FREQUENTLY ASKED QUESTIONS

What is Colorectal Cancer (CRC)?
Colorectal cancer (CRC) is cancer of the large intestine (colon), the lower part of the digestive system. Rectal cancer is cancer of the last several inches of the colon. Together, they're often referred to as colorectal cancer or CRC.

CRC usually develops slowly and begins as small, noncancerous (benign) clumps of cells called adenomatous polyps. CRC usually develops slowly and often begins as precancerous adenomatous polyps. Over time some of these polyps can become colon cancers.¹

What is the incidence of CRC?
In 2016, there will be an estimated 134,490 new cases of colorectal cancer diagnosed in the U.S., and 49,190 people will die from the disease. Colorectal cancer is the second-leading cause of cancer-related death in the United States (behind only lung cancer) among men and women.²

What are the risk factors for CRC?
Several lifestyle-related factors have been linked to CRC—these include certain types of diets, being overweight or obese, smoking and heavy alcohol use. Other risk factors include a personal or family history of colorectal polyps or CRC, as well as a personal history of inflammatory bowel disease, ulcerative colitis or Crohn’s disease.

One of the greatest risk factors for CRC is age. While younger adults can develop CRC, a person’s chances of getting the disease increase significantly after the age of 50.³ In fact, 90% of new cases of CRC and 93% of deaths from CRC occur in people age 50 and older.⁴

Who should be screened for CRC and when?
The American Cancer Society (ACS) recommends that all Americans at average risk for CRC begin screening at age 50,⁵ while those at increased/high risk should begin screening earlier.⁶ The U.S. Preventive Services Task Force (USPSTF) recommends that adults age 50 to 75 be screened for CRC and

http://www.mayoclinic.org/diseases-conditions/colon-cancer/basics/definition/con-20031877
² American Cancer Society, Cancer Facts & Figures 2016
³ American Cancer Society Colorectal cancer risk factors.
⁴ American Cancer Society Colorectal Cancer Facts & Figures 2014-2016
⁵ American Cancer Society recommendations for CRC early detection
⁶ Centers for Disease Control and Prevention (CDC): “Vital Signs: CRC Screening”
http://www.cdc.gov/vitalsigns/colorectalcancerscreening/
adults 75 to 85 talk with their healthcare provider about whether they should be screened. African-Americans have the highest CRC incidence and mortality rates of all racial groups in the U.S., and research shows that African-Americans are diagnosed at a younger average age than other people.

All patients should speak with their physicians about their individual risk factors to determine the screening program that is right for them.

**Why is screening for CRC important?**
CRC is often considered the most preventable, yet least prevented cancer in the U.S.

Precancerous polyps can take 10 to 15 years to develop from benign to malignant, so early identification and removal (through routine screening) can effectively prevent cancer from ever forming. Because most polyps and early-stage cancers cause no symptoms, the only way to detect them early is through regular screening.

The good news is that for people whose CRC is detected at an early (localized) stage, the five-year survival rate is greater than 90%. Unfortunately, 23 million Americans age 50 and over who are at average risk do not get screened as recommended. In fact, America’s CRC screening rate has been nearly stagnant since 2005, hovering between 50-60%. Among some groups—including Hispanics, African-Americans, Medicare patients and low income Americans—screening rates are even lower. While data show that more than half of CRC-related deaths could be avoided with regular screening, the lack of patient compliance means that more than half of all CRC cases are not detected until the late stages, when treatment is difficult and the five-year survival rate a mere 13%.

**What screening options are available to patients and how do they compare?**
In June 2016, the USPSTF issued updated guidelines for CRC screening. While the Task Force notes that, generally, the best test is the one that gets done, it recommends several options, including:

- **Colonoscopy**—An invasive procedure in which a thin tube is used to look inside the rectum and colon for abnormalities. The procedure requires lengthy bowel preparation, dietary restrictions

---


13 Centers for Disease Control (CDC) National Health Interview Survey (NHIS) results as published in the CDC’s Morbidity and Mortality Weekly Report (MMWR) between 2006 and 2015.


and often sedation, but allows doctors to inspect, sample and remove abnormal tissue during the same procedure. Colonoscopy is recommended every 10 years for average risk patients.

- **Fecal Occult Blood Test (FOBT)**—There are two types of FOBT tests: one uses the chemical guaiac while the other, the fecal immunochemical test (FIT), uses antibodies to detect blood in the stool. Patients with average risk are usually recommended for screening with FIT or FOBT every year.

- **CT Colonography**—A procedure that uses a series of X-rays called computed tomography to image the colon. The images may show abnormalities on the inside surface of the colon. Patients with average risk are usually recommended for CT colonography every five years.

- **Stool DNA Test (sDNA, also referred to as FIT-DNA, multi-target stool DNA test or Cologuard®)**—Prescribed by a health care provider, this noninvasive test allows the patient to collect a sample of their stool in the privacy of their home, send it to a lab for analysis for the presence of blood AND altered DNA from abnormal cancerous or precancerous cells. The American Cancer Society recommends patients at average risk screen with sDNA at a three-year interval.16

**What is Cologuard®?**

Cologuard, developed by Exact Sciences, is the first and only FDA-approved, at-home, noninvasive, sDNA CRC screening test for adults 50 and over who are at average risk for colorectal cancer and is available by prescription only.

