In the Clinic

Screening for Colorectal Cancer

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CME Objective: To review current evidence for prevention, screening, and practice improvement of screening for colorectal cancer.

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Colorectal cancer (CRC) is the third leading cause of cancer death among men and women in the United States (1), but its incidence has been decreasing in the United States by 2%–3% per year over the past 15 years (2). Ample evidence shows that screening with any of several available strategies significantly decreases CRC incidence and mortality. Although still not optimal, screening rates in average-risk populations continue to increase, now exceeding 60% of the eligible population (3).

The lifetime risk for CRC in men and women in the United States is approximately 6%. About 93% of diagnoses are in patients older than 50 years, with the remaining 7% in those aged 40–50 years. CRC before 40 years of age is rare. Women are at modestly lower age-related risk for the disease than men but have an equivalent lifetime risk given their longer average life spans. Data suggest different relationships between age and disease incidence by sex and ethnic group, but these differences are generally not considered large enough to warrant specific, targeted screening recommendations (4, 5).

What if a family history of CRC is present?

As befits a common disease, about 10% of people report a family history of CRC in a first-degree relative (6)—that is, a relative who shares about half of their genes, such as a parent, sibling, or child. The overall increased risk for CRC with a family history in a first-degree relative is about 2-fold (7). Persons at greatest risk are those with 2 or more affected first-degree relatives or a single first-degree relative diagnosed at a young age (<60 years); such persons may have as much as a 3- to 4-fold increased risk for CRC (8). The contribution to individual risk of affected second- and third-degree relatives with CRC is small (7). The degree of risk conferred by having a single first-degree relative diagnosed after age 60 years—the most common clinical scenario—is less than 2-fold (7, 8).

Current guidelines recommend that persons with multiple affected first-degree relatives or a single first-degree relative diagnosed with CRC before age 60 years receive screening colonoscopy at age 40 years, or 10 years before the youngest affected first-degree relative, and continue thereafter with colonoscopy every 5 years. In those with a first-degree relative diagnosed after age 60 years, the recommendation is to have colon cancer screening at age 40 years, with intervals for follow-up that are equivalent to those for average-risk persons (9).

A subgroup analysis from a cohort study evaluating the benefit of endoscopic screening showed a decrease in CRC incidence with more frequent endoscopic testing in patients with a family history of the disease (10). A family history of CRC has been shown to strongly influence the timing of surveillance colonoscopy in practice (11), but the yield of more aggressive screening and surveillance in patients with a family history is largely unknown and requires further study.

Colon cancer syndromes driven by specific known mutations, such as hereditary non-polyposis colorectal cancer (HNPCC) or familial adenomatous polyposis (FAP), are uncommon, but the lifetime colon cancer risk can exceed 80% without preventive screening. Concern about such a syndrome is suggested by the presence of multiple affected first-degree relatives and early-onset CRC in the family before age 50 years (12).
Can patients reduce their risk for CRC by modifying their health behaviors or using certain drugs? Epidemiologic studies have shown associations between some health behaviors and CRC, so clinicians should advise patients about the potential benefits of these behaviors in modifying CRC risk (see the Box: Health Behaviors That May Reduce Risk for CRC). These behaviors have been associated with 0.5- to 2.0-fold risk reductions. Persons who are nonadherent to CRC screening are also more likely than adherent persons to have other behavior-related risk factors for CRC (13).

Several other micronutrients, including calcium; vitamins A, D, and E; folate; and selenium, have been associated with a decreased risk for CRC, but further study is necessary before supplemental intake of these agents can be routinely recommended.

Use of postmenopausal estrogen, aspirin, and other nonsteroidal anti-inflammatory drugs can decrease the risk for CRC and adenomatous polyps, but the balance of benefits and harms does not favor their use for primary prevention. Aspirin, for example, is effective as a primary chemopreventive agent for CRC (daily aspirin for 5 years reduces CRC incidence and mortality by 30%-40%) and as secondary prevention (recurrent adenoma rate is reduced by roughly 20%) (14). However, the U.S. Preventive Services Task Force recommends against the routine use of these drugs for CRC or polyp prevention in average-risk persons because of the risk for major bleeding (15).

Does screening prevent CRC? Screening not only prevents disease-associated morbidity and mortality but can also reduce cancer incidence. Cancer incidence reduction is the result of identification and removal of precancerous adenomatous polyps, some of which would have evolved into cancer if they had not been removed (6, 16, 17).

