Colorectal Cancer Screenings | Facts for Clinicians

This document addresses some of the most common questions from clinicians relating to colorectal cancer (CRC) screening.

<table>
<thead>
<tr>
<th><strong>QUESTIONS</strong></th>
<th><strong>ANSWERS</strong></th>
</tr>
</thead>
</table>
| **Who needs to be screened for colorectal cancer (CRC)?** | ▪ There is a consensus in the medical community, all adults male and female age 50-75 need to be screened for CRC.  
▪ The U.S. Preventive Services Task Force (USPSTF) gives CRC screening an A recommendation.  
▪ Some patients may need to begin screening earlier based on certain risk factors (see Appendix B). |
| **What are current recommended screening guidelines?** | There are a variety of testing options for average-risk patients, beginning at age 50. The most common include:  
▪ Fecal Immunochemical Test (FIT) annually and if positive proceed with colonoscopy  
▪ Colonoscopy every 10 years  
▪ See Appendix A for full USPSTF screening guidelines. |
| **What is the FIT test and what evidence is available supporting its efficacy in clinical practice?** | ▪ FIT looks for hidden blood in the stool, specifically for non-digested human blood from the colon; FIT results are not impacted by food or medication; FIT requires collection of 1 or 2 specimens for a completed test; sensitivity and specificity varies with the test used  
▪ Use stool tests only for average risk patients (no personal or family history of CRC, adenomas, or genetic syndromes); high-risk patients should have colonoscopy screening  
▪ FIT is as effective as any other screening method when strict adherence and needed follow-up occurs at recommended intervals over a lifetime  
▪ For sensitivity and specificity of individual FIT brands, see Appendix C  
▪ Stool samples obtained by digital rectal exam (DRE) have low sensitivity for cancer (missing 19 of 21 cancers in one study with guaiac-based FOBT) and should never be used for CRC screening |
| **What is the FIT-DNA (Cologuard) test and what evidence is available supporting its efficacy in clinical practice?** | ▪ Cologuard is a stool-based test which detects DNA mutations present in colorectal cancer cells and adenomatous polyps; it also detects blood in the stool by FIT  
▪ Screening interval is every 3 years  
▪ Cost of the FIT-DNA is significantly more than a FIT, and abnormal results will require a follow-up colonoscopy  
▪ Sensitivity 92.3%; specificity 84.4%  
▪ Patients should check with their insurance about coverage |
| **What is the cost and insurance reimbursement available for these take-home methods?** | ▪ The lowest out-of-pocket cost option for CRC screening is a FIT; a colonoscopy is required if the take-home test is positive  
▪ Coverage of CRC screening is mandated under the Affordable Care Act (ACA) preventive benefit requirement  
▪ Grandfathered health plans may or may not cover CRC screening; 49% of insured North Dakotans have a grandfathered health plan; patients should be encouraged to contact their insurance company directly to learn details of their coverage  
▪ Patient navigation services can assist patients in reducing their individualized cost and other barriers; consider offering these services at your facility |
| **What is the difference between a screening and diagnostic colonoscopy?** | ▪ A screening test is one provided to a patient in the absence of signs or symptoms to detect or prevent a disease; whether a polyp or cancer is ultimately found does not change the screening intent of that procedure.  
▪ Diagnostic colonoscopy is a test performed because of an abnormal finding, sign or symptom (such as abdominal pain, bleeding, diarrhea, etc.); Medicare and most payers do not waive the co-pay and |
<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
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| What insurance reimbursement is available for screening colonoscopy?    | - As part of the ACA, most third-party payers are required to cover screening colonoscopies without a co-pay or deductible; Medicare beneficiaries may be subject to co-pays with polyp removal; Individuals on grandfathered health plans may also be subject to co-pays or deductibles.  
  - When the visit intent is screening and findings (i.e., polyps) result in a diagnostic or therapeutic service (i.e., polyp removal), the order of other codes submitted and pathology can affect how payers process the claim  
  - There is considerable variation in how payers process claims, and the order of the diagnosis code may affect whether the patient has out-of-pocket expenses for the procedure  
  - Encourage patients to check with their insurance company to determine their individual coverage options. |
| How do we connect uninsured or underinsured patients to get screened?   | - Take-home stool test is the lowest out-of-pocket cost option; if the stool test is positive, the patient will need a follow-up colonoscopy  
  - Ask about any charity-care programs the organization performing the colonoscopy may have and eligibility  
  - Connect patient to appropriate person for Medicaid or Medicaid Expansion enrollment information, if applicable. |
| How can we reduce patient barriers and ensure quality completion of CRC screening? | For take-home stool tests:  
  - Ensure patient receives instructions in their own language and at the appropriate literacy level; consider using demos or pictures to enhance comprehension  
  - Consider offering return postage and a “due by” date  
  - For patients who have not returned their kits, follow up with a reminder (i.e., phone call, mail, electronic)  
  - Track returns and results, and refer patients with a positive result to colonoscopy  