**How does Cologuard work?**

Every day, cells are shed from the colon wall. As part of this process, normal cells, along with abnormal cells from cancer or precancer, are shed and picked up by the stool as it passes through the colon. Cologuard is designed to detect these altered DNA and blood biomarkers released into the stool. At the Exact Sciences lab, stool samples are processed through a series of sophisticated, automated procedures to isolate specific DNA targets and detect the presence of blood.

**How do patients use Cologuard?**

First, a physician determines if Cologuard is appropriate for the patient and orders the test. A collection kit is then sent to the patient’s home. The patient should carefully review all the instructions and cautions listed in the Cologuard Patient Guide before beginning.

The Cologuard kit includes two collection containers: a large one for collecting the stool sample for sDNA testing and a small tube for testing for the presence of blood. First, the patient collects a stool sample at home and at his/her convenience in the large container. Then, the patient unscrews the tube, which contains a small brush, lightly scrapes the stool sample and returns the brush to the tube. Next, the patient pours a solution into the large container to preserve the sample as it’s transported to the lab. Patients should not drink the preservative liquid.

Once the process is complete, the patient ships the sample directly to the Exact Sciences lab via a prepaid mailer. The laboratory must receive the patient specimens within 72 hours of collection to ensure the integrity of the sample for testing. Therefore, pre-paid shipping is provided so that patients can send stool samples to the laboratory immediately after collection. The kit also includes a step-by-

16 American Cancer Society recommendations for CRC early detection

A step guide for collecting the stool sample and preparing the kit for shipment. In addition, patients have access to a support hotline and website provided by Exact Sciences.

There are no medications, dietary restrictions, bowel preparation, sedation, time off of work or transportation required with Cologuard.

The patient receives the test results from the prescribing healthcare provider in about two weeks.

**What do Cologuard results mean and what are the next steps following testing?**

A positive result means that the test detected altered DNA and/or blood in the stool that could mean there is cancer or precancer present. The patient will be referred for a diagnostic colonoscopy.

A negative result means that the test did not detect altered DNA and/or blood in the sample. A negative Cologuard test result does not guarantee absence of cancer or advanced adenoma. Patients with a negative Cologuard test result should be advised to continue participating in a colorectal cancer screening program at an interval and with a method appropriate for the individual patient based on a conversation with the prescribing physician.

Cologuard may produce false negative or false positive results. A false positive result occurs when Cologuard produces a positive result, even though a colonoscopy will not find cancer or precancerous polyps. A false negative result occurs when Cologuard does not detect a precancerous polyp or colorectal cancer even when a colonoscopy identifies the positive result.

**Who is Cologuard appropriate for?**

Cologuard is indicated to screen adults of either sex, 50 years or older, who are at typical average-risk for CRC.

**What is Cologuard’s indication for use?**

Cologuard is intended for the qualitative detection of colorectal neoplasia-associated DNA markers and for the presence of occult hemoglobin in human stool. A positive result may indicate the presence of colorectal cancer or advanced adenoma and should be followed by diagnostic colonoscopy. Cologuard is indicated to screen adults of either sex, 50 years or older, who are at typical average-risk for CRC. Cologuard is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.

**Is Cologuard an appropriate screening method for people over the age of 75?**

CRC screening guidelines vary for persons over the age of 75. The decision to screen persons over the age of 75 should be made on an individual basis in consultation with a healthcare provider. Cologuard test results should be interpreted with caution in older patients as the rate of false positives increases with age.

**Who should not use Cologuard?**

Cologuard was not clinically evaluated for the following types of patients:

- Patients with a history of CRC, adenomas or other related cancers
- Patients who have had a positive result from another CRC screening method within the last six months
- Patients who have been diagnosed with a condition that is associated with high risk for CRC—these include but are not limited to:
Inflammatory bowel disease
- Chronic ulcerative colitis
- Crohn’s disease
- Familial adenomatous polyposis
- Family history of CRC

- Patients who have been diagnosed with a relevant familial (hereditary) cancer syndrome, such as Hereditary non-polyposis CRC syndrome (HNPCCC or Lynch Syndrome), Peutz-Jeghers Syndrome, MYH-Associated Polyposis (MAP), Gardner’s syndrome, Turcot’s (or Crail’s) syndrome, Cowden’s syndrome, Juvenile Polyposis, Cronkhite-Canada syndrome, Neurofibromatosis and Familial Hyperplastic Polyposis.

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

Are there times when patients should not collect a sample for Cologuard?
Patients should not provide a sample for Cologuard if they have diarrhea or if they have blood in their urine or stool (e.g., from bleeding hemorrhoids, bleeding cuts or wounds on their hands, rectal bleeding or menstruation).

How do patients get Cologuard?
Cologuard is prescribed by a healthcare provider. Patients should speak with their healthcare providers to determine if Cologuard is appropriate for them.