Prevention... Although such health behaviors as improving dietary intake, increasing physical exercise, or taking aspirin regularly can decrease CRC risk, the benefits of these behaviors seem modest and do not play a major role in primary prevention compared with screening, which is a powerful way to reduce CRC incidence and mortality. Screening programs are being instituted worldwide because of their proven public health benefit.

Health Behaviors That May Reduce Risk for CRC
- Moderate intake of red meat and fat (both saturated and unsaturated)
- Regular physical activity
- Maintenance of normal body weight
- Avoidance of alcohol and tobacco
- Consumption of 5–7 daily servings of fresh fruits and vegetables

CLINICAL BOTTOM LINE

What are the precursors of CRC? Adenomatous polyps are the acknowledged precursors of CRC.

Identification and removal of polyps is the focal point of screening. The pathologic terminology...
for adenomas can be confusing because many modifiers are used in clinical practice, including “tubular,” “tubulovillous,” “villous,” “mixed,” and “serrated.” “Advanced” adenomas are those that measure at least 1 cm, have a villous component (tubulovillous or villous), or have foci of high-grade dysplasia. Advanced adenomas are important because they identify patients with increased long-term risk for cancer, even years after colonoscopy (18), and those with advanced adenomas merit more frequent surveillance. The prevalence of advanced adenomas at screening colonoscopy is 5%–10% (19).

Serrated lesions, which have a sawtooth appearance on histologic evaluation, were originally considered hyperplastic polyps and were not believed to be associated with cancer. However, recent research has identified a subset of serrated lesions that are precursors of colon cancer, especially in the proximal bowel. The terms “sessile serrated adenoma” and “serrated polyp” are synonymous, and both refer to a growth that should be considered an adenoma and a precursor of cancer.

Adenoma terminology is important to the internist because the number and type of adenoma dictate the recommended surveillance interval after initial identification. However, surveillance colonoscopy is often improperly timed, with patients who need colonoscopy not receiving it and others having it too frequently (11). Table 1 lists the current recommendations for surveillance colonoscopy (20).

The occurrence of CRC after screening (particularly colonoscopy), known as interval cancer, has raised concern. Interval cancer may account for as much as 5%–8% of all cases (21) and is, in part, to missed lesions, presumably caused by suboptimal colonoscopy quality. The adenoma detection rate (ADR) for an endoscopist is the percentage of cases in which adenomas are detected. This measure has emerged as a validated marker of colonoscopy quality. In Poland, an ADR less than 20% was associated with an 11-fold increase in interval CRC diagnoses within 5 years (22). The presumption is that undetected adenomas can evolve into cancer. Practitioners with lower ADRs may put patients at increased risk for subsequent but preventable CRC (23).

Most colonoscopy quality guidelines recommend an overall ADR of around 25% (the specific rate is under debate), which shows adequate removal of all relevant precursors.

Table 1. Surveillance Recommendations for Colorectal Polyps

<table>
<thead>
<tr>
<th>Type of Polyp</th>
<th>Next Recommended Interval Test, y</th>
<th>Subsequent Recommended Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperplastic polyp</td>
<td>10</td>
<td>Based on results of most recent examination</td>
</tr>
<tr>
<td>1–2 Nonadvanced adenomas</td>
<td>5–10</td>
<td>Based on results of most recent examination</td>
</tr>
<tr>
<td>3 Nonadvanced adenomas</td>
<td>3</td>
<td>Uncertain*</td>
</tr>
<tr>
<td>Advanced adenoma (≥ 1 cm, with villous components, or with high-grade dysplasia)</td>
<td>3</td>
<td>5†</td>
</tr>
</tbody>
</table>

*Whether or how a history of multiple nonadvanced adenomas should influence subsequent testing frequency is unclear. If the examination following one in which 3 adenomas were detected is normal, repeated colonoscopy with an interval of at least 5 years is reasonable.

†Patients with an advanced adenoma should have surveillance every 5 years, even if an intervening examination is normal.
What methods are effective in screening for CRC?

Available evidence supports several screening tests for CRC, including fecal occult blood testing (FOBT), fecal immunochemical testing (FIT), flexible sigmoidoscopy, and colonoscopy. Randomized trials of screening efficacy are available for FOBT and flexible sigmoidoscopy and show benefit (Table 2). Evidence for colonoscopy is ample but indirect. Newer methods, such as DNA-based stool tests and computed tomography (CT) colonography (also known as “virtual colonoscopy”), show promise, but definitive evidence of their effectiveness is not yet available.