For colonoscopy:  
  - Assess possible barriers such as transportation to and from colonoscopy, availability of support person/driver after procedure, cost barriers, paid time off from work and connect to appropriate resources  
  - Ensure patient understands the colonoscopy prep process and receives instructions in their own language and at the appropriate literacy level; consider using pictures to enhance comprehension. |
| How should we respond to the increase in colorectal cancer incidence in young adults with our patients? | - A recent study led by the American Cancer Society found new cases of CRC are occurring at an increasing rate among young and middle-aged adults in the US; the study also found people younger than 55 are more likely to be diagnosed with late-stage disease than older people.  
  - Healthcare professionals should educate young patients, even children, about healthy lifestyle behaviors, ask about family history, and encourage patients to be seen for new symptoms  
  - Screening guidelines for colorectal cancer apply to asymptomatic patients; it is important symptomatic patients, including those under 50, have a diagnostic work-up  
  - Colorectal cancer may cause one or more of these symptoms:  
    - A change in bowel habits, such as diarrhea, constipation, or narrowing of the stool that lasts for more than a few days  
    - A feeling of needing to have a bowel movement that is not relieved by having one  
    - Rectal bleeding with bright red blood or dark stool  
    - Cramping or abdominal pain  
    - Weakness and fatigue  
    - Unintended weight loss  
    - Anemia. |

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The North Dakota Colorectal Cancer Roundtable (NDCRT), led by the American Cancer Society and the North Dakota Department of Health, is a statewide coalition of organizations dedicated to reducing the incidence and mortality from colorectal cancer in our state through coordinated leadership and strategic planning. The ultimate goal of the state's Roundtable is to increase the use of proven colorectal cancer screening tests among the entire population for whom screening is appropriate. To learn more, contact shannon.bacon@cancer.org.
APPENDIX A – USPSTF Recommended Tests for Colorectal Cancer Screening

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms. It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment. The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

### Stool-Based Tests

<table>
<thead>
<tr>
<th>Screening Method</th>
<th>Frequency</th>
<th>Evidence of Efficacy</th>
<th>Other Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>gFOBT</td>
<td>Every year</td>
<td>RCTs with mortality end points: High-sensitivity versions (eg, Hemoccult SENSA) have superior test performance characteristics than older tests (eg, Hemoccult II)</td>
<td>Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)</td>
</tr>
<tr>
<td>FIT</td>
<td>Every year</td>
<td>Test characteristic studies: Improved accuracy compared with gFOBT Can be done with a single specimen</td>
<td>Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)</td>
</tr>
<tr>
<td>FIT-DNA</td>
<td>Every 1 or 3 y</td>
<td>Test characteristic studies: Specificity is lower than for FIT, resulting in more false-positive results, more diagnostic colonoscopies, and more associated adverse events per screening test Improved sensitivity compared with FIT per single screening test</td>
<td>There is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of the test</td>
</tr>
</tbody>
</table>

### Direct Visualization Tests

<table>
<thead>
<tr>
<th>Screening Method</th>
<th>Frequency</th>
<th>Evidence of Efficacy</th>
<th>Other Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopy</td>
<td>Every 10 y</td>
<td>Prospective cohort study with mortality end point</td>
<td>Requires less frequent screening. Screening and diagnostic follow-up of positive results can be performed during the same examination.</td>
</tr>
<tr>
<td>CT colonography</td>
<td>Every 5 y</td>
<td>Test characteristic studies</td>
<td>There is insufficient evidence about the potential harms of associated extra colonic findings, which are common</td>
</tr>
<tr>
<td>Flexible sigmoidoscopy</td>
<td>Every 5 y</td>
<td>RCTs with mortality end points:</td>
<td>Test availability has declined in the United States</td>
</tr>
</tbody>
</table>

