

# Screening for Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement

U.S. Preventive Services Task Force\*

**Description:** Update of the 2002 U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for colorectal cancer.

**Methods:** To update its recommendation, the USPSTF commissioned 2 studies: 1) a targeted systematic evidence review on 4 selected questions relating to test characteristics and benefits and harms of screening technologies, and 2) a decision analytic modeling analysis using population modeling techniques to compare the expected health outcomes and resource requirements of available screening modalities when used in a programmatic way over time.

**Recommendations:** The USPSTF recommends screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults, beginning at age 50 years and continuing until age 75 years. The risks and benefits of these screening methods vary. (A recommendation)

The USPSTF recommends against routine screening for colorectal cancer in adults 76 to 85 years of age. There may be considerations that support colorectal cancer screening in an individual patient. (C recommendation)

The USPSTF recommends against screening for colorectal cancer in adults older than age 85 years. (D recommendation)

The USPSTF concludes that the evidence is insufficient to assess the benefits and harms of computed tomographic colonography and fecal DNA testing as screening modalities for colorectal cancer. (I statement)

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[www.annals.org](http://www.annals.org)

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\*For a list of the members of the U.S. Preventive Services Task Force, see the **Appendix**, available at [www.annals.org](http://www.annals.org).

**T**he U.S. Preventive Services Task Force (USPSTF) makes recommendations about preventive care services for patients without recognized signs or symptoms of the target condition.

*It bases its recommendations on a systematic review of the evidence of the benefits and harms and an assessment of the net benefit of the service.*

*The USPSTF recognizes that clinical or policy decisions involve more considerations than this body of evidence alone. Clinicians and policymakers should understand the evidence but individualize decision-making to the specific patient or situation.*

## SUMMARY OF RECOMMENDATION AND EVIDENCE

The USPSTF recommends screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults, beginning at age 50 years and continuing until age 75 years.

The risks and benefits of these screening methods vary. See the Rationale and Clinical Considerations sections for comparisons of the risks and benefits of different screening regimens, as well as the specific intervals for different recommended tests.

This is an A recommendation.

The USPSTF recommends against routine screening for colorectal cancer in adults age 76 to 85 years. There may be considerations that support colorectal cancer screening in an individual patient. This is a C recommendation.

The USPSTF recommends against screening for colorectal cancer in adults older than age 85 years. This is a D recommendation.

The USPSTF concludes that the evidence is insufficient to assess the benefits and harms of computed tomographic (CT) colonography and fecal DNA testing as screening modalities for colorectal cancer. This is an I statement.

See also:

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See the **Figure** for a summary of the recommendations and suggestions for clinical practice.

See **Table 1** for a description of the USPSTF grades and **Table 2** for a description of the USPSTF classification of levels of certainty about net benefit.

## RATIONALE

### Importance

Colorectal cancer is the third most common type of cancer and the second leading cause of cancer death in the United States. Current levels of screening in this country lag behind those of other effective cancer screening tests; it has been estimated that attainment of goals for population colorectal cancer screening could save 18 800 lives per year (1). Colorectal cancer incidence and mortality show health disparities, with a disproportionate burden occurring in certain minority populations, including African Americans and Alaska Natives (2, 3).

### Detection

The evidence is convincing that screening for colorectal cancer with fecal occult blood testing, sigmoidoscopy, or colonoscopy detects early-stage cancer and adenomatous polyps.

Although colonoscopy is considered to be the reference standard against which the sensitivity of other colorectal cancer screening tests are compared, it is not perfect. Two types of studies to assess the sensitivity of colonoscopy—tandem colonoscopy studies, in which the same patient is studied twice, and studies comparing colonoscopy and CT colonography—show that colonoscopy may miss even polyps larger than 10 mm and colorectal cancer. In addition, most of the evidence about the sensitivity of colonoscopy comes from experienced examiners in research settings. The evidence is inadequate to estimate the sensitivity in community practice; however, it is likely to be lower than in research settings.

Although single test performance is an important issue in the detection of colorectal neoplasia, the sensitivity of the test over time is more important in an ongoing screening program. Unfortunately, data that permit assessment and comparison of screening methods to detect colorectal neoplasia in a testing program over time from a population perspective are limited to data from analytic modeling.

