Colorectal Cancer Screening Fact Sheet

Why is colorectal cancer screening so important?

- Colorectal cancer (CRC) is the 2nd leading cause of cancer death in the U.S., with over 140,000 Americans expected to be diagnosed with CRC in 2018. More than 50,000 people in the U.S. die annually of CRC.[1]
- When colorectal cancer is found at an early stage before it has spread, the 5-year relative survival rate is about 90 percent, yet 1 in 3 people in the U.S. who should be tested for colorectal cancer have never been screened.[2]

Who should be screened for Colorectal Cancer?

- CRC screening is generally recommended for all average-risk patients aged 50-75, with individualized plans made for patients aged 76-85 based on the patient's overall health and prior screening history.[3]
- People who have a family member with colorectal cancer or polyps are at increased risk and might need to start colorectal cancer screening before age 50.[4]
- The American Cancer Society recently released its 2018 guideline which recommends that average-risk adults aged 45 years and older undergo regular colorectal cancer screening.[5]
    - The change in starting age is designated as a "qualified recommendation," because there is less direct evidence related to CRC screening in adults aged 45-49 since most studies only include adults over 50.[5]
    - The recommendation for adults aged 50 years and older is designated as a "strong recommendation," based on the greater strength of the evidence and the judgment of the overall benefit. [5]
- African Americans have the highest rate of mortality and lowest survival when compared with all other racial groups in the United States, due to low awareness of benefits of CRC screening, limited access to health care, and insurance status.[6]
    - The American College of Gastroenterology and the American Society for Gastrointestinal Endoscopy recommend CRC screening in African Americans to begin at age 45.[6]

What is the most effective screening test for CRC?

- Preventing cancer is always better than finding cancer. Colonoscopy is the gold standard of CRC screening methods because of its ability to view the entire colon and both detect and remove pre-cancerous polyps during the same procedure.[4] It is the only suitable test for people who have risk factors such as family history of CRC.[4]
- In 2017, the U.S. Multi-Society Task Force on Colorectal Cancer (MSTF) ranked colonoscopy in the highest of three tiers among available CRC screening options, based on performance features, costs, and practical considerations. The MSTF recommends offering colonoscopy first with annual fecal immunohistochemical testing (FIT) offered to patients who decline colonoscopy, followed by second-tier tests for patients who decline FIT.[7]
    - First-tier options are colonoscopy every 10 years or annual FIT.[7]
    - Second-tier options include CT colonography every 5 years, Cologuard® every three years, or flexible sigmoidoscopy every five to 10 years.[7]
    - Third-tier tests include capsule endoscopy every five years due to limited evidence and barriers to access.
    - MSTF does not recommend the Septin9 serum assay (Epi proColon) due to low-quality evidence.[7]
- Medicare will cover at 100 percent of the initial CRC screening test chosen by a patient. If the initial test is positive, then subsequent testing (e.g., colonoscopy after a positive Cologuard® or FIT) may result in a large patient deductible and/or co-insurance bill because the second test would be considered a diagnostic or therapeutic service under Medicare billing codes.[8]

For patients who cannot or will not get a colonoscopy, what other screening tests are available, and how effective are they at detecting CRC and precancerous colon polyps?

- MSTF included two stool-based CRC screening tests in its recommendations, FIT and Cologuard®.[7]
- Stool-based screening tests are more effective at detecting CRC than those tests used to be, but they are NOT as effective as colonoscopy at accurately detecting pre-cancerous polyps.

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[1] American Cancer Society. Cancer Statistics Center: Colorectum. https://cancerstatisticscenter.cancer.org/#!/cancer-site/Colorectum. Accessed July 12, 2018.
[2] American Cancer Society. Colorectal Cancer: Early Detection, Diagnosis, and Staging. https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/detection.html. Accessed July 12, 2018.
[3] US Preventive Services Task Force. Screening for Colorectal Cancer US Preventive Services Task Force Recommendation Statement. JAMA, 2016;315(23):2564–2575. http://doi.org/10.1001/jama.2016.5989.
[4] American Society for Gastrointestinal Endoscopy. Media backgrounder on Colorectal Cancer Screening. https://www.asge.org/home/about-asge/newsroom/media-backgrounders-detail/colorectal-cancer-screening. Accessed July 12, 2018.
[5] American Cancer Society. American Cancer Society Updates Colorectal Cancer Screening. http://pressroom.cancer.org/releases?item=770. Accessed July 12, 2018.
[6] Williams, R., White, P., Nieto, J., Vieira, D., Francois, F., & Hamilton, F. (2016). Colorectal Cancer in African Americans: An Update: Prepared by the Committee on Minority Affairs and Cultural Diversity, American College of Gastroenterology. Clinical and Translational Gastroenterology, 7(7), e185. http://doi.org/10.1038/ctg.2016.36.
[7] Rex D, Boland C, Dominitz J et al. Colorectal Cancer Screening: Recommendations for Physicians and Patients from the U.S. Multi-Society Task Force on Colorectal Cancer. The American Journal of Gastroenterology 2017;112:1016-1030. http://doi.org/10.1038/ajg.2017.174.
[8] American Cancer Society. Colorectal Cancer: Early Detection, Diagnosis, and Staging: Insurance Coverage for Colorectal Cancer Screening. https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/screening-coverage-laws.html. Accessed July 12, 2018.

