We can estimate how many of the 56,300 people who die annually of colorectal cancer whose survival could have been lengthened if their disease had been prevented or detected early: more than 50 percent. Risk of colorectal cancer may be reduced by regular physical activity and appropriate diet, and it can be effectively treated when it is detected early. Only lung cancer, which is expected to take the lives of 156,900 American men and women in 2000, outpaces colorectal cancer in the potential impact prevention strategies could have. Increased screening and adenoma removal, which prevents progression to invasive cancer, have been credited with the 2.1 percent annual decline in incidence between 1992 and 1996. Early detection translates into a 91.4 percent 5-year relative survival rate for about 37 percent of all cases diagnosed. Another 37 percent are diagnosed when disease is regional, and the survival rate for these cases falls to 66.1 percent. For those remaining cases diagnosed when cancer has metastasized to a distant site, the survival rate is only 8.5 percent.

In the United States, men have higher rates of colorectal cancer incidence and mortality than do women, but mortality rate graph lines tended to intertwine from 1930 to about 1960, when the mortality rate began to decline steadily and in women fell distinctly lower than in men. Cumulative lifetime risk for colorectal cancer is 6 percent. In the United States, a gap exists between overall survival rates by race: the rate for whites (63 percent) surpasses that of African Americans (52.5 percent), and researchers blame more than half of the difference on African Americans’ more advanced stage of disease at diagnosis.

Globally, incidence of cancer of the colon and rectum is highest in Australia/New Zealand, North America, Western Europe, Northern Europe, and Japan and lowest in Northern, Western, and Middle Africa along with South Central Asia. Worldwide it occurs slightly more frequently in men than in women.

**RISK FACTORS**

To determine a patient’s level of colorectal cancer risk and take an appropriate approach to surveillance, physicians should profile personal and familial health history to identify the patient’s level of risk. In asymptomatic persons who have no risk factors other than increased age, routine screening begins at age 50. For those whose risk of having colorectal cancer is higher than average, screening should begin at age 40 or 10 years before the age at which the youngest case in the family was diagnosed, whichever is earlier.
of colon cancer is also higher in those whose family medical history is characterized by familial adenomatous polyposis, including familial polyposis and Gardner’s syndrome, or hereditary non-polyposis colorectal cancer (HNPPC), including family cancer syndrome and site-specific inherited colorectal cancer.

Also increasing the risk of colorectal cancer is inflammatory bowel disease (chronic ulcerative colitis or Crohn’s disease), intestinal adenomatous polyps (especially if of the villous type or larger than 1 cm), a history of colon cancer, or a history of ovarian or uterine cancer. A history of breast cancer has been found in a retrospective review of 227,165 cases to be not associated with increased risk and was in fact associated with colorectal cancer risk reduction. Obesity has been shown to put men at increased risk. Also raising risk is Turcot’s syndrome or juvenile polyposis. In addition, dietary animal fats have been linked to an increased risk of colorectal cancer.

Reductions in risk have been associated with fruit and vegetable intake, regular physical activity, estrogen replacement therapy in postmenopausal women, and taking acetylsalicylic acid or other nonsteroidal anti-inflammatory drugs including sulindac and proxicam.

SCREENING

General agreement on testing with the fecal occult blood test (FOBT), sigmoidoscopy, a combination of FOBT and sigmoidoscopy, double-contrast barium enema with x-ray studies, or colonoscopy has been reached (Table 4–1) by government, professional, and patient-centered organizations, paving the way for unified educational efforts to improve screening rates. Also encouraging wider compliance is the U.S. government’s Health Care Financing Administration’s expansion in January 1998 of Medicare coverage to include routine colorectal cancer screening. The coverage permits annual fecal occult blood testing, with sigmoidoscopy every 4 years for those with average risk. For those at high risk, coverage includes colonoscopy every 2 years. Provider requests for substitution of double-contrast barium enema imaging evaluations for colonoscopy will be honored.