### Benefits of Detection and Early Intervention

There is convincing evidence that screening with any of the 3 recommended tests reduces colorectal cancer mortality in adults age 50 to 75 years. Follow-up of positive screening test results requires colonoscopy regardless of the screening test used. Because of the harms of colonoscopy described below, the chief benefit of less invasive screening tests is that they may reduce the number of colonoscopies required and their attendant risks.

There is adequate evidence that the benefits of detection and early intervention decline after age 75 years. The

lead time between the detection and treatment of colorectal neoplasia and a mortality benefit is substantial, and competing causes of mortality make it progressively less likely that this benefit will be realized with advancing age.

### Harms of Detection and Early Intervention

The primary established harms of colorectal cancer screening are due to the use of invasive procedures initially or in the evaluation sequence. Harms may arise from the preparation the patient undergoes to have the procedure, the sedation used during the procedure, and the procedure itself.

#### Colonoscopy

Evidence is adequate to estimate the harms of colonoscopy. In the United States, perforation of the colon occurs in an estimated 3.8 per 10 000 procedures (4). Serious complications—defined as deaths attributable to colonoscopy or adverse events requiring hospital admission, including perforation, major bleeding, diverticulitis, severe abdominal pain, and cardiovascular events—are significantly more common, occurring in an estimated 25 per 10 000 procedures (5).

#### Flexible Sigmoidoscopy

Evidence is adequate that serious complications occur in approximately 3.4 per 10 000 procedures (5).

#### Fecal Tests

Evidence about the harms of fecal tests is lacking (inadequate), but the USPSTF assesses them to be no greater than small.

#### CT Colonography

Computed tomographic colonography images more than the colon. Up to 16% of people having their first CT colonography are found to have extracolonic abnormalities that require further testing (5, 6). Evidence is inadequate to assess the clinical consequences of identifying these abnormalities, but there is potential for both benefit and harm. Potential harms arise from additional diagnostic testing and procedures for lesions found incidentally, which may have no clinical significance. This additional testing also has the potential to burden the patient and adversely impact the health system.

The risks for perforation associated with screening CT colonography in research settings are estimated to be 0 to 6 per 10 000 CT colonography studies (4). However, these estimates may be higher than what can be expected in screened populations because the studies included symptomatic populations.

Radiation exposure resulting from CT colonography is reported to be 10 mSv per examination. The harms of radiation at this dose are not certain, but the linear no-threshold model predicts that 1 additional individual per

1000 would develop cancer in his or her lifetime at this level of exposure (7). The lifetime cumulative radiation risk from the use of CT colonography to screen for colorectal cancer should be considered in the context of the growing cumulative radiation exposure from the use of other diagnostic and screening tests that involve radiation exposure. On the other hand, improvements in CT colonography technology and practice are lowering this radiation dose.

### USPSTF Assessment

The USPSTF concludes that, for fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy to screen for colorectal cancer, there is high certainty that the net benefit is substantial for adults age 50 to 75 years. See Clinical Considerations for a comparison of the regimens for each of these tests.

The USPSTF concludes that, for adults age 76 to 85 years, there is moderate certainty that the net benefits of screening are small.

The USPSTF concludes that, for adults older than age 85 years, there is moderate certainty that the benefits of screening do not outweigh the harms.

The USPSTF concludes that there is insufficient evidence to assess the sensitivity and specificity of fecal DNA testing for colorectal neoplasia, and that therefore the balance of benefits and harms cannot be determined for this test.

The USPSTF concludes that, for CT colonography, evidence to assess the harms related to extracolonic findings is insufficient, and the balance of benefits and harms cannot be determined.

## CLINICAL CONSIDERATIONS

### Patient Population under Consideration

These recommendations apply to adults 50 years of age and older, excluding those with specific inherited syndromes (the Lynch syndrome or familial adenomatous polyposis) and those with inflammatory bowel disease. The recommendations do apply to those with first-degree relatives who have had colorectal adenomas or cancer, although for those with first-degree relatives who developed cancer at a younger age or those with multiple affected first-degree relatives, an earlier start to screening may be reasonable. Data suggest that colorectal cancer has a higher mortality rate in African Americans. The reasons for this differential are not well known, and the recommendations are intended to apply to all ethnic and racial groups.

When the screening test results in the diagnosis of clinically significant colorectal adenomas or cancer, the patient will be followed by a surveillance regimen and recommendations for screening are no longer applicable. The USPSTF did not address evidence for the effectiveness of any particular surveillance regimen after diagnosis and/or removal of adenomatous polyps.

