Colorectal Cancer Screening for Average-Risk Adults: 2018 Guideline Update From the American Cancer Society

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Additional supporting information may be found online in the Supporting Information section at the end of the article.

Abstract: In the United States, colorectal cancer (CRC) is the fourth most common cancer diagnosed among adults and the second leading cause of death from cancer. For this guideline update, the American Cancer Society (ACS) used an existing systematic evidence review of the CRC screening literature and microsimulation modeling analyses, including a new evaluation of the age to begin screening by race and sex and additional modeling that incorporates changes in US CRC incidence. Screening with any one of multiple options is associated with a significant reduction in CRC incidence through the detection and removal of adenomatous polyps and other precancerous lesions and with a reduction in mortality through incidence reduction and early detection of CRC. Results from modeling analyses identified efficient and model-recommendable strategies that started screening at age 45 years. The ACS Guideline Development Group applied the Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) criteria in developing and rating the recommendations. The ACS recommends that adults aged 45 years and older with an average risk of CRC undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability. As a part of the screening process, all positive results on noncolonoscopy screening tests should be followed up with timely colonoscopy. The recommendation to begin screening at age 45 years is a *qualified recommendation*. The recommendation for regular screening in adults aged 50 years and older is a *strong recommendation*. The ACS recommends (*qualified recommendations*) that: 1) average-risk adults in good health with a life expectancy of more than 10 years continue CRC screening through the age of 75 years; 2) clinicians individualize CRC screening decisions for individuals aged 76 through 85 years based on patient preferences, life expectancy, health status, and prior screening history; and 3) clinicians discourage individuals older than 85 years from continuing CRC screening. The options for CRC screening are: fecal immunochemical test annually; high-sensitivity, guaiac-based fecal occult blood test annually; multitarget stool DNA test every 3 years; colonoscopy every 10 years; computed tomography colonography every 5 years; and flexible sigmoidoscopy every 5 years. *CA Cancer J Clin 2018;000:000-000.* © *2018 American Cancer Society.*

Keywords: adenoma, colonoscopy, computed tomography colonoscopy, colorectal and rectal neoplasms, mass screening and early detection, mortality, occult blood, radiography, sigmoidoscopy, stool testing

Introduction

Colorectal cancer (CRC) is the fourth most commonly diagnosed cancer among adults in the United States.[1] Over 140,000 Americans are expected to be diagnosed with CRC in 2018. It is the second leading cause of cancer death, leading to over 50,000 deaths annually.[1] CRC disease burden varies across racial groups, with the highest incidence and mortality rates in blacks, American Indians, and Alaska Natives.[2]

Temporal trends in CRC incidence and mortality among adults aged 55 years and older have shown a decline for several decades that accelerated around 2000, particularly among adults aged 65 years and older.[2,3] Although changes in exposure to risk factors account for an estimated one-half of the reduction in incidence and one-third of the reduction in mortality before 2000, subsequent accelerated declines in incidence and mortality since 2000 are largely attributable to increased uptake of screening, with improved treatment also contributing to mortality reductions.[3-6] In contrast, among adults younger than 55 years, there was a 51% increase in the incidence of CRC from 1994 to 2014 and an 11% increase in mortality from 2005 to 2015.[7,8]

Risk factors associated with a Western lifestyle that have been shown to increase CRC risk include: cigarette smoking; excess body weight; diet, including high consumption of alcohol and red and processed meat and low consumption of fruits/vegetables, dietary fiber, and dietary calcium; and physical inactivity.[9,10] Islami et al estimated that a significant proportion of CRC incidence among women and men in 2014 (50.8% and 58.2%, respectively) was attributable to these lifestyle factors.[10] Thus, there is an important opportunity to reduce risk across the population through lifestyle modification. The use of aspirin in selected individuals has also been demonstrated to reduce the likelihood of developing CRC.[11-14] Risk for developing CRC is associated with several identified hereditary CRC conditions; a family history of CRC[15]; medical conditions, including chronic inflammatory bowel disease[16] and type 2 diabetes[17]; and a history of abdominal or pelvic radiation for a previous cancer.[18-21]

The detection and subsequent removal of precursor lesions detected during screening and the detection of CRC at an earlier, more favorable stage have been shown to significantly reduce incidence and mortality. The increased understanding of the natural history of CRC and precursor lesions and the development and accumulation of evidence on screening technologies have supported the evolution of screening recommendations and implementation of CRC screening in clinical practice and public health programs.[22]

This guideline is intended to provide guidance to adults at average risk of CRC, to clinicians who counsel and refer patients to CRC screening, and to health care systems to support best practices in the early detection and prevention of CRC. The American Cancer Society (ACS) first published evidence-based recommendations for early detection of cancer of the colon and rectum in 1980.[23] The most recent update of recommendations for individuals at average risk occurred in 2008 and was based on an evidence-based consensus process that included the ACS, the US Multi-Society Task Force (USMSTF) on Colorectal Cancer (representing the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy), and the American College of Radiology.[24] Since 2008, evidence has accumulated on the different screening modalities, test performance in population-based screening programs, and the changing risk of CRC.[3,25,26] This guideline update is based on an assessment of the underlying burden of disease; the strength of evidence and the balance of benefits and harms for available screening tests; and consideration of patient values and preferences, including the importance of choice in the selection of screening test options.

Materials and Methods

The ACS follows a protocol for developing and disseminating guidelines that is designed to maintain transparency, consistency, and rigor.[27,28] This process includes the use of systematic evidence reviews on the topic, consideration of the overall balance of benefits and harms of interventions and patient preferences, a guidelines panel of scientific

experts without any direct professional specialization in the issue under review, a transparent disclosure and management process that minimize biases and conflicts of interest, explicit explanation of the logical relationships between screening interventions and health outcomes, and ratings of both the quality of evidence and the strength of the recommendations.

The ACS Guideline Development Group (GDG), a multidisciplinary panel of volunteers comprising generalist clinicians, biostatisticians, epidemiologists, economists, and a patient representative, is charged with the development and update of the ACS cancer screening guidelines. The GDG has full responsibility for interpretation of the evidence, formulating the recommendations, deliberation and voting on the recommendations and strength, and writing the guideline. A record of voting on the recommendations is kept without attribution. While the GDG attempts to achieve complete agreement, a three-quarters majority is considered acceptable for adopting a recommendation and assigning strength. For the update of the CRC screening guideline, a subcommittee consisting of 6 GDG members had primary responsibility for reviewing the evidence, drafting recommendations, and preparing the manuscript for publication, although the entire GDG reviewed and voted on the updated guideline. ACS staff members served as guideline methodologists and in an administrative capacity to support the GDG. ACS staff members also contributed cancer screening and CRC expertise to the GDG evaluation of the evidence and participated in preparation of the manuscript but did not formulate recommendations or vote to approve the final guideline. Guideline development is supported by ACS general operating funds.