FOBT

Screening average-risk persons older than 50 years with annual or biennial FOBT has been shown in several randomized trials to reduce CRC incidence and mortality (24, 25).

A large, long-duration trial in the United States randomly assigned 46,551 volunteers aged 50–80 years to annual FOBT with a guaiac-based test (no rehydration in the first 3 years of the trial and rehydration afterward), biennial FOBT, or usual care. Cumulative 18-year CRC mortality was 33% lower in the annual group than in the control group, whereas the biennial group had a 21% lower mortality rate than the control group (26, 27).

This study was recently updated with longer follow-up. Thirty years from study initiation, CRC mortality was reduced by 32% (28).

Overall, a meta-analysis of FOBT trials showed that participants assigned to screening had a 16% reduction in CRC death (relative risk, 0.84 [95% CI, 0.77 to 0.93]). In an analysis of only participants who adhered to screening, the risk reduction was 23% (29).

FIT

FIT measures intact human globin protein (as opposed to heme) in the stool and is replacing FOBT in many screening programs because it offers several advantages. It requires only 1 stool specimen (as opposed to 3 for FOBT) and requires less stool handling (30). Dietary restrictions are not necessary because animal heme from

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>Author (Reference)</th>
<th>Location</th>
<th>Patients, n (thousands)</th>
<th>Interval</th>
<th>Follow-up, y</th>
<th>CRC Mortality Reduction (95% CI), %</th>
<th>CRC Incidence Reduction (95% CI), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal occult blood test</td>
<td>Mandel (16)</td>
<td>Minnesota</td>
<td>47</td>
<td>Annual/biennial</td>
<td>18</td>
<td>Annual: 33 (17–49); biennial: 20 (3–38)</td>
<td>Annual: 20 (10–30); biennial: 17 (6–27)</td>
</tr>
<tr>
<td></td>
<td>Kronborg (66)</td>
<td>Denmark</td>
<td>62</td>
<td>Biennial</td>
<td>10</td>
<td>18 (1–32)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Hardcastle (25)</td>
<td>United Kingdom</td>
<td>153</td>
<td>Biennial</td>
<td>8</td>
<td>15 (2–26)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Lindholm (67)</td>
<td>Sweden</td>
<td>68</td>
<td>Biennial</td>
<td>9</td>
<td>16 (1–29)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Faivre (68)</td>
<td>France</td>
<td>91</td>
<td>Biennial</td>
<td>11</td>
<td>16 (1–29)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>Flexiscope (17)</td>
<td>United Kingdom</td>
<td>170</td>
<td>One-time FSG</td>
<td>11</td>
<td>31 (18–41)</td>
<td>23 (16–30)</td>
</tr>
<tr>
<td></td>
<td>SCORE (38)</td>
<td>Italy</td>
<td>34</td>
<td>One-time FSG</td>
<td>11</td>
<td>22 (8–54)*</td>
<td>18 (4–31)</td>
</tr>
<tr>
<td></td>
<td>PLCO (6)</td>
<td>United States</td>
<td>155</td>
<td>Two FSGs, 3–5 y</td>
<td>12</td>
<td>26 (13–37)</td>
<td>21 (15–28)</td>
</tr>
</tbody>
</table>

CRC = colorectal cancer; FSG = flexible sigmoidoscopy; NS = not significant.

*Mortality reduction was not statistically significant.
meat will not trigger a false-positive result. FIT is also more specific for lower gastrointestinal bleeding because human globin is degraded as it passes through the small intestine. A meta-analysis showed that participation in FIT screening exceeds that of FOBT (31).

The biggest potential advantage of FIT is evidence suggesting that it detects more advanced adenomas than FOBT (32–34) without a significant loss of specificity or increased false-positive results. Use of FIT also offers the option of varying the cutoff that determines the result. A lower cutoff for positive results increases sensitivity for neoplasm detection but also identifies more patients needing diagnostic follow-up (35). The cutoff can be based on public health resources. For example, in developing countries, the limited availability of diagnostic colonoscopy may encourage a higher cutoff for positive results.

In a French study, 10,673 patients received FOBT and FIT. A positive result on either test prompt subsequent colonoscopy. When the FIT threshold for positivity was set at 50 ng/ml, the test detected twice as many cases of advanced neoplasia as FOBT with no loss of specificity (32).