### Screening Tests

The relative sensitivity and specificity of the different colorectal screening tests with adequate data to assess cancer detection—colonoscopy, flexible sigmoidoscopy, and fecal tests—can be depicted as follows:

Sensitivity: Hemoccult II < fecal immunochemical tests  $\leq$  Hemoccult SENSEA  $\approx$  flexible sigmoidoscopy < colonoscopy

Specificity: Hemoccult SENSEA < fecal immunochemical tests  $\approx$  Hemoccult II < flexible sigmoidoscopy = colonoscopy

For the operator-dependent tests—flexible sigmoidoscopy, CT colonography, and colonoscopy—better operator training and more experience have a high likelihood of improving sensitivity. Approaches related to certification, such as quality standards and possibly minimum volume requirements, could be used to achieve the goal of improving operator performance and therefore test sensitivity. Assurance of performance of high-quality endoscopy should be part of all screening programs.

Because several screening strategies have similar efficacy, efforts to reduce colon cancer deaths should focus on implementation of strategies that maximize the number of individuals who get screening of some type. The different options for colorectal cancer screening tests are variably acceptable to patients; eliciting patient preferences is one step in improving adherence. Ideally, shared decision making between clinicians and patients would incorporate information on local test availability and quality as well as patient preference.

### Screening Intervals and Starting and Stopping Ages

Screening for colorectal cancer reduces mortality through detection and treatment of early-stage cancer and detection and removal of adenomatous polyps. The degree to which each of these mechanisms contributes to a reduction in mortality is unknown, although it is likely that the largest reduction in colorectal cancer mortality during the 10 years after initial screening comes from the detection and removal of early-stage cancer. Colonoscopy is a necessary step in any screening program that reduces mortality from colorectal cancer. This reduction in mortality does come at the expense of significant morbidity associated with colonoscopy. Evidence does not currently allow a differential estimate of colonoscopy-related morbidity for different age groups or for examinations done with or without biopsy.

In this context, the best measure for the morbidity that results from any screening program for colorectal cancer is the number of colonoscopies required to achieve a reduction in mortality. Although improvements in mortality will generally be associated with increasing morbidity that results from the screening and surveillance program, the goal of a screening program should be to maximize the number of life-years gained while minimizing the harms.

In a report prepared for the USPSTF by 2 groups in

the Cancer Intervention and Surveillance Modeling Network (CISNET), investigators conducted microsimulation analyses that applied programs of screening to standard populations of adults in the United States (5). These analyses permitted a comparison of expected outcomes among testing strategies involving the fecal tests, flexible sigmoidoscopy, or colonoscopy (as noted below). In the models, the predicted total number of colonoscopies included those resulting from surveillance after detection of colorectal neoplasia. The models assumed lifetime monitoring by colonoscopy every 3 to 5 years depending on the number and size of the adenomas detected. It is not the intent of the USPSTF to endorse this particular approach to surveillance, but standardizing the approach to surveillance is necessary to compare screening strategies in the models.

For all screening modalities, starting screening at age 50 resulted in a balance between life-years gained and colonoscopy risks that was more favorable than commencing screening earlier. Despite the increasing incidence of colorectal adenomas with age, for individuals previously screened the gain in life-years associated with extending screening from age 75 years to 85 years was small in comparison to the risks of screening people in this decade. For adults who have not previously been screened, decisions about first-time screening in this age group should be made in the context of the individual's health status and competing risks, given that the benefit of screening is not seen in trials until at least 7 years later. For persons older than 85 years, competing causes of mortality preclude a mortality benefit that outweighs the harms.

Screening programs incorporating fecal occult blood testing, sigmoidoscopy, or colonoscopy will all be effective in reducing mortality. Modeling evidence suggests that population screening programs between the ages of 50 and 75 years using any of the following 3 regimens will be approximately equally effective in life-years gained, assuming 100% adherence to the same regimen for that period (8): 1) annual high-sensitivity fecal occult blood testing, 2) sigmoidoscopy every 5 years combined with high-sensitivity fecal occult blood testing every 3 years, and 3) screening colonoscopy at intervals of 10 years.

The strategies differ in the total number of colonoscopies that would be required to gain similar numbers of life-years. The first strategy, use of annual high-sensitivity fecal occult blood testing (sensitivity for cancer  $\geq 70\%$ ) that has a false-positive rate less than 10% (that is, specificity  $>90\%$ ), is estimated to require the fewest colonoscopies while achieving a gain in life-years similar to that seen with screening colonoscopy every 10 years. Currently available tests that meet both specifications include SENSEA guaiac testing (Beckman Coulter, Fullerton, California) and fecal immunochemical tests with characteristics similar to those of the Magstream quantitative test (Fujirebio, Tokyo, Japan).