Fecal Occult Blood Test

The FOBT performed annually has demonstrated benefit in reducing mortality from colorectal cancer (for a review, see Towler and colleagues). Testing annually is recommended because randomized trials have shown that testing every 2 years is less effective than testing annually because cost and inconvenience are little affected by frequency and because testing annually may mean detection of disease that, though undetected on previous tests, has not reached a less curable stage. A review of FOBT trials found that reductions in mortality in the annually screened groups ranged from 37 to 14 percent in those studies reporting mortality statistics. One of these trials found that testing annually reduced mortality in the screened group by 33 percent, whereas testing biennially reduced mortality by 5 percent, which was identified as a nonsignificant difference from not screening at all.

The major shortcoming of screening by this method is its high false-positive rate, which means that many disease-free persons will undergo unnecessary colonoscopy with its attendant risks and stresses. The likelihood ratio, a test’s sensitivity divided by its false-positive rate, is a calculation meant to further refine risk definition and has been identified as substantially better than any other predictors of colorectal cancer risk, including age and family history. It compares the risk of someone who has had the test and had positive results to that of another who has had the test and had negative results. In this ratio, the false-positive rate equals the difference between 100 percent and the specificity rate (or true negative results). For example, sensitivity of FOBT screening divided by its false-positive rate (0.60/1-0.92), using Winawer and colleagues’ best estimates for sensitivity and specificity, results in a likelihood of having cancer of 7.5 times that of another whose test result was negative. Calculations of likelihood ratios from studies of FOBT screening indicate a likelihood ratio of 12 for hydrated testing in the Minnesota trial and a likelihood ratio of 50 in the Danish trial, according to Young, Macrae, and St John. The failure of FOBT screening to produce more consistent and more dramatic mortality reductions needs to prompt development of better tests with
lower false-positive rates and improved adenoma and cancer detection capability. But even after such tests come to market, physicians will have to continue helping patients undergoing screening gain perspective on their risks as indicated by the test results and negotiate the emotional and sometimes physical consequences of testing that yields false-positive and false-negative findings.²⁰

**Flexible Sigmoidoscopy**

Recommendations to use sigmoidoscopy to screen for colorectal cancer are based on case-control research and on work showing that colorectal cancer risk is reduced when adenomatous polyps are removed.²²,²³ Rigid as well as flexible sigmoidoscopes have been used in research used to support screening with sigmoidoscopy.¹⁴ Flexible sigmoidoscopes, 60 cm in length, have largely replaced screening with the rigid 25-cm scope in most countries because of their increased scope, their greater clarity, and their reputation for better patient tolerance. Of course, the percentage of polyps and cancers detectable by sigmoidoscopy is proportional to the length of the scope. Winawer and colleagues report that when fully inserted, the 60-cm scope can detect 40 to 60 percent of adenomatous polyps and colorectal cancers; the 35-cm scope, 30 to 40 percent; and the 25-cm scope, 20 to 30 percent.¹⁴

The chief virtues of flexible sigmoidoscopy are its sensitivity and specificity: sensitivity is 96.7 percent for cancer and large polyps and 73.3 percent for small polyps; specificity is 94 percent for cancer and large polyps and 92 percent for small polyps.¹⁴ Also important is its ability to produce direct visualization of the colon and to allow biopsy of suspicious lesions. For these benefits, however, the patient must submit to the associated risk of bowel perforation (2/10,000). The complication rate rises slightly when biopsy or polypectomy is incorporated in the

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Table 4-1. COLORECTAL CANCER SCREENING RECOMMENDATIONS FOR ASYMPTOMATIC MEN AND WOMEN 50 YEARS OF AGE OR OLDER

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Fecal occult blood test (FOBT)</td>
<td>Annually plus flexible sigmoidoscopy every 5 years</td>
<td>Annually</td>
<td>Annually</td>
<td>Annually plus flexible sigmoidoscopy every 5 years</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>Flexible sigmoidoscopy every 5 years plus FOBT annually</td>
<td>Flexible sigmoidoscopy every 5 years</td>
<td>Flexible or rigid sigmoidoscopy recommended but insufficient evidence to recommend periodicity</td>
<td>Flexible sigmoidoscopy every 5 years plus FOBT annually</td>
</tr>
<tr>
<td>Combination of FOBT and sigmoidoscopy</td>
<td>FOBT annually plus flexible sigmoidoscopy every 5 years</td>
<td>FOBT annually plus flexible sigmoidoscopy every 5 years</td>
<td>Both “effective” but “insufficient evidence to determine which of these methods is preferable or whether the combination... produces greater benefits than either test alone”</td>
<td>FOBT annually plus flexible sigmoidoscopy every 5 years</td>
</tr>
<tr>
<td>Double-contrast barium enema with x-ray studies</td>
<td>Every 5–10 years</td>
<td>Every 5–10 years</td>
<td>“Insufficient evidence” to recommend for or against routine screening</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Every 10 years</td>
<td>Every 10 years</td>
<td>“Insufficient evidence” to recommend for or against routine screening</td>
<td>Every 10 years</td>
</tr>
</tbody>
</table>