When FOBT or FIT is used to screen for CRC, the test must be done correctly, with specimens obtained at home by the patient. A single test done during a digital rectal examination in the office is not adequate for screening (36). FOBT or FIT as a screening method requires organized, programmatic use over time. Testing should be repeated annually, and 1 or more positive slides is a positive result that warrants follow-up colonoscopy. However, inadequate follow-up is frequently reported in primary care settings (37).

Flexible Sigmoidoscopy

Three large prospective trials from the United Kingdom (17), Italy (38), and the United States (6) provide compelling evidence that flexible sigmoidoscopy reduces CRC incidence by 18%–23% and mortality by 22%–31% compared with usual care. All of the trials showed a greater benefit in the distal colon (splenic flexure to rectum) than in the proximal colon (cecum to splenic flexure). Distal colon cancer mortality was reduced by approximately 50% in the U.K. and U.S. trials. The U.S. trial found a 14% reduction in proximal colon cancer incidence, but none of the studies demonstrated a reduction in proximal colon cancer mortality. Of note, the statistically significant benefit in the proximal colon that was uniquely observed in the U.S. study was associated with a higher rate of colonoscopy use than in the European studies, suggesting that primary colonoscopy, rather than colonoscopy only after an abnormal flexible sigmoidoscopy result, may be a more powerful approach to combating proximal colon cancer.

A recent meta-analysis showed that sigmoidoscopy screening was associated with an 18% reduction in incidence (relative risk, 0.82 [CI, 0.73–0.91]; P < 0.001; number needed to screen to prevent 1 CRC case, 361) and a 28% reduction in CRC mortality (relative risk, 0.72 [CI, 0.65–0.80]; P < 0.001; number needed to screen to prevent 1 CRC death, 850). Among patients who adhered to sigmoidoscopy screening, CRC incidence was reduced by 32% (P < 0.001) and CRC-related mortality was reduced by 50% (P < 0.001) (39).

Colonoscopy

Colonoscopy permits visual examination of the entire colon. Several studies have shown increased detection of adenomas and carcinomas with colonoscopy compared with FOBT, FIT, or flexible sigmoidoscopy (40, 41).

There are no data from randomized, controlled trials evaluating the efficacy of screening colonoscopy in reducing morbidity or mortality from CRC. Although studies are
under way in the Nordic countries, Spain, and the United States, results are not expected for 10 years. Case-control studies show colonoscopy to be effective in both the distal and proximal colon.

A nested case-control study enrolled 1039 average-risk persons from 4 large U.S. health plans. Screening colonoscopy rates preceding the diagnosis of stage Iib or greater CRC in 471 such patients were compared with screening rates in 509 matched control participants without CRC. The adjusted odds ratio associated with preceding colonoscopy was 0.29 (CI, 0.15–0.58) for any CRC, 0.36 (CI, 0.16–0.80) for right-sided colon cancer, and 0.26 (CI, 0.06–1.11) for left-sided cancer (42).

A population-based case-control study in Germany assessed the association between previous colonoscopy and risk for CRC in 1688 patients with CRC and 1932 control participants. Overall, colonoscopy in the preceding 10 years was associated with a 77% lower risk for CRC. This effect was most pronounced against left-sided cancer (84% reduction [CI, 80%–88%]) but was also seen for right-sided cancer (56% reduction [CI, 45%–65%]) (43).

Data from the Nurses’ Health Study and the Health Professionals Follow-up Study show a reduction in CRC incidence after polypectomy (hazard ratio [HR], 0.57), negative sigmoidoscopy result (HR, 0.60), and negative colonoscopy result (HR, 0.44) compared with patients who did not have endoscopy (10). Screening sigmoidoscopy (HR, 0.59) and screening colonoscopy (HR, 0.32) were associated with a reduction in CRC mortality. Only colonoscopy was associated with decreased colon cancer mortality in the proximal colon (HR, 0.47). The investigators estimated that 40% of incident CRC could have been avoided with colonoscopy, with a greater effect in the distal colon (61% reduction) than in the proximal colon (22% reduction).

Although some studies suggest a reduction of as much as 90% in CRC incidence with colonoscopy (44), overall effectiveness is probably lower. Effectiveness is greater in the distal than in the proximal colon because polyps in the proximal colon have a greater tendency to be flat and are thus more difficult to detect (45), preparation in the proximal colon is often not as good, and the biology of polyps in the proximal colon may be distinct with a more aggressive behavior (46).

As with any procedure, colonoscopy is operator-dependent and quality standards must be ensured. The metrics that most accurately capture a “quality” endoscopy are under study, but a cecal intubation rate greater than 95% and adequate ADRs are essential (47).