Fecal immunohistochemical test (FIT)

- Detects human blood in fecal specimens. A positive result should be followed up with additional diagnostic procedures, such as colonoscopy, to determine the exact cause and source of blood in the feces.[9] The test is less expensive ($20 per test) than Cologuard® ($500-600 per test).[9]
- A 2014 study in the New England Journal of Medicine of nearly 10,000 patients comparing FIT and Cologuard® to screening colonoscopy for CRC and polyp detection found that FIT was shown to have 73.8 percent sensitivity for detecting CRC compared to screening colonoscopy.[10]
    - A FIT test will miss a majority of advanced precancerous lesions and nearly all dangerous "flat" lesions.
        - The sensitivity of FIT was 46.2 percent for detecting advanced polyps with high-grade dysplasia and 23.8 percent for detecting advanced precancerous lesions.[10]
        - When compared to screening colonoscopy, FIT was 5.1 percent sensitive at detecting serrated polyps >1cm.[10] Studies have shown that 20 to 30 percent of colorectal cancers likely arise through the serrated polyp pathway.[11]
- FIT specificity (true negative rate) for CRC was 94.9 percent (5.1 percent false positive rate).[10]

Who should use FIT?

- FIT is recommended by major health organizations as an annual screening option for people age 50 or older who are at average risk for colon cancer. [1,2,3,4,5,6,7]
- The MSTF recommends offering colonoscopy first with annual FIT offered to patients who decline colonoscopy, followed by second-tier tests for patients who decline FIT.[7]

Cologuard®

- Cologuard® uses an Enzyme-Linked Immunosorbent Assay (ELISA) FIT test to quantify Hemoglobin in stool, but also contains a test for markers of altered DNA - methylated target DNA (NDRG4, BMP3), specific DNA point mutations (KRAS) and total human DNA (ACTB) - that are lost from tumors and polyps and shed in stool.[12] All positive test results should lead to a colonoscopy.[12]
- Cologuard® costs approximately $600 for privately insured patients and about $500 for Medicare patients.[7]
- A 2014 study in the New England Journal of Medicine of nearly 10,000 patients comparing FIT and Cologuard® to screening colonoscopy for CRC and polyp detection found that Cologuard® was shown to have 92.3 percent sensitivity for detecting CRC compared to screening colonoscopy.[10]
    - The sensitivity of Cologuard® was 69.3 percent for detecting advanced polyps with high-grade dysplasia and 42.4 percent for detecting advanced precancerous lesions.[10]
    - Cologuard® was only 42.4 percent sensitive at detecting serrated polyps >1cm.[10] Studies have shown that 20 to 30 percent of colorectal cancers likely arise through the serrated polyp pathway.[11]
    - The lower specificity (86.6 percent) of Cologuard® leads to a very high false positive rate (13.4 percent).[10]

Who should use Cologuard®?

- Cologuard® is approved for patients age 50 years and older who are at average risk for colon cancer and is not intended to replace diagnostic colonoscopy or surveillance colonoscopy in high-risk patients.[12]
- NO other screening test should be used within 10 years of a high-quality negative screening colonoscopy.[3,7]
- Cologuard® is NOT approved for patients with high risk, including those who have been diagnosed with a condition that is associated with high risk for colorectal cancer. These include but are not limited to:
    - Personal history of polyps;
    - Inflammatory Bowel Disease;
    - Chronic ulcerative colitis;
    - Crohn's disease;
    - Familial adenomatous polyposis; and
    - Family history of colorectal cancer.[12]

[9] Labcorp. Occult Blood, Fecal, Immunoassay. https://www.labcorp.com/test-menu/32161/occult-blood-fecal-immunoassay. Accessed July 12, 2018.
[10] Imperiale T, Ransohoff D, Itzkowitz S, et al. Multitarget Stool DNA Testing for Colorectal-Cancer Screening. New England Journal of Medicine, 2014;370:1287-1297.
[11] Makkar R, Pai R, Burke C. Cleveland Clinic Journal of Medicine. 2012 December;79(12):865-871. http://doi.org/10.3949/ccjm.79a.12034.
[12] U.S. Food and Drug Administration. Summary of Safety and Effectiveness Data (SSED). https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130017b.pdf. Accessed July 12, 2018.