Individuals with recognized clinical and research expertise in the areas of CRC natural history, detection, diagnosis, and decision making were invited to advise the GDG and to provide broader knowledge and understanding of the complexity of CRC screening (see Supporting Information). The GDG consulted the expert advisors at several stages in the guideline development process: the expert advisors were requested to respond to questions about the key evidence questions and the evidence and logic underlying screening recommendations and to assess the primary evidence reports and suggest additional data for consideration. In addition, they served as external reviewers of the draft recommendation statements and the guideline manuscript before publication.

Participants (GDG members, ACS staff, expert advisors) in all stages of the guideline development process were required to disclose all financial and nonfinancial (personal, intellectual, practice-related) relationships and activities that might be perceived as posing a conflict of interest in the update of the CRC screening guideline. The GDG chairpersons had the responsibility to ensure balanced perspectives were considered in deliberations and decision making.

For the update of the CRC screening guideline, the GDG chose to use 2 reports commissioned by the US Preventive Services Task Force (USPSTF) for its 2016 CRC screening recommendation update as sources of evidence to inform recommendations: a systematic evidence review on CRC screening and a report of simulation modeling findings from the Cancer Intervention and Surveillance Modeling Network (CISNET) CRC group.[26,29-31] The evidence synthesis conducted for the USPSTF addressed 3 issues: the effectiveness of screening in reducing incidence and mortality from CRC, the test performance characteristics of different screening tests for detecting CRC and important precursor lesions, and the adverse effects associated with different screening tests. Three microsimulation models of CRC screening developed as part of the CISNET consortium estimated the impact of a variety of programmatic screening strategies for the screening-eligible US population. The CISNET-CRC group consists of 3 CRC microsimulation models that were independently developed for the evaluation of interventions, and their use to date principally has focused on screening. The 3 models differ somewhat in their underlying assumptions about the natural history of CRC, which allows for estimation of outcomes based on these different assumptions. The CISNET-CRC models include: 1) MISCAN-CRC, with investigators from Erasmus University Medical Center and Memorial Sloan Kettering Cancer Center; 2) SimCRC from the University of Minnesota and Massachusetts General Hospital; and 3) CRC-SPIN from RAND Corporation.[32]

To gain additional understanding of outcomes associated with different screening strategies (particularly starting age) for black and white adults, the ACS commissioned a modeling study by the MISCAN and SimCRC investigators (2 of the CISNET modeling groups) that extended the previous analysis conducted for the USPSTF. The objective was to assess the potential benefit (life-years gained and CRC deaths averted) and the burden of different CRC screening strategies for black and white women and men.[33] Subsequently, the GDG determined that recent evidence demonstrating a significant increase in CRC incidence among individuals younger than 55 years, which was attributable to a strong birth-cohort effect,[3] warranted a reevaluation of the optimal age to start screening in the average-risk population. Additional modeling analyses by the MISCAN investigators incorporated recent Surveillance, Epidemiology, and End Results (SEER) incidence data and evaluated screening outcomes for the general US population.[34] Analyses of outcomes for race-specific and sex-specific groups by MISCAN and SimCRC, which initially were carried out

under the assumption of stable incidence, were repeated to incorporate recent SEER incidence data.[33]

Under the direction of the GDG, the ACS staff performed a supplemental literature review to examine differential risk and screening outcomes in racial and ethnic subgroups. In addition, literature searches were conducted to identify relevant new studies that have addressed screening outcomes since completion of the USPSTF evidence review. The GDG also examined data provided by the ACS Surveillance and Health Services Research Program on disease burden using data from the SEER program.[35] Unless otherwise indicated, all incidence and mortality rates are per 100,000 person-years and age-adjusted to the US standard population.

While the primary source of evidence for this guideline used a different rating system for the appraisal of evidence,[26,29] the GDG applied the principles of the Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) and GRADE Evidence-to-Decision (EtD) frameworks in formulating and assigning the strength of recommendations.[36,37] The principal GRADE decision-making criteria are: 1) balance between desirable and undesirable effects—the greater the difference between desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted, and the narrower the difference, the higher the likelihood that a qualified recommendation is warranted; 2) quality of evidence—the higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted; and 3) values and preferences—the greater the uniformity or certainty in values and preferences, the higher the likelihood that a strong recommendation is warranted. Each recommendation was designated by the GDG as either *strong* or *qualified*, in accordance with GRADE guidance.[38] A strong recommendation conveys the consensus that the benefits of adherence to the intervention outweigh the undesirable effects and that most patients would choose the intervention. A qualified recommendation indicates there is clear evidence of benefit (or harm) but less certainty either about the balance of benefits and harms or about patients' values and preferences, which could lead to different individual decisions. Additional elements included in the GRADE EtD framework and considered in this guideline are the impact on health equity, feasibility, and acceptability.[37] The ACS does not apply cost and resource use as a decision-making criterion for recommendations. Actual costs of CRC screening tests and follow-up examinations vary widely in the United States, and costs, coverage, and reimbursement may be important considerations for individuals when making decisions about screening tests (see Patient considerations of cost and reimbursement, below).

Before final preparation of a manuscript for publication, the guideline was submitted to the ACS Mission Outcomes Committee and Board of Directors for review and approval of the proposed recommendations. The expert advisors and representatives from 30 relevant outside organizations were then invited to participate in an external review of the guideline. Responses were documented and reviewed by the GDG to determine whether modifications in the recommendations or narrative were warranted, and adopted changes were incorporated in the final manuscript.

Considerations in Developing Recommendations

Outcomes of Screening

The GDG identified reduction in CRC mortality (measured as life-years gained [LYGs] in the modeling reports) and incidence as the principal benefits of screening. Although the previous ACS guideline gave priority to CRC incidence reduction, in this update, the GDG did not prioritize incidence reduction over mortality reduction. There is variability in prevention potential among the available screening tests, but all noncolonoscopy screening tests contribute to prevention through colonoscopy follow-up and adenoma removal after a positive initial screening test, as demonstrated by the reduction in incidence in the US guaiac fecal occult blood test (gFOBT) randomized trial.[39] Although prevention is highly valued by patients, test preparation, invasiveness, potential costs, and other considerations will lead some patients to prefer a noncolonoscopy test for screening. Greater value was placed on the role of patient preferences and on the potential to increase CRC screening utilization through offering choice in screening test options. The GDG recognized the potential relevance of other beneficial outcomes, including reduction of disease and treatment morbidity and improved quality of life, but identified no studies that demonstrated direct associations with screening.