Although use of an annual fecal occult blood screening

test with a lower sensitivity has been demonstrated to reduce colorectal cancer mortality in randomized, controlled trials, modeling suggests that the number of life-years gained will be greater with the strategies using higher-sensitivity tests.

For all screening modalities, the effectiveness decreases substantially as adherence to the regimen declines. At the individual level, adherence to a screening regimen will be more important in life-years gained than will the particular regimen selected. Current data are insufficient to predict adherence to any specific screening regimen at the population level.

### Considerations for Practice When Evidence Is Insufficient CT Colonography

*Potential Preventable Burden.* A screening program that incorporates the option of CT colonography could help reduce colorectal cancer mortality in the population if patients who would otherwise refuse screening found it an acceptable alternative.

*Potential Harms.* The potential harms from evaluation of incidental findings found with CT colonography may be large. The lifetime cumulative radiation risk from use of CT colonography to screen for colorectal cancer should be considered, as well as the growing cumulative radiation exposure from the use of other kinds of diagnostic and screening that involve radiation exposure.

*Current Practice.* Computed tomographic colonography performed by trained and experienced radiographers may not be currently available in many parts of the United States.

*Costs.* Patient time and burden to participate in colorectal cancer screening using test strategies that require bowel preparation are substantial. A CT colonography screening strategy that did not involve bowel preparation would decrease the burden of adherence. The cost of CT colonography is high.

### Fecal DNA

*Potential Preventable Burden.* Fecal DNA has potential as a highly specific test, and it could reduce harms associated with follow-up of false-positive test results.

*Current Practice.* Fecal DNA tests are evolving, and no test is widely used.

*Costs.* Fecal DNA is likely to have a high monetary cost per test.

### Other Approaches to Prevention

Dietary approaches, such as avoidance of red meat and alcohol or consumption of diets very high in fiber, have been suggested to protect against the risk for colorectal adenomas, but these claims are based on associations present in observational studies that have thus far not been substantiated in trials. Certain nonsteroidal anti-inflammatory drugs (NSAIDs) are associated with regression and decreased incidence of colonic adenomas, but the harms of

daily NSAID use in asymptomatic persons led the USPSTF to recommend against this use in persons not at increased risk (see below.)

### Useful Resources

In 2007, the USPSTF recommended against the use of aspirin or NSAIDs for prevention of colorectal cancer (D recommendation, available at [www.ahrq.gov/clinic/uspstf/uspsasco.htm](http://www.ahrq.gov/clinic/uspstf/uspsasco.htm)).

## OTHER CONSIDERATIONS

### Research Needs and Gaps

Our understanding of optimal screening strategies would be significantly enhanced if higher-quality data were available about the natural history of small adenomas. Also, the importance of detecting flat adenomas is controversial, and there is a pressing need for further research on the natural history of these lesions.

Information is needed about the age-specific and biopsy-related harms of colonoscopy. Also needed are studies of the benefits and risks of detection and subsequent evaluation of extracolonic lesions through CT colonography. Finally, randomized trials are needed to compare screening programs using different modalities in order to define more clearly their relative benefits and harms.

Ultimately, all screening tests are merely tools, and the most important step is their actual use by patients; as such, further research into systems approaches to promoting the use of colorectal cancer screening could have a large impact on increasing the use of the tools that are available.

## DISCUSSION

### Burden of Disease

As noted earlier, colorectal cancer is the third most common type of cancer in both men and women in the United States (9). Progress has been achieved in reducing the cancer burden in the United States with declining rates in overall cancer deaths since the 1990s (3). However, the increasing proportion of the population older than 65 years has contributed to the increasing absolute total number of cancer deaths (2, 10). For 2008, it is estimated that 148 810 individuals will be diagnosed and that 49 960 will die of colorectal cancer (11).

More than 80% of diagnosed cases of colorectal cancer occur in patients older than 55 years. The age-adjusted incidence for colorectal cancer is 51.6 per 100 000 persons, with a lifetime risk of diagnosis of 5.7% for men and 5.1% for women. Increased age, along with male sex and black race, are associated with increasing colorectal cancer incidence (11). Despite these disparities, the incidence rate for colorectal cancer has declined over the past 20 years among men of all racial and ethnic groups except for Hispanics/

Latinos and Alaska Natives, and has stabilized among women of all racial and ethnic groups except Alaska Natives (3, 9).