Colonoscopy is a “one-stop shop” with combined diagnosis and treatment, whereas less invasive tests, such as FIT or sigmoidoscopy, require subsequent referral for treatment with colonoscopy. Disadvantages of colonoscopy include colonic preparation, patient sedation, lost time from work, need for a companion for transportation home, cost, and the invasive nature of the procedure. Although the risks of colonoscopy and polypectomy are small, the procedure may result in bleeding, perforation, or other complications (48).

A prospective study of 502 asymptomatic patients who had colonoscopy for screening, surveillance, or follow-up of another positive screening test result found that although 34% of patients reported mild complications (bloating and pain), only 6 (1.1%) had unexpected hospitalizations or emergency department visits within 30 days after colonoscopy. Ninety-four percent of patients lost 2 or fewer days of normal activity due to the process of preparation, colonoscopy, and recovery (49).

CT Colonography

CT colonography is another potential screening tool for CRC. A recent meta-analysis included more than 4000 average-risk participants. Compared with a gold standard of optical

References

In recent Dutch study, average-risk persons were randomly invited to have either CT colonography or optical colonoscopy. Initial acceptance was 34% for CT colonography and 22% for optical colonoscopy \((P < 0.001)\). However, the diagnostic yield for advanced neoplasia (larger polyps and cancer) was 8.7 per 100 patients for optical colonoscopy versus 6.1 per 100 patients for CT colonography \((P = 0.02)\). As a result, similar numbers of advanced neoplasia were detected per patient invited, suggesting that either test could be used for population screening.

CT colonography is a noninvasive test that can examine the entire colon and has a minimal complication rate. However, colonic preparation is required. Methods to perform the test without bowel preparation are under study but are thus far associated with an unacceptable decrement in performance \((52)\).

Studies of patient preference between virtual and optical colonoscopy have shown mixed results, especially when patients are queried both before and after each test \((53)\).

Colonoscopy is required for the removal of polyps detected by CT colonography. The overall cost and, hence, cost-effectiveness of CT colonography will be enhanced if CT colonography increases patient participation but is also significantly affected by test sensitivity and specificity and frequency of referral for optical colonoscopy.

The growing importance of morphologically “flat” polyps in the proximal colon may further compromise the utility of CT colonography, which is more effective in visualizing lesions that protrude into the lumen. Studies that use a gold standard comparison with endoscopists who detect flat lesions at high frequency will be needed to definitively determine the effectiveness of CT colonography. Prospective studies that track patient outcome over time are needed to evaluate the longer-term efficacy of this technique.

What are the emerging CRC screening techniques?

Because all current CRC screening methods have drawbacks, the search for new and improved blood-, stool-, or image-based methods continues \((56)\). One emerging technology poised for wider implementation may be fecal DNA testing. Colonic mucosal cells are continually shed into the fecal stream, as are cells exfoliated by colonic neoplasms. Cells possessing specific genetic or epigenetic changes can be selectively identified, allowing for the noninvasive detection of CRC and perhaps even large adenomas.
Most analyses of commercially available fecal DNA testing strategies have found testing to be cost-effective compared with no testing but not compared with other standard CRC screening methods (57). However, these analyses were of less sophisticated fecal DNA tests. In a study of 1003 persons, fecal DNA testing had a sensitivity of 97% and a specificity of 90% for CRC stages I to III. In addition, sensitivity for advanced adenomas measuring at least 1 cm was 57% (58). In a recent observational trial that used colonoscopy as a reference standard, 10 000 participants received fecal DNA testing combined with FIT. Sixty-four cancer cases and 752 adenomas were detected. The combination of fecal DNA testing and FIT had a sensitivity of 92% and a specificity of 90% for CRC stages I to III. In addition, the effectiveness of an automated stool DNA assay for detection of colorectal neoplasia in asymptomatic adults: a prospective evaluation. Ann Intern Med. 2012;156:692-702. [PMID: 22586008]

Although colonoscopy has become a favorite screening method in the United States, one should not assume that it is necessarily the best polyp, a benefit not offered by conventional stool-based screening methods (60). For now, cost remains the primary obstacle inhibiting broader adoption of fecal DNA testing.

How should clinicians and patients select from among different screening methods?

Because there is no clear evidence that one screening method outperforms another and because each test has advantages and disadvantages (Table 3), clinicians and patients can currently choose from stool testing, such as FOBT or FIT; sigmoidoscopy with or without FOBT or FIT every 5 years; or colonoscopy every 10 years.