The principal recognized harms of CRC screening, which are rare, are those associated with colonoscopy (bleeding, perforation, cardiorespiratory complications of sedation) as a primary screening test or as a follow-up of other positive noncolonoscopy tests.[26,40,41] The harm conventionally associated with workup of false-positive test results is partly mitigated when a normal follow-up examination removes the patient from the screening pool for 10 years. In addition to estimating the number of colonoscopy-related complications, the CISNET modeling group used the number of colonoscopies required as a proxy for harms and a measure of the burden of CRC screening.[30] The GDG regarded the number of colonoscopies (and related risk of complications) as a proxy for harms. Individual patient burden was considered primarily in the context of patient decision making on the basis of test attributes. For computed tomography colonography (CTC), attention was given to additional

potential harms associated with radiation exposure and workup of incidental findings not leading to residual benefit. Screening test performance measures (sensitivity, specificity, etc) were included as important outcomes in evaluating the evidence on screening tests. Relatively low importance was ascribed to the beneficial effect of reassurance from a negative screening test as well as to the burden of anxiety precipitated by a false-positive test result.

Evidence-Based Inferential Reasoning

Results from randomized controlled trials (RCTs) of CRC screening with either a stool-based test (gFOBT) or a structural examination (flexible sigmoidoscopy [FS]) have demonstrated mortality reductions associated with the detection of advanced neoplasia in asymptomatic adults.[26] The evidence of benefit for all other screening tests is limited to test performance data demonstrating the ability to detect early stage CRC and/or advanced adenomas and observational studies. In addition to this body of evidence for the individual modalities, the GDG adopted evidence-based inferential reasoning to extrapolate from the evidence establishing a rationale for using the detection of occult blood as an effective screening tool to support fecal immunochemical testing (FIT) and multitarget stool DNA (mt-sDNA) testing, which includes multiple molecular assays combined with a hemoglobin immunoassay. Similarly, findings from RCTs of FS provide a compelling "proof of concept" for structural evaluation of the colon to detect both CRC and adenomas as an effective approach to reducing CRC incidence and mortality. In addition to examining the test performance and observational data on the other 2 currently available structural examinations (colonoscopy and CTC), the GDG made the judgment to extrapolate the RCT evidence on FS.

Use of Modeling Studies

Given the limited evidence on long-term outcomes for the different screening options as well as direct comparisons, modeling studies have been used to compare the potential effectiveness of different screening strategies, and the results of these studies have influenced the USPSTF CRC screening recommendations.[30,42-44] The CISNET investigators have devised a methodology to identify model-recommended screening strategies for consideration among the numerous unique strategies that are generated by combinations of tests with different starting and stopping ages and screening intervals.

Model-recommended screening strategies for individual tests are based on the balance of benefits, expressed as LYGs (corrected for life-years lost because of screening complications) versus burden and harms, expressed as the number of colonoscopies required for a given strategy (screening, follow-up, surveillance, and diagnosis of symptomatic cancer). The burden of noncolonoscopy tests is addressed by grouping and comparing screening options that have similar test characteristics, resulting in 4 separate classes of screening tests (ie, colonoscopy, all stool tests, FS, and CTC). Strategies within each class that achieve the highest LYGs for a given number of colonoscopies are deemed efficient, whereas strategies that achieve at least 98% of the highest LYGs are deemed "near-efficient." For all efficient and near-efficient strategies, an efficiency ratio (ER) is estimated, which is a measure of burden to benefit based on the ratio of the incremental number of colonoscopies divided by the incremental number of LYGs compared with the nearest less effective efficient strategy. From the efficient or near-efficient strategies in each class, model-recommendable strategies are those that have an acceptable overall benefit and ER (balance of burden to benefit).[33,34]

The limitations of modeling arise from the uncertainty inherent in the parameters and assumptions that underpin the model inputs. One such assumption in the CISNET models[30,31] is 100% adherence to all screening strategies, including 100% adherence to follow-up colonoscopy for positive initial noncolonoscopic screening examinations. The assumption of full adherence allows for comparison of the screening options under a uniform scenario. However, actual screening and follow-up adherence rates vary by test, setting, and population group, meaning that actual outcomes could diverge from predicted outcomes based on differential uptake and follow-up. These limitations are acknowledged by the CISNET investigators and were acknowledged by the GDG in integrating modeling results with empirical evidence.

Patient Preferences, Choice, and Adherence

CRC screening presents a unique challenge and opportunity, as there are multiple screening tests with variability in supporting evidence of effectiveness, risk of harm, prevention potential, and patient burden. There is no consistent, direct evidence that adults prefer any one CRC screening tool or strategy over others. Individual preferences can be influenced by patient education about screening, test characteristics (ie, accuracy, degree of invasiveness, test preparation, required screening interval, and cost), and clinician recommendation.[45-50] The ACS is committed to increasing utilization to achieve the benefits of CRC screening by recommending that patients be given an opportunity to choose a testing strategy, thus increasing the likelihood of adherence. Patient preference is an important consideration, although the choice of test must be predicated on high-quality screening test options that are accessible to the patient, and there must be access to follow-up colonoscopy if needed.

TABLE 1. American Cancer Society Guideline for CRC Screening, 2018

Recommendations[a]

The ACS recommends that adults aged 45 y and older with an average risk[b] of CRC undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability. As a part of the screening process, all positive results on noncolonoscopy screening tests should be followed up with timely colonoscopy.

The recommendation to begin screening at age 45 y is a *qualified recommendation*.

The recommendation for regular screening in adults aged 50 y and older is a *strong recommendation*.

The ACS recommends that average-risk adults in good health with a life expectancy of greater than 10 y continue CRC screening through the age of 75 y *(qualified recommendation)*.

The ACS recommends that clinicians individualize CRC screening decisions for individuals aged 76 through 85 y based on patient preferences, life expectancy, health status, and prior screening history *(qualified recommendation)*.

The ACS recommends that clinicians discourage individuals over age 85 y from continuing CRC screening *(qualified recommendation)*.

Options for CRC screening

Stool-based tests

- Fecal immunochemical test every y
- High-sensitivity, guaiac-based fecal occult blood test every y
- Multitarget stool DNA test every 3 y

Structural examinations

- Colonoscopy every 10 y
- CT colonography every 5 y
- Flexible sigmoidoscopy every 5 y

ACS, American Cancer Society; CRC, colorectal cancer; CT, computed tomography. [a]A strong recommendation conveys the consensus that the benefits of adherence to that intervention outweigh the undesirable effects that may result from screening. Qualified recommendations indicate there is clear evidence of benefit (or harm) of screening but less certainty about the balance of benefits and harms or about patients' values and preferences, which could lead to different decisions about screening. [b]These recommendations represent guidance from the ACS for persons without a history of adenomatous polyps or CRC and not at increased risk for CRC due to a family history of CRC, a confirmed or suspected hereditary CRC syndrome (such as familial adenomatous polyposis or Lynch syndrome), a personal history of abdominal or pelvic radiation for a previous cancer, or a personal history of inflammatory bowel disease.

Recommendations

The ACS recommends that adults aged 45 years and older with an average risk of colorectal cancer undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability. As a part of the screening process, all positive results on noncolonoscopy screening tests should be followed up with timely colonoscopy. The recommendation to begin screening at age 45 years is a *qualified recommendation*. The recommendation for regular screening in adults aged 50 years and older is a *strong recommendation* (Table 1).