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1 https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/colorectal-cancer-screening2#Pod1
Modeling suggests it provides less benefit than when combined with FIT or compared with other strategies

| Flexible sigmoidoscopy with FIT<sup>c</sup> | Flexible sigmoidoscopy every 10 y plus FIT every year | RCT with mortality end point (subgroup analysis) | Test availability has declined in the United States
Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy

| **Abbreviations:** | FIT=fecal immunochemical test; FIT-DNA=multi-targeted stool DNA test; gFOBT=guaiac-based fecal occult blood test; RCT=randomized clinical trial. |
---|---|---|---|
<sup>a</sup> Although a serology test to detect methylated SEPT9 DNA was included in the systematic evidence review, this screening method currently has limited evidence evaluating its use (a single published test characteristic study met inclusion criteria, which found it had a sensitivity to detect colorectal cancer of <50%).<sup>1</sup> It is therefore not included in this table.<sup>a</sup>
<sup>b</sup> 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.<sup>b</sup>
<sup>c</sup> Strategy yields comparable life-years gained (ie, the life-years gained with the noncolonoscopy strategies were within 90% of those gained with the colonoscopy strategy) and an efficient balance of benefits and harms in CISNET modeling.<sup>2</sup>
<sup>d</sup> Suggested by manufacturer.<sup>d</sup>
<sup>e</sup> Strategy yields comparable life-years gained (ie, the life-years gained with the noncolonoscopy strategies were within 90% of those gained with the colonoscopy strategy) and an efficient balance of benefits and harms in CISNET modeling when lifetime number of colonoscopies is used as the proxy measure for the burden of screening, but not if lifetime number of cathartic bowel preparations is used as the proxy measure.<sup>2</sup>
APPENDIX B – RISK ASSESSMENT

The following tips regarding CRC Risk Assessment come from the American Cancer Society & National Colorectal Cancer Roundtable’s manual, Steps for Increasing Colorectal Cancer Screening Rates: A Manual for Community Health Centers:

Understanding Risk Levels for CRC

- **Average-risk**: Individual has no personal history of either adenomatous polyps or colorectal cancer, no first-degree relatives (parent, sibling, or child) with a history of either of these problems, and no history of inflammatory bowel disease.
- **Increased-risk**: Patient has a personal or family history of adenomatous polyps or colorectal cancer.
- **High-risk**: Patients include those with hereditary colorectal cancer syndromes: hereditary non-polyposis colorectal cancer (HNPCC) also called Lynch Syndrome, familial adenomatous polyposis (FAP), and another form of FAP, called Attenuated FAP (AFAP), which is a milder version of the disease. Other high-risk patients include those with Crohn’s disease or ulcerative colitis, whose risk increases with the extent and duration of the disease (usually after at least eight years).

Questions to Determine Risk

- Have you or any members of your family had colorectal cancer?
- Have you or any members of your family had an adenomatous polyp? (Request old pathology records if possible since most people will not know the type of polyp)
- Has any member of your family had a CRC or adenomatous polyp when they were under the age of 50? (If yes, consider a hereditary syndrome.)
- Do you have a history of Crohn’s disease or ulcerative colitis (more than eight years)?
- Do you or any members of your family have a history of cancer of the endometrium, small bowel, ureter, or renal pelvis? If the answer to any one of these is yes, a genogram will help assess for other cancers at young ages associated with hereditary non-polyposis colorectal cancer (HNPCC).

Genetic testing should be offered to those who have a personal or family history suggestive of one of the hereditary colorectal cancer syndromes. Genetic testing is often located in cancer centers that are interested in serving the community. If there is suspicion of a high-risk situation, send the patient for colonoscopy.

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Guidelines from the American Cancer Society, the US Preventive Services Task Force, and others recommend Fecal Immunochemical Tests (FIT), High-Sensitivity Guaiac-Based Fecal Occult Blood Tests (HS-gFOBT) and FIT-DNA tests as options for colorectal cancer (CRC) screening in men and women at average risk for developing colorectal cancer.

This document provides state-of-the-science information about these tests.

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3 http://nccrt.org/resource/fobt-clinicians-reference-resource/
The following factors make stool tests a good option for colorectal cancer screening

- Colorectal cancer screening with guaiac-based FOBT has been shown to decrease both incidence and mortality in randomized controlled trials.

- Modeling studies suggest that lives saved through a high-quality stool-based screening program are nearly the same as with a high-quality, colonoscopy-based screening program when strict adherence to screening and needed follow-up occurs at recommended intervals over a lifetime.

All patients should be aware that stool tests are a recommended screening option, along with invasive exams like colonoscopy. When given a choice, a significant number of patients prefer stool tests. In addition, access to colonoscopy and other invasive tests may be limited or non-existent for many patients.

High-sensitivity gFOBT and FIT should be repeated annually; FIT-DNA tests should be repeated every 3 years based on current screening guidelines.

Three types of stool tests are available – FIT, guaiac-based FOBT, and FIT-DNA

Fecal Immunochemical Tests (FITs) look for hidden blood in the stool and are specific for human blood while older guaiac-based tests (gFOBTs) are not. Unlike gFOBT, FIT results are not impacted by food or medication. There is evidence that patient adherence with FIT may be higher than with gFOBT possibly because no dietary and medication restrictions are required before collecting.
samples, or because some brands of FIT require collection of only 1 or 2 specimens for a completed test. It is important to note that not all FITs are equally effective. As of July 2016, there are 26 FDA-cleared FITs available for purchase in the US, however most do not have published data on their performance for detection of cancer. To assist with choosing a FIT for use in your setting, the table below includes FITs that have published data on sensitivity and specificity for cancer.