### Table 3. Colorectal Cancer Screening Options

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOBT</td>
<td>Annual</td>
<td>Inexpensive/noninvasive; RCTs show effectiveness in decreasing colorectal cancer mortality and incidence</td>
<td>Positive results require follow-up colonoscopy; many false-positive results; repeated testing needed to achieve adequate sensitivity</td>
</tr>
<tr>
<td>Fecal immunochemical testing</td>
<td>Annual</td>
<td>More sensitive for detection of advanced adenoma than FOBT; no dietary restrictions; only 1 stool sample required; fewer false-positive results than with FOBT</td>
<td>Positive results require follow-up colonoscopy; repeated testing needed to improve sensitivity</td>
</tr>
<tr>
<td>Flexible sigmoidoscopy (with or without annual FOBT)</td>
<td>Every 5 y</td>
<td>No sedation needed; less-intensive preparation; less expensive; RCTs show reduction in incidence and mortality</td>
<td>Requires colonoscopy for removal of larger polyps; can be limited by patient discomfort (no sedation); not widely available</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Every 10 y</td>
<td>Allows visualization of entire colon and rectum; allows for biopsy and polypectomy; screening is a one-step process; potentially most effective means of reducing CRC mortality and incidence</td>
<td>Requires intensive colonic preparation and anesthesia; loss of workday and requires accompanying home; serious complications include perforation and bleeding; expensive; many patients have negative results; efficacy depends on quality</td>
</tr>
<tr>
<td>CT colonography</td>
<td>Every 5 y</td>
<td>Allows visualization of entire colon and rectum; no sedation required; detection of larger adenomas equivalent to that of colonoscopy</td>
<td>Requires colonoscopy for polyp removal; expensive; requires bowel preparation; performance in detection of flat polyps uncertain</td>
</tr>
</tbody>
</table>

CT = computed tomography; FOBT = fecal occult blood test; RCT = randomized, controlled trial.

test, especially because patient compliance may be better with the simpler, less demanding fecal tests. In a population-based Spanish trial comparing FIT with colonoscopy (41), the participation rate after the first round of testing was higher for FIT than for colonoscopy (36% vs. 24%).

To study the effect of choice on CRC screening uptake, 997 average-risk participants were randomly assigned to receive a recommendation for screening with FOBT, colonoscopy, or their choice of the two. The primary outcome was screening uptake within 12 months. Participants who were recommended to receive colonoscopy screened at a significantly lower rate (38%) than those who were recommended for FOBT (67%) (P<0.001) or given a choice of screening method (69%) (P<0.001) (61).

In a test of outreach to encourage screening in an underserved U.S. population, screening uptake was greater for FIT than for colonoscopy (62). Physicians and patients should weigh costs, convenience, availability, and patient preference when choosing a screening option.

Is CRC screening cost-effective? Cost-effectiveness analyses have found CRC screening to be effective at costs similar to those of other recommended cancer screening procedures. A 2002 systematic review of 7 cost-effectiveness analyses found that commonly used screening methods cost between $10 000 and $25 000 per year of life saved compared with no CRC screening. Which strategy had the best cost-effectiveness ratio was unclear (63). As the cost of treating established CRC has accelerated with the development of expensive targeted therapies, such as vascular endothelial growth factor inhibitors and epidermal growth factor receptor inhibitors, the ability of screening to reduce cancer incidence, leading to fewer patients requiring treatment, ensures the cost-effectiveness of screening.

What are the risks for patients? Clinicians and patients should understand that most adenomas detected and removed via screening are unlikely to progress to CRC. The screening process operates on “overkill.” Many patients have negative testing results and many patients have polyps that are discovered and treated, thus exposing them to potential risks that do not contribute to benefit. Because we do not know and cannot tell which adenomas will progress, we remove all of them. The data show that this approach substantially reduces CRC mortality and incidence.

At what age should patients begin screening? Average-risk persons should initiate screening at age 50 years.

How frequently should patients repeat screening? Screening with FOBT or FIT should be repeated annually, flexible sigmoidoscopy should be repeated every 5 years, and colonoscopy should be repeated every 10 years when no adenomas are found. The timing for surveillance examinations, when adenomas are detected, is presented in Table 1. The histologic type, number, and size of the polyps guide frequency of follow-up.