This recommendation for CRC screening in average-risk adults is based on the GDG's judgment of the preponderance of benefits of CRC screening over harms, the overall quality of the evidence on screening outcomes, recent evidence related to the incidence of disease, evidence demonstrating the influence of test preference on adherence to recommendations, and the high value individuals place on preventing and avoiding death from CRC.[51,52] The GDG chose to issue a general overall recommendation for CRC screening rather than recommendations for the use of specific individual tests. Although there is significant variability among the available screening tests in the volume and quality of supporting evidence, the overall quality of the evidence was judged to be good and sufficient to support a recommendation for screening with any of the 6 included strategies (Table 1). On the basis of the strength of the evidence and on the judgment of an overall preponderance of benefit, the recommendation for regular screening in adults aged 50 years and older has been designated as a "strong" recommendation. The recommendation to begin screening at age 45 years is based on disease burden, results from microsimulation modeling, and the reasonable expectation that screening will perform similarly in adults aged 45 to 49 years as in persons for whom screening is currently recommended. However, the long-standing recommendation to initiate CRC screening at age 50 years means that there are limited data on screening outcomes in adults aged 45 to 49 years. Because of differences in the type and quality of evidence for screening in adults younger than 50 years, as described below, the recommendation to start screening at age 45 years has been designated as "qualified."

Age to Begin CRC Screening

Burden of disease

When initiating this guideline update and examining the burden of disease, the GDG initially focused on higher than average incidence before age 50 years in some racial subgroups.[35,53] Beginning screening earlier in these groups would be consistent with a disease burden approach and could contribute to reducing disparities.[2,54,55] Some organizations already have recommended that blacks and Alaska Natives begin screening before age 50 years based on their higher incidence at younger ages.[56-58] However, prior reports showing the persistence of a trend of increasing CRC incidence in adults younger than 50 years[59-62] and the recent work by Siegel et al[3] demonstrating that this rising incidence was the result of a strong birth-cohort effect that would carry forward with age led the GDG to reevaluate the age to initiate screening in all US adults.

CRC incidence rates in the United States have historically varied by sex as well as by race and ethnicity. Among all races combined, CRC incidence is similar in women and men until age 35 years but, thereafter, is higher for men, and the disparity widens with age. CRC incidence among blacks, including those younger than 50 years, has historically been higher than that among whites, Hispanics, and Asian Americans.[2] However, while incidence rates in whites younger than 50 years have risen, incidence rates for blacks younger than 50 years have remained generally stable, resulting in comparable contemporary incidence between the 2 groups (Fig. 1). The CRC incidence rate for individuals younger than 50 years is higher among Alaska Natives than for any other racial/ethnic group in the United States.[2,63] High rates have been reported for some American Indian groups, although this varies by tribe and geographic region.[64]

CRC incidence has declined steadily over the past 2 decades in the population aged 50 years and older because of the combined influence of screening and changes in exposure to risk factors,[4] but there has been a 51% *increase* in CRC among those younger than 50 years since 1994 (Fig. 2).[3] Increased incidence rates have been particularly notable for rectal cancer, which doubled between 1991 (2.6 of 100,000) and 2014 (5.2 of 100,000) in individuals aged 20 to 49 years.[7] A recent analysis found that adults born around 1990 have twice the risk of colon cancer and 4 times the risk of rectal cancer compared with adults born around 1950, who have the lowest risk.[3]

The factors contributing to this increase in incidence are not understood.[2,3] The increase in incidence observed in the youngest birth cohorts is not likely due to detection bias arising from increased use of colonoscopy, because negligible screening and case finding occur in the youngest cohorts, and the increased incidence in whites is accompanied by an increase in mortality, which is contrary to what would be expected if increased incidence in this group was because of
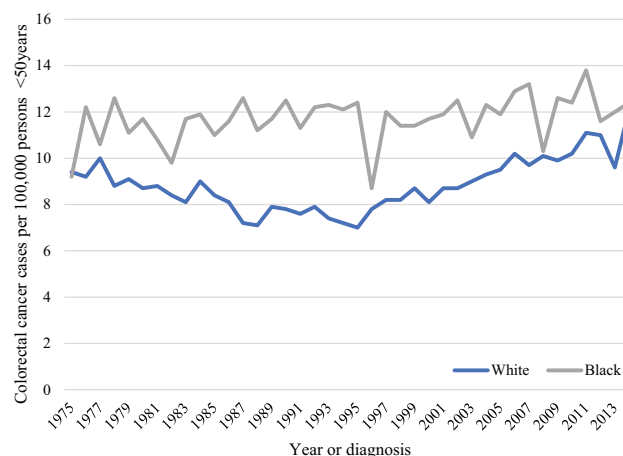

FIGURE 1. Trends in Colorectal Cancer Incidence Rates in Adults Younger Than Age 50 Years by Race, 1975 to 2014.

increased screening.[3] The observation that CRC incidence is increasing in successively younger birth cohorts suggests that the greater burden of CRC in the population younger than 50 years is not just a transient epidemiological phenomenon. Rather, these birth cohorts are carrying the elevated risk with them as they age; increases in colon cancer incidence began in the mid-1980s and have continued through 2013 for the groups aged 20 to 29 years (2.4% per year) and aged 30 to 39 years (1% per year) and in the mid-1990s for the groups aged 40 to 49 years (1.3% per year) and 50 to 54 years (0.5% per year). Rectal cancer incidence rates increased 3.2% per year from 1974 to 2013 in adults aged 20 to 29 years, 3.2% per year from 1980 to 2013 in adults aged 30 to 39 years, and 2.3% per year from the early to mid-1990s to 2013 in adults aged 40 to 54 years.[3] Siegel et al also noted a recent convergence of CRC incidence rates in the groups aged 50 to 54 years and 55 to 59 years (Fig. 3); in the early 1990s CRC incidence rates in adults aged 50 to 54 years were one-half of those in the group aged 55 to 59 years, whereas in 2012-2013 there was just a 12.4% difference in colon cancer rates, and rectal cancer rates were the same for the 2 age groups.[3] This rising incidence in younger age groups coinciding with rapid declines in older age groups has led to a large shift in the age-adjusted proportion of CRC in adults younger than 55 years, from 11.6% during 1989 to 1990 to 16.6% during 2012 to 2013 for colon tumors and from 14.6% to 29.2%, respectively, for rectal tumors.[3]