### Scope of Review

In 2002, the USPSTF released a strong recommendation on colorectal cancer screening for average-risk adults age 50 years or older (12). To update this recommendation, the scope of the current review was determined to encompass 2 parts: a targeted systematic evidence review (5) to update information on selected questions from the prior review (13), and a decision analytic modeling analysis commissioned by the USPSTF to use population modeling techniques (8, 14).

The targeted systematic evidence review focused on the following key questions:

1. Do colorectal cancer screening programs have demonstrated benefit in reducing colorectal cancer mortality?
2. What is the efficacy of newer screening technologies—the high-sensitivity guaiac fecal occult blood test, the fecal immunochemical test, the fecal DNA test, and CT colonography?
3. What is the effectiveness of optical colonoscopy and flexible sigmoidoscopy in community practice?
4. What are the harms of newer screening technologies and optical colonoscopy and flexible sigmoidoscopy in community practice?

The USPSTF also requested a report from 2 decision analytic modeling groups to offer guidance on the optimal ages at which to start and stop screening, as well as the optimal intervals for different screening modalities. The analyses were carried out by using 2 microsimulation population models, both parts of the larger CISNET collaboration funded by the National Cancer Institute.

As each individual ages, there is a chance that an adenomatous lesion—the benign precursor to colorectal cancer—will develop. Because the time between the development of an adenoma and the occurrence of a clinically observable cancer is unknown, the models incorporate different assumptions about the adenoma–carcinoma sequence that yield different estimates of the average time between adenoma development and cancer diagnosis among cancer cases: a 10-year average in one model and a 22-year average in the other. Life expectancy was calculated for different screening strategies, including no screening given a 40-year-old cohort of asymptomatic individuals in the United States. The primary outcome was life-years gained relative to no screening, relative to the number of colonoscopies (14).

This update of the 2002 recommendation did not consider barium enema because it has substantially lower sensitivity than modern test strategies, it has not been subjected to screening trials, and its use as a screening test for colorectal cancer is declining.

### Accuracy of Screening Tests

Currently, there are 2 recognized approaches for colorectal cancer screening: assessment of stool for blood or DNA and visual inspection of the colon and rectum to find precancerous adenomas or early cancer. Since the 2002 review, several new stool-based screening modalities have become available: immunochemical fecal occult blood testing and fecal DNA testing. Certain fecal immunochemical tests have shown gains in sensitivity without excess loss of specificity when compared with established stool tests (15, 16). Screening with fecal DNA is still an evolving technology, with only 1 fair-quality study in average-risk patients providing data on sensitivity (better than Hemoccult II) and on the proportion of all tests that have positive results (higher than Hemoccult II) (17).

Direct visualization techniques offer substantial benefit over fecal tests, with greater sensitivity, when considered as a single test (5). Reduced screening accuracy in the community setting, due to inadequate bowel preparation or provider skill level, may decrease the sensitivity of optical colonoscopy and flexible sigmoidoscopy. Despite these operational constraints, these screening modalities remain an important means for detecting and treating colorectal cancer and its precursor lesions.

Recent clinical studies of CT colonography suggest that this screening method may be at least as sensitive as optical colonoscopy at identifying colorectal cancer and large adenomas in the community setting (18–20).

### Effectiveness of Early Detection

In 2002, the USPSTF concluded that there was fair-to-good evidence that several screening methods were effective in reducing mortality from colorectal cancer (12). The only method with direct evidence for reduction of mortality is a program that tests for blood-positive stools over several years. Since the last recommendation in 2002, the mortality reduction previously reported in FUBT trials was maintained in longer-term follow-up, and a recent meta-analysis estimates the overall colorectal cancer mortality reduction at 15% for biennial fecal occult blood testing (21).

There are no new trials that report on mortality for the other optical screening modalities (colonoscopy and sigmoidoscopy) or newer screening methods, such as fecal DNA and fecal immunochemical testing. The decision analytic modeling analysis performed for the USPSTF projected a comparative benefit to screening with colonoscopy, high-sensitivity fecal blood test, or flexible sigmoidoscopy every 5 years in combination with fecal testing every 3 years or mid-interval screening, relative to the other techniques studied (8). Despite the lack of direct evidence from clinical trials to ascertain which is the most effective strategy, any of the recommended screening methods is effective compared with no screening (22).

