancer: Facts & Figures 2023-2025*. American Cancer Society; 2023.
2. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10-45. doi:10.3322/caac.21871
3. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250-281. doi:10.3322/caac.21457
4. US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Screening for colorectal cancer: US preventive services task force recommendation statement. *JAMA*. 2021;325(19):1965. doi:10.1001/jama.2021.6238
5. Shaukat A, Burke CA, Chan AT, et al. Clinical Validation of a Circulating Tumor DNA–Based Blood Test to Screen for Colorectal Cancer. *JAMA*. 2025;334(1):56-63. doi:10.1001/jama.2025.7515

Rx ONLY **IVD**