Although the current age-specific incidence rate among adults aged 45 to 49 years (31.4 per 100,000) is lower compared with that among adults aged 50 to 54 years (58.4 per 100,000),[35] the higher rate in the group aged 50 to 54 years is influenced by lead time associated with the uptake of screening as well as rising incidence because of increasing age. Data from the National Health Interview Survey revealed that approximately 45.3% of adults aged 50 to 54 years reported recent screening with either colonoscopy or
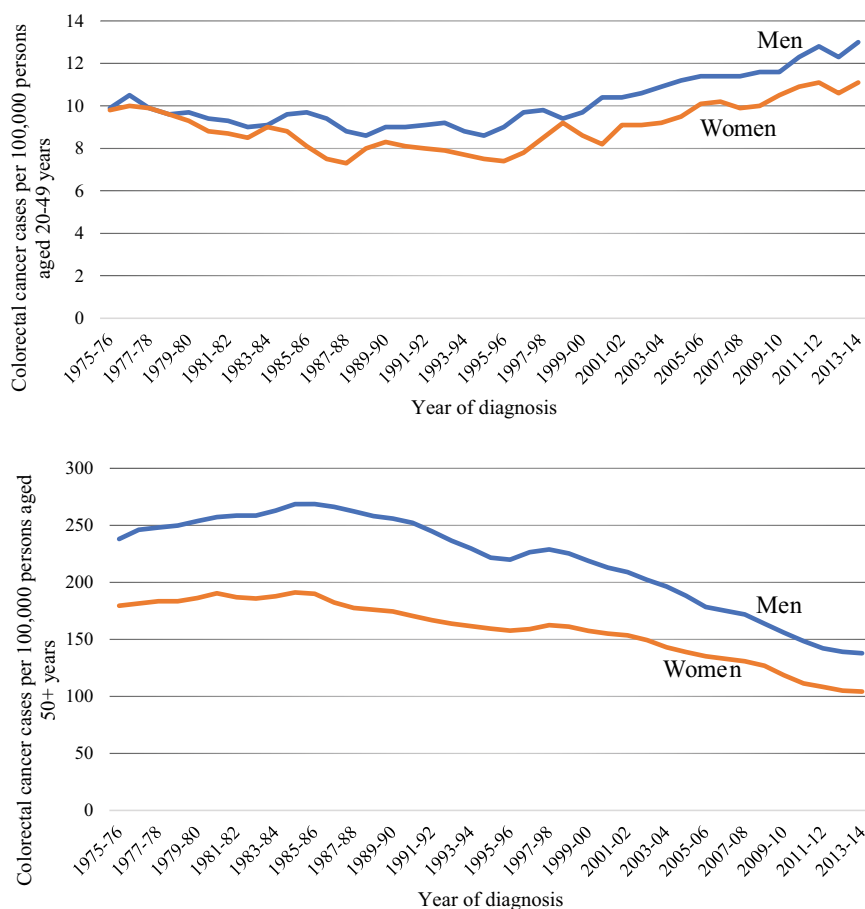
FIGURE 2. Trends in Colorectal Cancer Incidence Rates by Age (Ages 20-49 and Ages 50+) and Sex, 1975 to 2014. Rates are adjusted for delays in reporting and are plotted as a 2-year moving average. Data source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2017.

FS in 2015 compared with approximately 17.8% of adults aged 40 to 49 years.[65] Thus, the true underlying risk in adults aged 45 to 49 years is likely closer to the risk in adults aged 50 to 54 years than the most recent age-specific rates would suggest. More noteworthy, however, is that the increase in the annual percentage change in the incidence rate for adults aged 40 to 49 years (1.3%) is more than twice that of adults aged 50 to 54 years (0.5%), suggesting that the risk for the younger cohort will continue to carry forward into the group aged 50 to 54 years.[3]

Although the data described above pertain to trends in the risk of invasive disease, Lieberman et al reported that the prevalence of polyps measuring 9 mm or greater among adults younger than 50 years was 4.2% in whites and 6.2% in blacks, similar to the prevalence of 5.3% in whites and 6.1% in blacks aged 50 to 59 years.[66] Insofar as prevention also is a goal of CRC screening, these data indicating a similar prevalence of large polyps in adults aged 45 to 49 years and 50 to 54 years point to the disease prevention potential of beginning screening at age 45 years.

Further confirmation of a change in underlying disease risk is the increase in CRC mortality among white adults aged 50 to 54 years since 2005, after decades of decline in an age group in which screening is recommended.[3] CRC mortality rates have been increasing since 1995 in whites aged 30 to 39 years and since 2005 in whites aged 40 to 54 years. In contrast, mortality rates have been decreasing since 1970 among blacks aged 20 to 54 years but still were about 50% higher compared with the rates among whites in this age group in 2014 (6.1 vs 4.1 per 100,000).

It is further noteworthy that, of all CRC deaths during 2010 through 2014, a similar proportion of decedents were diagnosed at ages 45 to 49 years (5.1%) compared with ages 50 to 54 years (7.6%) (Fig. 4A). Likewise, of all estimated premature mortality from the disease measured by years of potential lives lost, 10% was because of diagnoses in persons aged 45 to 49 years compared with 13% attributable to diagnoses in those aged 50 to 54 years (Fig. 4B).

Evidence of the effectiveness of screening in adults aged 45 to 49 years

There is limited direct evidence of screening effectiveness in adults younger than 50 years, in large part because of early
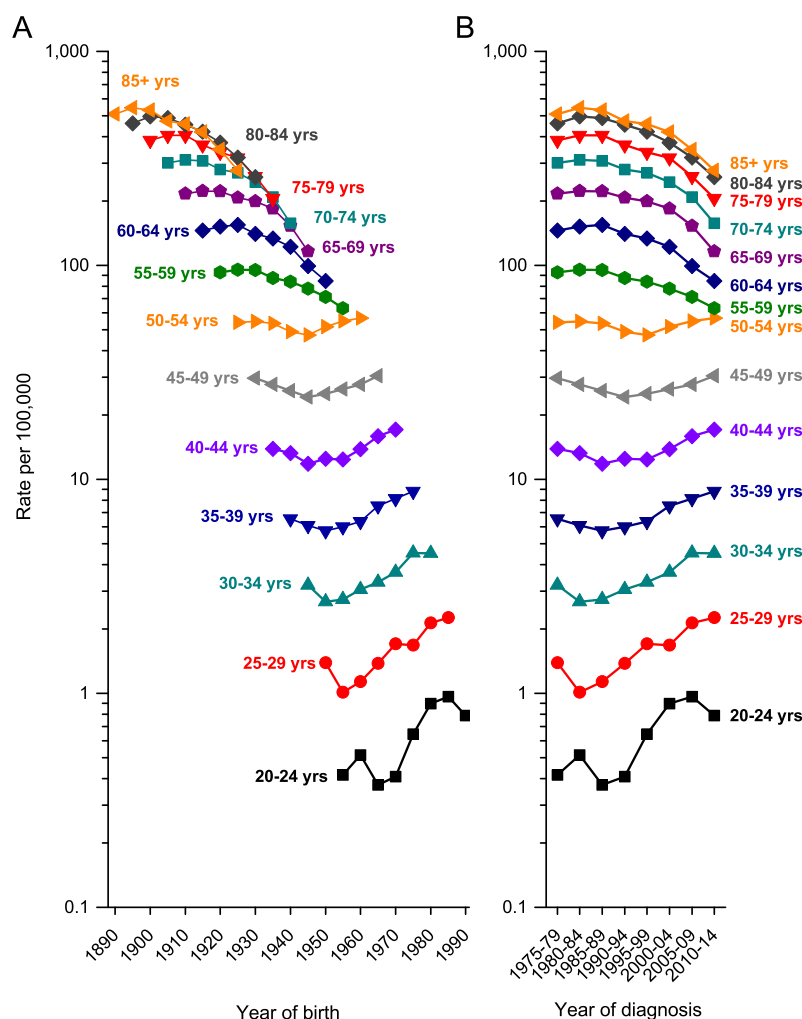
FIGURE 3. Trends in Colorectal Cancer Incidence Rates by Age and Year of Birth, and by Age and Year of Diagnosis, United States, 1975 to 2014. Data source: Surveillance, Epidemiology, and End Results (SEER) program, SEER 9 registries, delayed adjusted rates, 1975-2014, National Cancer Institute.