<table>
<thead>
<tr>
<th>FIT BRAND NAME</th>
<th>MANUFACTURER</th>
<th>SENSITIVITY FOR CANCER†,‡</th>
<th>SPECIFICITY FOR CANCER†,‡</th>
<th>NUMBER OF STOOL SAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Automated (non-CLIA waived) FITs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OC Auto-FIT*</td>
<td>Polymedco</td>
<td>65%-92.3%3,4</td>
<td>87.2%-95.5%3,4</td>
<td>1</td>
</tr>
<tr>
<td>CLIA-waived FITs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OC-Light iFOB Test (also called OC Light S FIT)</td>
<td>Polymedco</td>
<td>78.6%-97.0%3,4</td>
<td>88.0%-92.8%3,4</td>
<td>1</td>
</tr>
<tr>
<td>QuickVue iFOB</td>
<td>Quidel</td>
<td>91.9%5</td>
<td>74.9%5</td>
<td>1</td>
</tr>
<tr>
<td>Hemosure One-Step iFOB Test</td>
<td>Hemosure, Inc.</td>
<td>54.5%3</td>
<td>90.5%3</td>
<td>1 or 2</td>
</tr>
<tr>
<td>InSure FIT</td>
<td>Clinical Genomics</td>
<td>75.0%6</td>
<td>96.6%6</td>
<td>2</td>
</tr>
<tr>
<td>Hemoccult-ICT</td>
<td>Beckman Coulter</td>
<td>23.2%-81.8%3</td>
<td>95.8%-96.9%3</td>
<td>2 or 3</td>
</tr>
</tbody>
</table>

*Used with OC-Sensor DIANA and OC-Auto Micro 80 automated analyzers.
†Detection limits for cancer vary across FIT brand and by study such that direct comparison between FIT brands is not possible.
‡Cited studies should be interpreted in the full context of the published literature given variation in study size and quality.

Guaiac-based FOBTs (gFOBTs) have been the most common form of stool tests used in the US prior to FIT becoming widely available. Modern high-sensitivity tests have much higher cancer and adenoma detection rates than older tests, resulting in fewer missed cancers. Hemoccult II SENSA is the only test in this category for which published performance data is available. Screening guidelines now specify that only high-sensitivity forms of guaiac-based tests should be used for colorectal cancer screening. Hemoccult II and similar older guaiac-based tests should not be used for colorectal cancer screening.

<table>
<thead>
<tr>
<th>GFOBT BRAND NAME</th>
<th>MANUFACTURER</th>
<th>SENSITIVITY FOR CANCER</th>
<th>SPECIFICITY FOR CANCER</th>
<th>NUMBER OF STOOL SAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoccult II SENSA</td>
<td>Beckman Coulter</td>
<td>61.5%‐79.4%4</td>
<td>86.7%‐96.4%4</td>
<td>3</td>
</tr>
</tbody>
</table>

FIT-DNA is a stool test that looks for increased levels of altered DNA biomarkers that are released into the stool as cells from colorectal cancer and adenomas degenerate. Cologuard is the only stool DNA test currently marketed in the US and combines testing for these DNA biomarkers with a high-quality FIT (a “FIT-DNA” test).

<table>
<thead>
<tr>
<th>FIT-DNA BRAND NAME</th>
<th>MANUFACTURER</th>
<th>SENSITIVITY FOR CANCER</th>
<th>SPECIFICITY FOR CANCER</th>
<th>NUMBER OF STOOL SAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cologuard</td>
<td>Exact Sciences</td>
<td>92.3%7</td>
<td>84.4%7</td>
<td>1</td>
</tr>
</tbody>
</table>
Key Sources

Other Information Sources

Visit nccrt.org or cancer.org / colonmd to find additional clinical practice tools and learn more about 80% by 2018.
About the North Dakota Colorectal Cancer Roundtable

The North Dakota Colorectal Cancer Roundtable (NDCCRT), co-lead by the American Cancer Society and the North Dakota Department of Health, is a statewide coalition of organizations dedicated to reducing the incidence of and mortality from colorectal cancer in our state, through coordinated leadership and strategic planning. The ultimate goal of the state’s Roundtable is to increase the use of proven colorectal cancer screening tests among the entire population for whom screening is appropriate.

Learn more:

Listen to a message for North Dakota healthcare providers from Dr. Wender, Chief Cancer Control Officer for the American Cancer Society

Contact us:
shannon.bacon@cancer.org or 701-433-7593