Data from the American Cancer Society,² Winawer et al.,¹⁴ U.S. Preventive Services Task Force,¹⁵ and the National Comprehensive Cancer Network.¹⁶
procedure. Patients may also feel inconvenienced or discomforted, but the introduction of flexible sigmoidoscopy was expected to increase compliance with screening practice by reducing discomfort associated with rigid sigmoidoscopy.

Screening intervals must be considered in relation to efficacy and safety and also in relation to such issues as cost, patient acceptability, and availability. For screening sigmoidoscopy, some researchers have found effectiveness to persist as long as 9 to 10 years, though others have reported a shorter protective effect. A panel of experts originally convened by the U.S. government’s Agency of Health Care Policy and Research and subsequently sponsored by a consortium of professional, patient, and other nonprofit groups estimated that transformation from polyp to invasive cancer took 10 years. Using a model, the U.S. Preventive Services Task Force (1996) found that the effectiveness of screening sigmoidoscopy was ensured with screening intervals of 10 years, but it based its model on a transformation period of 10 to 14 years.

Despite the advantages offered by sigmoidoscopy, its effectiveness is limited to that part of the colon within reach of its scope. Two other methods facilitate detection in the proximal colon.

**Double-Contrast Barium Enema**

It was not carefully conducted trials of double-contrast barium enema (DCBE) imaging but general evidence indicating a reduction in colorectal cancer mortality when polyps and cancers were detected early that prompted experts to consider DCBE imaging for colorectal cancer screening. Double-contrast barium enema outperforms the FOBT and extends beyond the reach of sigmoidoscopy, matching the scope of colonoscopy by imaging the entire colon.

Winawer and colleagues reported that DCBE’s sensitivity and specificity were better than those of the FOBT and flexible sigmoidoscopy, but recently reported findings comparing barium enema with colonoscopy indicate that barium enema detects about half or fewer of the adenomas detected by colonoscopy, the test that has a range it most closely matches. Press deadlines permit only a brief mention (see discussion).

**Colonoscopy**

Recommendations to use colonoscopy for colorectal screening are based on its supporting role in FOBT trials in which screening produced a reduction in colorectal cancer mortality and on its similarity to sigmoidoscopy, which has proved to be effective. Advantages include its ability to permit visualization of the entire colon and the efficiency afforded by its being both a diagnostic and therapeutic tool. Sensitivity is high in detecting cancers (96.7 percent) and large polyps (85 percent), but lower in detecting small polyps (78.5 percent). Specificity for all measures is 98 percent.

Like the recommendation for performing the test, the recommended interval for the test has been set in part based on experience with sigmoidoscopy. It is also based on the success rate for this procedure and the 10-year estimate for polyp transformation in those with average risk.

**RECOMMENDED COLORECTAL CANCER SCREENING GUIDELINES**

It is widely agreed that screening for colorectal cancer in asymptomatic adults should begin at age 50. An age at which to stop screening has not been set, but certainly the onset of other significant disease or diseases is an example of when screening would appropriately end. Also of concern would be the patient’s ability or willingness to tolerate the screening procedure and any procedure that logically would be recommended subsequently in follow-up of positive findings. Patient and physician must examine the patient’s personal and familial health history to identify the patient’s level of risk and therefore the appropriate surveillance strategy (Table 4–2).