expert judgments, based on disease burden, that screening should begin at age 50 years.[23,67,68] Most of the RCTs of CRC screening demonstrating benefit had a starting age of 50 years, as do the RCTs of colonoscopy/FIT[25,69] and CTC/colonoscopy/FIT/FS[70-72] that are currently in progress. Three of the European gFOBT trials conducted in the 1980s and 1990s that demonstrated a CRC mortality benefit enrolled persons starting at age 45 years (45-74 years or 75 years).[26] However, all were underpowered for age subgroup analyses, and age-specific outcomes were not reported. Much of the observational evidence demonstrating effectiveness of CRC screening is similarly limited to a starting age of 50 years.

Modeling Analyses

Given the limited empirical data on long-term screening outcomes across screening modalities and strategies and the paucity of comparative data, recommendations for CRC screening over the past decade increasingly have relied on modeling analyses of screening outcomes.[30,42] It should be noted that the modeling report prepared for the USPSTF 2016 CRC screening recommendations determined that, "for all modalities, strategies with screening beginning at age 45 years predominated on the efficient frontier; that is, these strategies generally provided additional LYGs at a lower number of additional colonoscopies than strategies with screening beginning at later ages."[30] However, beginning screening at age 45 years while maintaining the 10-year screening interval, resulted in an increase in the estimated lifetime number of colonoscopies. In 2 models (SimCRC and CRC-SPIN), starting screening at age 45 years but extending the screening interval to 15 years resulted in slightly more LYGs and a similar lifetime number of colonoscopies compared with screening with colonoscopy every 10 years from aged 50 to 75 years.[30] Ultimately, the USPSTF elected not to recommend the younger starting age, judging that the estimated additional LYGs would be "modest," also noting that 1 of the 3 models in the 2016 report (the MISCAN model) did not corroborate the modest increase in LYGs associated with the younger starting
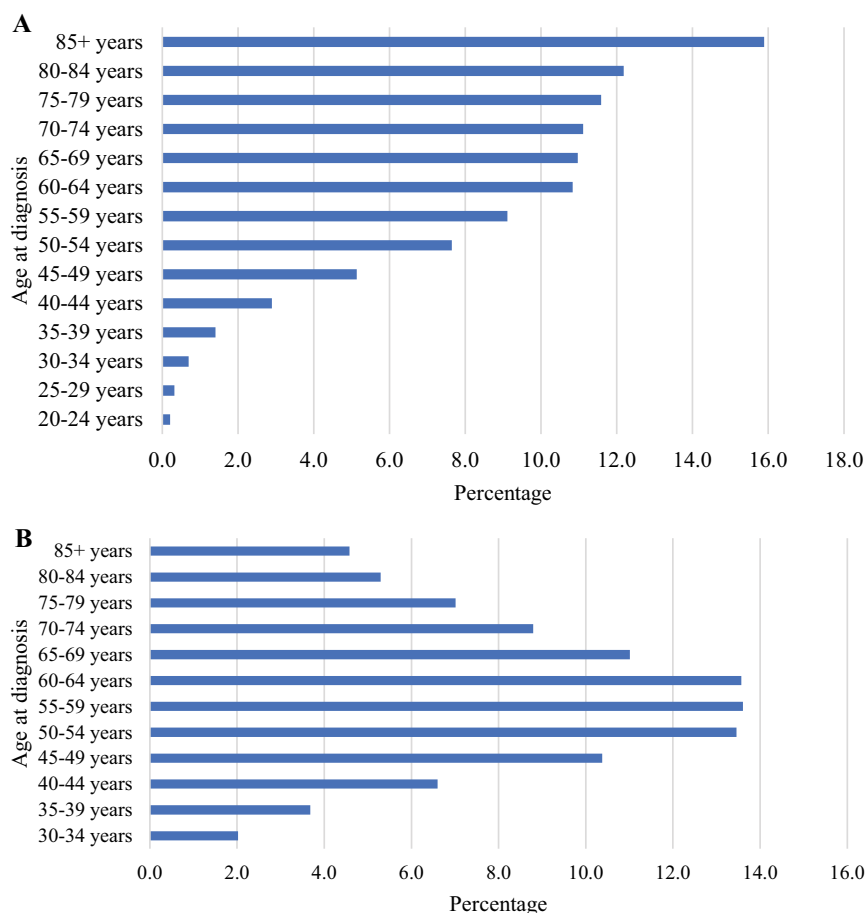
A

B

FIGURE 4. Distribution of Colorectal Cancer Burden by Age at Diagnosis, 2010 to 2014. (A) The distribution of colorectal cancer (CRC) deaths by age at diagnosis (n = 20,198) is illustrated among patients who were followed for 20 years after diagnosis. (B) The distribution of person-years of life lost (YLL) because of CRC by age at diagnosis is illustrated among patients who were followed for 20 years after diagnosis. Source: SEER 9 registries.

age and a 15-year screening interval, and citing the lack of empirical evidence for screening younger populations and a 15-year screening interval.[44]

The CISNET modeling analyses used for the 2016 USPSTF update were based on historical CRC incidence data from the prescreening era (1975-1979) to reflect risk without the influence of screening on incidence (prevention and early detection). Although this was a reasonable methodological decision, the model outputs did not reflect changes in incidence because of underlying changes in risk that may have occurred over time. On the basis of the recent trends in CRC incidence before age 55 years described previously[3] and the higher burden of disease in blacks compared with whites, the ACS worked with 2 of the CISNET groups (MISCAN and SimCRC) to reexamine optimal screening strategies, with emphasis on the influence of observed trends in incidence on the age to begin screening. Outcomes of different screening strategies were predicted for the general population under the increased-risk scenario (MISCAN only)[34] and for population subgroups defined by race and sex under both the stable-risk scenario and the increased-risk scenario (MISCAN and SimCRC models).[33]

With respect to the reevaluation of screening strategies for the general population with emphasis on observed trends in incidence, the analyses were similar to those carried out for the USPSTF, with the principal exception of the application of incidence multipliers to adjust risk proportional to the observed increase in incidence in adults younger than 40 years (to rule out any potential contamination from screening). The models also accounted for the higher proportion of tumors in the rectum and distal colon observed in the incidence trends among younger adults.[3] This adjustment in risk was based on the observation that increased incidence in adults younger than 55 years is attributable to a strong birth-cohort effect that began in the 1950s and is carrying over as these cohorts age. Six screening modalities (colonoscopy, CTC, FS, mt-sDNA, FIT, and high-sensitivity gFOBT [HSgFOBT]) were evaluated with variation in the starting age (40, 45, and 50 years), ending age (70, 75, and 80 years), and screening intervals, which varied by screening test, for a total of 132 unique CRC screening strategies.