At what age should average-risk patients stop screening? The age to stop CRC screening depends on life expectancy and the anticipated benefit of screening. Clinicians and patients should temper enthusiasm for screening elderly adults. At age 75 years, the average woman can expect to live an additional 12.1 years and the average man will live an additional 10.2 years. At age 85 years, life expectancies are 6.7 and 5.6 years, respectively. Limited life expectancy reduces the potential benefit of screening. The harms of screening may increase for elderly patients. A recent overview of several CRC screening...
Guidelines concluded that it was appropriate to stop CRC screening at age 75 years or in persons with life expectancies less than 10 years (9).

A cross-sectional study that evaluated 1244 patients who had screening colonoscopy found neoplasia in 13.8% of those aged 50–54 years, 26.5% of those aged 25–79 years, and 28.6% of those aged 80 years or older. However, this study estimated that the mean extension of life expectancy among patients older than 80 years was only 15% that of patients aged 50–54 years (64).

Screening... Colorectal cancer screening, accomplished through a number of accepted methods, is a key component of preventive health care for the general population. Unless there is a compelling contraindication, this cost-effective intervention should begin at 50 years of age and continue at regular intervals well into later adulthood.

What measures do U.S. stakeholders use to evaluate the quality of CRC screening? The Centers for Medicare & Medicaid Services has issued specifications for measures that make up the Physician Quality Reporting Initiative. Of these, 2 relate to CRC screening: the percentage of adults aged 50–75 years who have had appropriate screening for CRC, which measures utilization of an effective screening test, and the percentage of patients who had screening colonoscopy without biopsy or polyp removal who had a recommended follow-up colonoscopy at least 10 years later, which measures overutilization of testing. More information about the measures, inclusion and exclusion criteria, and implementation suggestions can be found at www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/index.html.

What do professional organizations recommend? All national organizations endorse CRC screening. The U.S. Preventive Services Task Force has endorsed CRC screening with a grade A recommendation, the highest level of approval, which exceeds the recommendations for mammography for breast cancer screening and prostate-specific antigen testing for prostate cancer screening (65).

What information should clinicians include in discussions with patients? When discussing CRC screening with patients, clinicians should inform them that CRC is common and that screening reduces incidence through the removal of polyps and mortality by identifying cancer at earlier, more easily treatable stages. Patients should be informed about the advantages and disadvantages of the recommended screening methods before selecting one. If colonoscopy is chosen, the clinician should inform the patient about the risks of the procedure and instruct them to limit fiber intake for several days before the test. In general, aspirin and other nonsteroidal anti-inflammatory drugs do not need to be discontinued before the procedure. Insulin and anticoagulants will require individualized adjustment. Patients should avoid anything by mouth for a few hours before the procedure to reduce the risk for aspiration. They should know that they will receive sedation and will need a ride home after the procedure but can expect to return to their usual activities the next day.

In the Clinic

Screening for Colorectal Cancer

ACP Smart Medicine Module
http://smartmedicine.acponline.org/content.aspx?gbosId=486
http://smartmedicine.acponline.org/content.aspx?gbosId=131
Access the American College of Physicians Smart Medicine modules on colorectal cancer (CRC) and CRC screening.

Patient Information
www.nlm.nih.gov/medlineplus/colorectal cancer.html
Information on colon cancer screening and on CRC from the National Institutes of Health MedlinePlus.
www.cancer.gov/cancertopics/pdq/screening/colorectal/patient
www.cancer.gov/cancertopics/wynk/colon-and-rectal
Information for patients on CRC screening, including the booklet “What You Need To Know About Cancer of the Colon and Rectum” from the National Cancer Institute.
www.cancer.gov/cancertopics/factsheet/detection/colorectal-screening
Description of tests to detect CRC and polyps from the National Cancer Institute.

Clinical Guidelines
http://annals.org/article.aspx?articleid=1090701
Guidance statement on screening for CRC from the American College of Physicians in 2012.
www.uspreventiveservicestaskforce.org/uspstf/uspscolo.htm
Guideline on screening and surveillance for the early detection of CRC and adenomatous polyps from the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology in 2008.
Guideline on CRC screening and surveillance from the American Society for Gastrointestinal Endoscopy in 2006.

Diagnostic Tests and Criteria
www.uspreventiveservicestaskforce.org/uspstf08/colocancer/colcanes2.pdf
Decision analysis on evaluating test strategies for CRC screening from the U.S. Preventive Services Task Force in 2009.