### Potential Harms

The USPSTF found evidence of harms associated with different colorectal screening programs. With all colorectal cancer screening modalities, a positive test result leads to follow-up testing, specifically colonoscopy, to resolve the diagnosis. This invasive procedure can result in serious morbidity as well as anxiety, inconvenience, discomfort, and additional medical expenses. Below, we first report known harms of each modality in single-use scenarios, and, at the end of this section, we describe the use of the accompanying decision model report to project the accumulated harms (that is, the number of colonoscopies) resulting from each program of screening over the lifetime of a hypothetical cohort of people.

#### Fecal Occult Blood Tests

No current studies adequately address any adverse effects of high-sensitivity stool tests for blood (SENSA, fecal immunochemical testing) (23).

#### Colonoscopy

Perforation from colonoscopy occurs in an estimated 3.8 per 10 000 procedures in the United States; major bleeding is estimated to occur in 12.3 per 10 000 procedures (95% CI, 7.8 to 19.3 per 10 000 procedures) (4). Serious complications—deaths from colonoscopies in asymptomatic populations or events requiring hospital admission, including perforation, major bleeding, diverticulitis, severe abdominal pain, and cardiovascular events—are estimated at 25 per 10 000 procedures (CI, 12 to 76 per 10 000 procedures) (5).

#### Flexible Sigmoidoscopy

Serious complications—deaths from flexible sigmoidoscopy in asymptomatic populations or events requiring hospital admission, including perforation, major bleeding, severe abdominal symptoms, and syncope—were fewer than with colonoscopy. The rate of serious complications is estimated at 3.4 per 10 000 procedures (CI, 0.6 to 19 per 10 000 procedures) (4). Perforation from flexible sigmoidoscopy was relatively uncommon, with a point estimate of 4.6 per 100 000 procedures (CI, 0.36 to 59 per 100 000 procedures) (4). Proportions for other complications were not calculated because of a lack of reliable data.

#### Fecal DNA

Information on harms from fecal DNA testing is limited at this time. Popular misunderstandings could occur about genetic profiling and insurability, but these are without basis because fecal DNA testing relies on the detection of de novo or somatic mutation in the mucosal lining of the bowel and is not related to hereditary (germ-line) mutations (24). Despite this distinction, general acceptability may limit the use of this test.

### CT Colonography

The risk for perforation, as studied in both symptomatic and asymptomatic populations, from CT colonography is estimated at 0 to 6 per 10 000 procedures (4). Because rates of perforation are higher for symptomatic persons undergoing CT colonography, the actual risk in a screening population would be expected to be on the low end of this range.

Computed tomographic colonography involves a wider area of examination than just the interior of the colon. Extracolonic findings of potential clinical significance are common and range from 7% to 16% of studies (4). It is not known whether the serendipitous discovery of these lesions results in better outcomes for patients; it is possible that they result in extra follow-up testing without associated benefit.

No studies directly addressed cancer-causing effects from CT colonography–associated radiation exposure. The ionizing radiation from a single CT colonography examination ranges from 1.2 to 23.4 mSv, with the median exposure at 10 mSv. The average radiation dose of 2-view chest radiography is 0.06 mSv (25), and the background radiation experienced by living in the United States is 3 mSv per year (7). However, the potential risk from this low-dose exposure remains uncertain. It is not yet possible to quantify accurately the potential harms of extracolonic findings or radiation exposure associated with CT colonography (4).

As mentioned above, the risks or harms from a single administration of a screening test must be considered in the framework of how often that test will be repeated in a patient's lifetime, as well as how many invasive procedures (that is, colonoscopies) will be required to follow up on abnormal screening test results. The model commissioned for this evidence review estimates that the USPSTF-recommended strategies would result in 3756 total colonoscopies per 1000 people for the "colonoscopy every 10 years" strategy, 2654 total colonoscopies for the "annual SENSE" strategy, 2295 for the "annual fecal immunochemical testing" strategy, and 1655 for the "flexible sigmoidoscopy every 5 years with SENSE every 3 years" strategy (14). Through the lens of minimizing harms associated with colonoscopy, the flexible sigmoidoscopy plus SENSE and the fecal immunochemical testing strategies are most successful.