Among 9 efficient and 5 near-efficient colonoscopy strategies, the strategy recommended by the model under the increased-risk scenario was screening every 10 years from
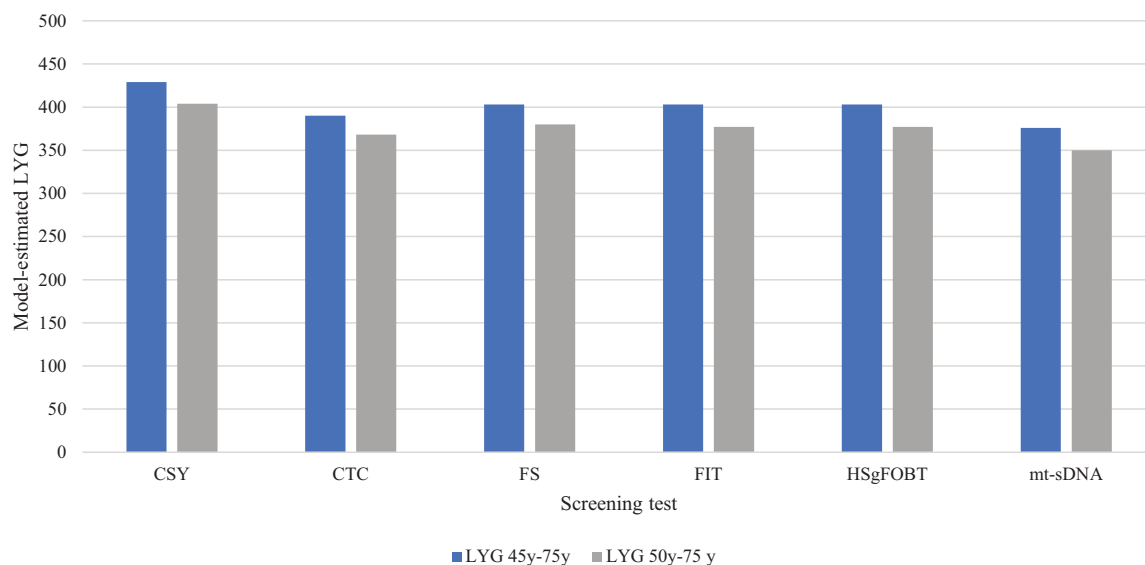
FIGURE 5. Model-Estimated Life-Years Gained (LYG) from Colorectal Cancer Screening Starting at Age 45 Years Versus 50 Years, per 1000 Screened Over a Lifetime. CSY indicates colonoscopy; CTC, computed tomography colonography; FSIG, flexible sigmoidoscopy; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood test; LYG, life-years gained; mt-sDNA, multitarget stool DNA. Adapted from: Peterse EFP, Meester RGS, Siegal RL, et al. The impact of the rising colorectal cancer incidence in young adults on the optimal age to start screening: microsimulation analysis I to inform the American Cancer Society colorectal cancer screening guideline. *Cancer*. 10.1002/cncr.31543 [epub ahead of print].[34]

ages 45 to 75 years, which, compared with screening every 10 years from ages 50 to 75 years, had 6.2% more LYGs and 17% more colonoscopies per 1000 adults over a lifetime of screening (Fig. 5).[34] This strategy was chosen as the benchmark strategy because it had the highest LYGs among strategies with ERs less than a predetermined benchmark. Other model-recommended strategies for adults aged 45 to 75 years under the increased-risk scenario included annual FIT, CTC every 5 years, and FS every 5 years (Table 2).[34]

In the analysis of race-specific and sex-specific strategies, using 2 CISNET models, CRC screening was evaluated under both stable-risk and increased-risk scenarios. For the analyses in which prescreening era incidence data were used to reflect risk (stable-risk scenario), both models concluded that colonoscopy screening from ages 45 to 75 years was recommendable for black women and men, although the MISCAN model recommended a 10-year interval, and the SimCRC model recommended a 15-year interval.[33] For whites, the SimCRC model recommended the same strategy that was recommended for blacks, while the MISCAN model recommended colonoscopy from ages 50 to 75 years every 10 years. When the models were adjusted for increased incidence, both models recommended screening strategies from ages 45 to 75 years (colonoscopy every 10 years, FIT annually, FS every 5 years, and CTC every 5 years) for both black women and men and white women. For white men aged 45 to 75 years, the SimCRC recommended these same strategies, while the MISCAN model only recommended screening with colonoscopy every 5 years.[33] Thus, under the increased-risk scenario, both overall and race-specific and sex-specific analyses[33,34] by the 2 independent

microsimulation models support the conclusion that starting screening at age 45 years is an efficient and recommendable strategy for the general population.

TABLE 2. Model-Estimated Benefits and Burdens of CRC Screening Starting at Age 45 Versus 50 Years, per 1000 Screened Over a Lifetime

SCREENING TEST	LYG	NO. OF CSY	MODEL RECOMMENDABLE
CSY every 10 y, 45-75	429	5646	Yes
CSY every 10 y, 50-75	404	4836	No
CTC every 5 y, 45-75	390	2666	Yes
CTC every 5 y, 50-75	368	2430	No
FSIG every 5 y, 45-75	403	3761	Yes
FSIG every 5 y, 50-75	380	3426	No
FIT yearly, 45-75	403	2698	Yes
FIT yearly, 50-75	377	2402	No
HSgFOBT yearly, 45-75	403	3364	No
HSgFOBT yearly, 50-75	377	2956	No
mt-sDNA every 3 y, 45-75	376	2640	No
mt-sDNA every 3 y, 50-75	350	2331	No

CRC, colorectal cancer; CSY, colonoscopy; CTC, computed tomography colonography; FIT, fecal immunochemical test; FSIG, flexible sigmoidoscopy; HSgFOBT, high-sensitivity, guaiac-based fecal occult blood test; LYG, life-years gained; mt-sDNA, multitarget stool DNA. Adapted from: Peterse EFP, Meester RGS, Siegel RL, et al. The impact of the rising colorectal cancer incidence in young adults on the optimal age to start screening: microsimulation analysis I to inform the American Cancer Society colorectal cancer screening guideline. *Cancer*. 10.1002/cncr.31543 [epub ahead of print].[34]

The MISCAN analyses for the general population also evaluated strategies starting screening at age 40 years. Results indicated a small increase in the number of LYGs (438 vs 429), with the same number of deaths averted (37) per 1000 adults, for colonoscopy every 10 years with a starting age of 40 years compared with 45 years.[34] The incremental burden of additional colonoscopies resulted in an ER for this strategy above 45, which is higher than the model-recommended strategy for starting screening at age 45 years. The incidence of CRC in adults aged 40 to 44 years is 17.6 per 100,000 versus 31.4 per 100,000 for adults aged 45 to 49 years (58.4 per 100,000 for adults aged 50-54 years).[35] Because of lower incidence, the years of life lost because of CRC among persons diagnosed at ages 40 to 44 years are measurably less than in the group ages 45 to 49 years (6% vs 10% of total years of potential lives lost) and well below those in the older age groups for whom screening is currently recommended (Fig. 4B). Trends in incidence and mortality in adults younger than 50 years and accumulating evidence on screening performance in younger populations will continue to be monitored and will be examined in future guideline updates.