Quality-of-Care Guidelines
Report on enhancing the use and quality of CRC screening from the Agency for Healthcare Research and Quality in 2010.
www.uspafi.org/afp/2008/0401/p995.html
Consensus guidelines on colonoscopy surveillance after polypectomy and CRC resection from the U.S. Multi-Society Task Force on Colorectal Cancer and the American Cancer Society in 2008.
WHAT YOU SHOULD KNOW ABOUT COLORECTAL CANCER SCREENING

Who should be screened for colorectal cancer?
- All adults should undergo screening beginning at age 50 years.
- Persons with family members who have colorectal cancer or other risk factors may start screening before age 50 years.
- Remember that when your doctor suggests a screening test, it does not mean he or she thinks you have cancer.

How does screening prevent cancer?
- Screening can find abnormal growths (polyps) so they can be removed before they turn into cancer.
- If cancer has developed, screening can detect it early, when it is highly curable.
- If colorectal cancer is found early, surgery can cure it, but cancer found later may not be curable.
- Colorectal cancer often does not cause symptoms until it has become advanced and spread.

What tests are used for screening?
- High-sensitivity fecal occult blood test examines stool under a microscope to see if it contains any blood, which can be a sign of polyps or cancer.
- Flexible sigmoidoscopy uses a thin, flexible, lighted tube to view inside the rectum and sigmoid colon (the lower part of the colon) for polyps or signs of cancer.
- Colonoscopy is similar to flexible sigmoidoscopy, except the doctor uses a longer, thin, flexible, lighted tube to view inside the entire colon.
- Most polyps and some cancer found during sigmoidoscopy or colonoscopy can be removed during the test.

If screening works, why do some people avoid it?
- About 1 in 3 adults aged 50 to 75 years have not been tested for colorectal cancer as recommended.
- Some people do not know they should be tested or are unaware of the benefits of regular screening.
- Some are worried that the test will be uncomfortable or embarrassing.
- Some are uncertain whether their insurance will cover the procedure.
- If you are worried, you can talk with your doctor about these and any other concerns.

For More Information
- www.healthfinder.gov/HealthTopics/Category/doctor-visits/screening-tests/get-tested-for-colorectal-cancer#take-action_1
- www.cdc.gov/cancer/colorectal/basic_info/screening
- www.cdc.gov/cancer/colorectal/basic_info/screening/questions.htm
- Facts on colorectal cancer screening and questions to ask your doctor from the Centers for Disease Control and Prevention.
- Guide to Colon Cancer Prevention from Consumer Reports.
- www.cancer.org/cancer/colonandrectumcancer/moreinformation/colonandrectumcancerearlydetection/index
- Information on tests to detect colorectal cancer and polyps from the American Cancer Society.
1. A 36-year-old woman is evaluated during a routine examination. She is generally healthy and has no gastrointestinal problems. She would like to discuss colorectal cancer screening recommendations. Her family history is as follows: father, colorectal cancer, age 45 years; mother, no known cancer or precancerous lesions; paternal aunt, endometrial cancer, age 37 years; paternal uncle, large (2.5-cm) colorectal adenoma (ascending colon), age 42 years; brother, colorectal cancer, age 48 years; physical examination, including cardiopulmonary examination, is normal.

Which of the following is the most appropriate management strategy?

A. Colonoscopy now
B. Colonoscopy now and referral to genetics counsellor
C. Colonoscopy at age 50 years
D. Fecal DNA testing now
E. CT colonography now

In addition to colonoscopy, which of the following should be recommended?

A. Aspirin
B. Other NSAIDs
C. Estrogen replacement
D. No specific medications

2. A 55-year-old woman is evaluated during a routine examination. Although her mother was diagnosed with colorectal cancer at age 74 years, the patient herself has not been previously screened. She inquires about initiating colorectal cancer risk reduction strategies, including nutritional and pharmacologic interventions. She is postmenopausal, is otherwise healthy, and takes no medications.

Physical examination is normal.

Which of the following should be recommended?

A. Aspirin
B. Other NSAIDs
C. Estrogen replacement
D. No specific medications
E. CT colonography now

3. A 74-year-old woman has been deferring colon cancer screening because she is afraid to undergo colonoscopy. She learned of a new technique called virtual colonoscopy that she thinks may be more tolerable and asks you about the relative merits of this procedure.

Which of the following statements is true regarding virtual colonoscopy?

A. It is a noninvasive procedure that images the colon using ultrasound
B. It does not require any bowel preparation
C. It detects colorectal cancer and large adenomas quite well but may miss small polyps
D. It visualizes flat polyps and polyps that protrude into the bowel lumen equally well
E. The study is limited to the colon without investigation of any extracolonic structures

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