### Estimate of Magnitude of Net Benefit

In considering the magnitude of benefit from a colorectal cancer screening program, the USPSTF noted with high certainty that there are substantial benefits to screening asymptomatic adults. Given the substantial benefit and small harms, the USPSTF recommends screening for colorectal cancer in all asymptomatic adults from 50 to 75 years of age. Balancing the small benefit and potential increased harms, the USPSTF does not recommend routine screening in asymptomatic adults from 75 to 85 years of

age and recommends against screening in asymptomatic adults older than 85 years of age who have previously been adequately screened.

The decision modeling analysis prepared for the USPSTF used a microsimulation approach to compare the life-year gains and the total colonoscopy burden expected with various strategies (14). The number of colonoscopies expected per 1000 individuals is a proxy for harm and burden of testing because colonoscopy is the final evaluative pathway for all the screening methods, with the highest risks for morbidity, hospitalization, and (rarely) death. The models generated outcomes for 1) no screening, 2) colonoscopy, 3) Hemoccult II, 4) Hemoccult SENSE, 5) fecal immunochemical testing, 6) flexible sigmoidoscopy with biopsy, and 7) flexible sigmoidoscopy with biopsy plus Hemoccult SENSE. This decision modeling analysis did not include colonography.

The modeling analysis used life-years gained relative to the number of colonoscopies required for each strategy to calculate the net benefit, where the number of colonoscopies represents a proxy for resource utilization as well as adverse events from screening. The life-years gained relative to the number of colonoscopies for the scenarios allowed for an ordinal ranking of the different screening modalities (14) as follows: 1) colonoscopy (associated with 271 life-years gained for every 1000 persons screened); 2) SENSE, fecal immunochemical testing, and flexible sigmoidoscopy/SENSE (associated with 259, 256, and 257 life-years gained, respectively, for every 1000 persons screened); and 3) Hemoccult II and flexible sigmoidoscopy (218 and 199 life-years gained, respectively, per 1000 persons screened).

### How Evidence Fits with Biological Understanding

Our knowledge about the development of colorectal cancer currently builds on the concept of an adenoma–carcinoma sequence, wherein it is expected that some adenomas will develop into carcinomas. The progression from a precursor lesion to colorectal cancer is a multistep process accompanied by alteration in several suppression genes over a period of 10 to 15 years (26). The long preclinical phase from the development of adenomas to colorectal cancer allows for opportunities to successfully screen, intervene, and save lives. The efficacy of screening with stool-based methods relies on the detection of bleeding or shedding of genetic material from adenomas or carcinomas. Compared with the older stool tests (for example, Hemoccult II), the newer stool-based tests are more sensitive but less specific. All optical methods rely on visual recognition of surface alterations, either texture or shape changes in the mucosa of the colorectum. Adequate preparation of the colorectum is critical to ensure visualization of these changes. The impetus for a noninvasive optical technique (that is, CT colonography) was to permit visualization with a much lower risk for perforation and other complications. However, because the field of exposure, both in terms of

radiation and scrutiny, is broad with CT colonography, more studies are required to determine all the risks and benefits associated with its use. Fecal DNA technology (that is, detection of particular gene loci) may advance significantly in the coming years; data on sensitivity and accuracy of this testing are needed. This type of technology may radically alter diagnosis, risk stratification, and surveillance of a wide range of cancerous and non-cancerous gastrointestinal conditions (27).

### Update of Previous USPSTF Recommendation

In contrast to the 2002 USPSTF recommendation, which applied to all adults 50 years of age or older without regard to an age at which to stop screening, routine colorectal cancer screening is now recommended in adults beginning at age 50 and continuing only until age 75 (in people with adequate screening histories). The following screening modalities are recommended: high-sensitivity FOBT, sigmoidoscopy with interval FOBT, or colonoscopy. The USPSTF does not recommend routine screening for adults 75 to 85 years of age and recommends against screening adults older than 85 years of age. With this statement, the USPSTF concludes that for CT colonography and fecal DNA, there is insufficient evidence to permit a recommendation.