How often will patients have to use Cologuard?
The ACS recommends screening with Cologuard every three years. The Centers for Medicare and Medicaid Services’ (CMS) assessment is that Cologuard will be reimbursed every three years for patients 50 and older who do not have symptoms of CRC and who do not have an increased risk of CRC. Medicare covers Cologuard for individuals age 50-85 fitting these criteria once every three years at no cost to patients. It is important for patients to speak with their healthcare provider about the established screening guidelines and where Cologuard fits into screening schedules for each individual patient.

What scientific data supports Cologuard?
Detailed data from Exact Sciences’ prospective, 90-site, 10,000-patient pivotal study, “Multitarget Stool DNA Testing for CRC Screening,” was published in April 2014 in the New England Journal of Medicine.

The study, which looked at average risk patients between the ages of 50 and 84, compared the performance of Cologuard to a leading FIT (OC FIT-CHEK® from Polymedco) using colonoscopy as the reference method. Key published data of Cologuard vs. FIT shows:

- Sensitivity of Cologuard in detecting patients with CRC was 92% versus 74% for FIT;
- Cologuard detected 42% of the advanced adenomas (polyps);

17 American Cancer Society: “American Cancer Society recommendations for colorectal cancer early detection.”
• Cologuard achieved a specificity of 87% versus FIT specificity at 95%.\textsuperscript{18}

Data recently published in the \textit{Mayo Clinic Proceedings} show that Cologuard performed similarly in the Alaskan Native population, a group that has among the world’s highest rates of CRC. Conventional screening approaches, such as colonoscopy, present access challenges because many live in remote, underserved communities, resulting in screening rates for some Alaska Native people as low as 23%. Results from the study of 661 average-risk Alaska Natives support Cologuard’s attractiveness as a screening approach for those in rural locations who have limited access to healthcare.\textsuperscript{19}

Some recent studies suggest that Cologuard may be reaching previously unscreened populations. A study of approximately 3,000 patients published in the March 2015 issue of \textit{The American Journal of Gastroenterology - Nature} showed that 42% of initial Cologuard users aged 50 - 74 had never been screened for colorectal cancer.\textsuperscript{20} Similarly, in a USMD Health System in Dallas study of nearly 400 Medicare patients who were previously non-compliant with recommended screening guidelines were offered Cologuard. 88% of the 400 patients completed Cologuard and of those patients with a positive Cologuard result 90% complied with follow-up colonoscopy.

**What national guidelines support the use of Cologuard?**

Cologuard is included in ACS’ colorectal cancer screening guidelines\textsuperscript{21} and the newly updated recommendations of the USPSTF.\textsuperscript{22} In addition, sDNA is included in the combined screening guidelines of the ACS/U.S. Multi-Society Task Force/American College of Radiology\textsuperscript{23} and the American College of Gastroenterology.\textsuperscript{24}

**What is the Cologuard Customer Care Center?**

While Cologuard offers patients a noninvasive, user-friendly screening option, a better test alone is not enough to change colorectal cancer compliance statistics. Cologuard is the only colorectal cancer screening method that is supported by a built-in patient and physician navigation service designed to actively encourage patients to complete their physician-ordered screening. This robust, 24/7 customer service program combines real-time, lab-based tracking software with the human touch to encourage patient and physician engagement and ensure high levels of screening success.

---


Customer care advocates follow up with those who have received a Cologuard kit to encourage them to complete the test and send it back for analysis. Representatives create patient screening reminders, conduct personal phone outreach and answer patient questions about sample collection, all with the goal of increasing the number of patients who follow through with their prescribed Cologuard screening.

**Are there any risks to using the Cologuard collection kit?**
The risks related to using the Cologuard collection kit are low. No serious adverse events were reported among the 10,000 people in the clinical study. Patients should be careful when opening and closing the lids to avoid the risk of hand strain. Patients should be advised of the cautions listed in the Cologuard Patient Guide. Patients should NOT drink the preservative liquid.

**How much does Cologuard cost? Will insurance cover it?**
Cologuard is available for $649 and is covered by Medicare and a growing number of private insurers, including Anthem Blue Cross and Blue Shield, Tufts Health Plan and Aetna Medicare Advantage. Medicare reimburses Cologuard at $508.87. More information about insurance coverage can be found here: [http://www.cologuardtest.com/insurance](http://www.cologuardtest.com/insurance).

**Are Medicare patients fully covered for Cologuard?**
Patients with Traditional Medicare and Medicare Advantage plans do not have any co-pays or deductible amounts.

**Where can patients get Cologuard if their healthcare provider does not currently offer it?**
Patients can be connected with a healthcare provider via Exact Sciences at 1-844-870-8870.

**Where can I find more information on Cologuard?**
To learn more, visit [www.CologuardTest.com](http://www.CologuardTest.com) or [www.exactsciences.com](http://www.exactsciences.com), where you can sign up for the company’s eNewsletter, or call 1-844-870-8870. Or visit the informational site on colon cancer and the importance of screening and early detection at [www.beseengetscreened.com](http://www.beseengetscreened.com).

Rx Only