**Average Risk**

Those considered to be at average risk are those who are symptom free and have no personal or family medical history characteristics that would categorize their risk as moderate or high. Anyone with symptoms should undergo a diagnostic work-up. Screening recommendations for those with average risk are
outlined in Table 4–1. Methods should be selected based on consideration of community screening resources and quality and the patient’s medical status. When one test fails to provide sufficient information, another test should serve as a supplement. Although digital rectal examinations are no longer a part of the annual recommendations for screening in asymptomatic adults, they are assumed to be a routine element of sigmoidoscopy, DCBE evaluations, and colonoscopy.

### Moderate Risk

Risk for colorectal cancer is higher in those who are symptom free but have a history of adenomatous polyps or of cancer, including ovarian, uterine, or colorectal cancer. Screening in these individuals and those at high risk becomes more aggressive: it may be initiated earlier, be performed more frequently, or become more intensive by the use of more sensitive methods.

Table 4–3 outlines the initial and subsequent tests recommended for preventing or detecting colorectal cancers early in those with factors that put them at moderate or high risk.\(^{24}\)

### High Risk

Higher risk requires higher level testing and associated intervention, making those methods capable of adenoma removal—colonoscopy and flexible sigmoidoscopy—the preferred evaluations for patients with a personal history of inflammatory bowel disease or a family history of familial adenomatous polyposis or HNPCC. Patients with inflammatory bowel disease can expect colorectal cancer that does develop to be equal to their bowel disease in duration and extent. Screening begins with colonoscopy and biopsy of random sites in the colon. Despite the absence of direct evidence of the effectiveness of this approach, the rationale informing it is that early detection of dysplasia would prompt management likely to lower the risk of invasive carcinoma.

Sigmoidoscopy is an option in screening those with familial adenomatous polyposis, not because the condition is limited but because screening only attempts to obtain an index of the extent of disease, inasmuch as polyps multiply uniformly throughout the colon. The overwhelming number of polyps that develop makes case management by polypectomy an impossibility. Equally stunning is the almost 100 percent likelihood in these cases that colorectal cancer will develop. In these cases, the combination of polyp volume and the ineffectiveness of current therapy to control it almost inevitably requires colectomy. Patient and physician decision making is reduced to determining when to schedule the procedure.

Unlike monitoring in familial adenomatous polyposis, screening in patients who have a family history or have the genetic trait of HNPCC does more than provide a guide to an inevitable outcome. Colonoscopy, the best of the screening evaluations, is necessary because polyps have been found to occur proximally more often than in an even, sporadic pattern throughout the colon. Testing begins earlier and is conducted more frequently because the transformation of HNPCC polyps is faster than that of other polyps. Genetic counseling and testing are necessities. Women with HNPCC have been found
to be at greater risk of endometrial cancer and should undergo accelerated screening for it.

**INITIATIVES AND NEW PROSPECTS FOR BETTER SCREENING AND COMPLIANCE**

In 1997, the Centers for Disease Control (CDC) found that as few as 9.2 percent of the residents of one state (95 percent confidence interval = 2.2) had had the FOBT during the preceding year, and the overall average for all states was below 20 percent. The percentage of those surveyed who reported having undergone sigmoidoscopy or proctoscopy within the preceding 5 years was also low: 30.4 percent. These and other earlier studies by the CDC along with other indications of poor screening compliance have prompted it and others to call for increased efforts to encourage colorectal cancer screening.

Making testing more comfortable for patients may improve compliance. Under study by radiologists is computed tomographic (CT) colonography, a noninvasive test meant to substitute for colorectal screening's most thorough, most expensive, yet least favorite test: colonoscopy. Sometimes called “virtual colonoscopy,” CT colonography, performed on patients who have and have not undergone bowel preparation, is an experimental screening method.