### RECOMMENDATIONS OF OTHERS

In March 2008, the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology (28) jointly recommended screening for colorectal cancer beginning at 50 years of age by 1) high-sensitivity FOBT or fecal immunochemical testing annually, 2) flexible sigmoidoscopy every 5 years, 3) double-contrast barium enema every 5 years, 4) CT colonography (virtual colonoscopy) every 5 years, 5) colonoscopy every 10 years, or 6) fecal DNA at an unspecified interval. The report stated that approaches offering visualization of the colon were preferred to indirect methods (available at <http://caonline.amcancersoc.org/cgi/reprint/58/3/130>). The American College of Obstetricians and Gynecologists recommends colonoscopy as the preferred method (29). In 2001, the Canadian Task Force on Preventive Health Care (30) concluded that there is good evidence for annual or biannual FOBT and fair evidence to include flexible sigmoidoscopy in periodic health examinations of asymptomatic people older than 50 years of age (available at [www.cmaj.ca/cgi/reprint/165/2/206](http://www.cmaj.ca/cgi/reprint/165/2/206)). The American College of Physicians, American Academy of Family Physicians, American College of Preventive Medicine, and Centers for Disease Control and Prevention have issued similar recommendations or endorsed the USPSTF recommendation.

From the U.S. Preventive Services Task Force, Agency for Healthcare Research and Quality, Rockville, Maryland

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Figure. Screening for colorectal cancer: clinical summary of a U.S. Preventive Services Task Force (USPSTF) recommendation.\*

**Annals of Internal Medicine**



**SCREENING FOR COLORECTAL CANCER  
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION**

Population	Adults Age 50 to 75 Years*	Adults Age 76 to 85 Years*	Adults Older Than 85 Years*
	Screen with high-sensitivity FOBT, sigmoidoscopy, or colonoscopy Grade: A	Do not screen routinely Grade: C	Do not screen Grade: D
Recommendation	<p><b>For all populations, evidence is insufficient to assess the benefits and harms of screening with computed tomographic colonography and fecal DNA testing.</b></p> <p><b>Grade: I (insufficient evidence)</b></p>		
Screening Tests	<p>High-sensitivity FOBT, sigmoidoscopy with FOBT, and colonoscopy are effective in decreasing colorectal cancer mortality. The risks and benefits of these screening methods vary. Colonoscopy and flexible sigmoidoscopy (to a lesser degree) entail possible serious complications.</p>		
Screening Test Intervals	<p><b>Intervals for recommended screening strategies:</b></p> <ul style="list-style-type: none"> <li>• Annual screening with high-sensitivity FOBT</li> <li>• Sigmoidoscopy every 5 years, with high-sensitivity FOBT every 3 years</li> <li>• Screening colonoscopy every 10 years</li> </ul>		
Balance of Harms and Benefits	<p>The benefits of screening outweigh the potential harms for 50- to 75-year-olds.</p>	<p>The likelihood that detection and early intervention will yield a mortality benefit declines after age 75 because of the long average time between adenoma development and cancer diagnosis.</p>	
Implementation	<p>Focus on strategies that maximize the number of individuals who get screened. Practice shared decision making; discussions with patients should incorporate information on test quality and availability. Individuals with a personal history of cancer or adenomatous polyps are followed by a surveillance regimen, and screening guidelines are not applicable.</p>		
Relevant USPSTF Recommendations	<p>The USPSTF recommends against the use of aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of colorectal cancer. This recommendation is available at <a href="http://www.preventiveservices.ahrq.gov">www.preventiveservices.ahrq.gov</a>.</p>		

For a summary of the evidence systematically reviewed in making these recommendations, the full recommendation statement, and supporting documents, please go to [www.preventiveservices.ahrq.gov](http://www.preventiveservices.ahrq.gov). FOBT = fecal occult blood testing.  
\* These recommendations do not apply to individuals with specific inherited syndromes (the Lynch syndrome or familial adenomatous polyposis) or those with inflammatory bowel disease.

**Table 1. What the U.S. Preventive Services Task Force Grades Mean and Suggestions for Practice\***

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if other considerations support offering or providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

\* USPSTF = U.S. Preventive Services Task Force.

**Table 2. U.S. Preventive Services Task Force Levels of Certainty Regarding Net Benefit**

Level of Certainty*	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by such factors as: the number, size, or quality of individual studies inconsistency of findings across individual studies limited generalizability of findings to routine primary care practice lack of coherence in the chain of evidence. As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: the limited number or size of studies important flaws in study design or methods inconsistency of findings across individual studies gaps in the chain of evidence findings that are not generalizable to routine primary care practice a lack of information on important health outcomes. More information may allow an estimation of effects on health outcomes.

\* The U.S. Preventive Services Task Force (USPSTF) defines *certainty* as “likelihood that the USPSTF assessment of the net benefit of a preventive service is correct.” The net benefit is defined as benefit minus harm of the preventive service as implemented in a general primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

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