### Table 4-3. RECOMMENDED SCREENING AND SURVEILLANCE FOR THOSE AT MODERATE AND HIGH RISK FOR COLORECTAL CANCER

<table>
<thead>
<tr>
<th>Risk Stratification</th>
<th>Initial Screening</th>
<th>Subsequent Screening or Surveillance Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MODERATE RISK</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Personal History</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenomatous polyps</td>
<td>Colonoscopy at time of polyp diagnosis</td>
<td>Repeat TCE* within 3 years of diagnosis. If findings are negative, follow average risk recommendations.</td>
</tr>
<tr>
<td>Single, small (&lt; 1 cm) polyps</td>
<td>Colonoscopy at time of polyp diagnosis</td>
<td>Repeat TCE within 3 years of initial polyp removal. If findings are negative, repeat TCE every 5 years.</td>
</tr>
<tr>
<td>Large (&gt; 1 cm) polyps or multiple polyps of any size</td>
<td>TCE within 1 year of resection and perioperative TCE</td>
<td>If normal, TCE in 3 years. If at 3 years normal, TCE every 5 years.</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>TCE at 40 years of age or 10 years earlier than age at diagnosis of earliest case diagnosed in family</td>
<td>TCE every 5 years</td>
</tr>
<tr>
<td>Family History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenomatous polyps or colorectal cancer</td>
<td>TCE within 1 year of diagnosis</td>
<td>TCE every 5 years</td>
</tr>
<tr>
<td>First-degree relative &lt; 60 years of age or two first-degree relatives with a history of these</td>
<td>TCE every 5 years</td>
<td></td>
</tr>
<tr>
<td><strong>HIGH RISK</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Personal History</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Colonoscopy with biopsy of dysplasia In pancolitis: 8 years after initial diagnosis In colitis on left side: 12–15 years after initial diagnosis</td>
<td>Repeat every 1–2 years</td>
</tr>
<tr>
<td>Family History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Familial adenomatous polyposis</td>
<td>At puberty, endoscopic surveillance, genetic testing counseling, and specialist referral</td>
<td>Consider colectomy if polyposis confirmed or genetic testing positive. Perform endoscopy every 1–2 years.</td>
</tr>
<tr>
<td>Hereditary nonpolyposis colon cancer</td>
<td>At 21 years of age, colonoscopy and counseling regarding genetic testing</td>
<td>Colonoscopy every 2 years until age 40 and then annually for patients whose genetic test is positive or for patients who do not undergo genetic testing</td>
</tr>
</tbody>
</table>

Adapted from Byers et al.²⁴

*TCE, total colon evaluation by colonoscopy or double-contrast barium enema studies.*
that relies on sophisticated graphics software to assemble from a 1- to 2-minute CT scan an endoluminal image including surface and volume characteristics.\textsuperscript{26,27} Interpretation requires 20 to 40 minutes.\textsuperscript{26} A recent workshop report having a larger subject population than that in published reports found that CT colonography sensitivity for polyps \( \geq 5 \) mm was 81.9 to 93.9 percent and concluded that it rivaled conventional colonoscopy.\textsuperscript{26} The new method detected all colon carcinomas that had been identified by colonoscopy and pathologic findings.

Making tests more effective is another approach. Fecal occult blood testing has already improved since many of the studies of its screening effectiveness. In the future, stool samples collected for colorectal cancer screening may be searched for gene mutations or loss of DNA heterozygosity rather than occult blood.\textsuperscript{6}

Continuing studies of tests will also call for re-evaluation of use. In a recently published comparison of colonoscopy and DCBE for surveillance after polypectomy, Winawer and colleagues\textsuperscript{28} found barium enema to be dramatically less effective than previously thought. In comparison with colonoscopic findings, they found that barium enema detected 32 percent of adenomas \( \leq 0.5 \) cm, 53 percent of adenomas \( 0.6 \) to \( 1.0 \) cm, and 48 percent of those \( > 1 \) cm. Their findings prompted them to recognize colonoscopy as a more effective surveillance tool than barium enema after polypectomy. Tests now under way of colonoscopy as a screening measure can also be expected to refine thinking.

Attracting more patients to screening, including those who are less likely to participate, especially minorities and low-income women, is important in reducing mortality, and research indicates that doctor recommendations could spark interest and action in these groups.\textsuperscript{17,29} Also important is choosing an appropriate surveillance strategy that matches the patient’s risk.\textsuperscript{30} Large public campaigns, such as the one organized by the American Digestive Health Foundation and employing multiple organizations whose constituencies are stakeholders in the effort, could benefit thousands at risk.\textsuperscript{25} In office practice, efforts can require no technology beyond a telephone: physician input, patient education, and patient reminders by telephone.\textsuperscript{31}

REFERENCES