As noted above, microsimulation modeling conducted to inform the 2016 update of the USPSTF CRC screening recommendations found that screening strategies beginning at age 45 years provided additional LYGs at a lower number of additional colonoscopies than strategies that began screening at a later age.[30] The analyses conducted for the 2018 ACS update address the principal concerns raised by the USPSTF in choosing not to recommend a younger starting age. First, the modeling analyses conducted for this update incorporating an increased-risk scenario provide stronger support for beginning screening at age 45 years.[33,34] When the MISCAN model, which was the nonconcordant model in the 2016 analysis, was adjusted to reflect increased incidence, screening beginning at age 45 years had a favorable balance of benefit to colonoscopy burden for all adults, and there was an improvement in LYGs compared with starting screening at age 50 years.[33,34] Second, although SimCRC still indicates that colonoscopy screening every 15 years is recommended under the stable-risk scenario, which was not corroborated by MISCAN, there was concordance between the 2 models on a 10-year interval under the increased-risk scenario.[33]

Summary: Age to begin screening

Although there is little evidence on screening outcomes in adults aged 45 to 49 years, observational studies suggest that both structural and stool-based CRC screening tests perform similarly in cancer and adenoma detection among individuals younger than 50 years and among older individuals.[73-75] The GDG acknowledged that the absolute benefit expected from screening in adults aged 45 to 49 years was lower than that in other age groups for which screening is currently recommended but judged that the tradeoff between reduced CRC mortality and incidence and increased number of colonoscopies was favorable.

The GDG considered other factors in formulating its recommendation for the age to start screening. First, the potential harms of colonoscopy (as either a primary screening or follow-up examination) are lower in younger versus older adults.[40] Second, recent estimates indicate that the current colonoscopy capacity in the United States should be able to accommodate the anticipated increase in colonoscopies, performed both as primary screens and as follow-up to positive noncolonoscopy tests.[76] Finally, starting CRC screening earlier also may contribute to reducing disparities in population groups with a higher disease burden (including blacks, Alaska Natives, and some American Indian groups). Although the modeling analyses were unable to include other racial groups or to distinguish Hispanic ethnicity, incidence rates for Asians and Hispanics are similar to those for whites. Therefore, the general recommendation to begin screening at age 45 years should be applicable to all groups.

In summary, based on the recent increase in CRC incidence in younger persons, the analyses demonstrating a favorable benefit-to-burden balance for initiating screening earlier, and the expected reduction in CRC mortality and incidence, the ACS recommends that all adults start CRC screening at age 45 years using any of the screening options presented in Table 1.

Choice of Screening Tests

The recommendation for CRC screening includes offering patients the opportunity to select either a structural (visual) examination or a high-sensitivity stool-based test, depending on patient preference and test availability. As detailed in Table 3, the screening options differ in the extent of patient burden and in ways that can affect a patient's choice of test and subsequent adherence, including screening frequency, screening location (home vs medical facility), need for dietary and/or bowel preparation, need for sedation, time and transportation required, relative ability to prevent versus detect CRC, out-of-pocket cost, risk of complications, and test accuracy. There is evidence that patients will have a preference for one type of screening test over others if provided sufficient information regarding these test attributes, although no single test appears to consistently dominate patient preferences, supporting a strategy of offering choice.[45,47,52,77,78] Intention to screen is also higher if the screening test ordered is consonant with the patient's preference.[47,77] Decision aids that help patients choose among options have been shown to improve knowledge and interest

TABLE 3. Considerations in Choosing a Colorectal Cancer Screening Test[a]

SCREENING TEST	RECOMMENDED SCREENING INTERVAL	EVIDENCE OF EFFECTIVENESS AND TEST PERFORMANCE	LIMITATIONS	PATIENT BURDEN	COST AND REIMBURSEMENT
Stool-based screening tests					
FIT with high sensitivity for cancer	Annual	• Indirect evidence of mortality reduction from RCTs of guaiac-based stool tests • Equivalent or superior performance compared with high-sensitivity gFOBT • Variability in test performance by version and brand	• High nonadherence to annual testing (especially in absence of reminder systems) • Less effective for advanced adenoma detection • Few available tests have published peer-reviewed performance data	• Is done at home • Many brands require only a single sample • No diet or medication restrictions	• Inexpensive compared with structural examinations and mt-sDNA • Follow-up colonoscopy for positive test may be subject to out-of-pocket costs
gFOBT with high sensitivity for cancer (HSgFOBT)	Annual	• Good RCT evidence for incidence and mortality reduction • Performance characteristics vary by version of the test (low-sensitivity gFOBT versions are not recommended for CRC screening)	• High nonadherence to annual testing (especially in absence of reminder system) • Less effective for advanced adenoma detection • Difficulty in ascertaining test performance among the many FDA-cleared tests	• Is done at home • Requires multiple samples • Requires dietary and medication restriction • Higher false-positive rate than FIT leads to more colonoscopies	• Inexpensive compared with structural examinations and mt-sDNA • Follow-up colonoscopy for positive test may be subject to out-of-pocket costs
mt-sDNA	Every 3 y (as per manufacturer)	• Indirect evidence of mortality reduction from RCTs of guaiac-based stool tests • Results from one large, manufacturer-funded trial showed improved sensitivity for cancer and advanced adenomas and poorer specificity compared with FIT	• This is a new test, with limited data on screening outcomes, and its performance needs to be monitored over time • There may be uncertainty in management of positive results followed by a negative colonoscopy	• Can be done at home • Higher false-positive rate than FIT	• More expensive than other stool-based tests • Follow-up colonoscopy for positive test may be subject to out-of-pocket costs

TABLE 3. Continued

SCREENING TEST	RECOMMENDED SCREENING INTERVAL	EVIDENCE OF EFFECTIVENESS AND TEST PERFORMANCE	LIMITATIONS	PATIENT BURDEN	COST AND REIMBURSEMENT
Structural (visual) examinations for screening					
Colonoscopy	Every 10 y	• Non-RCT evidence of incidence and mortality reduction • Extrapolation from RCTs of sigmoidoscopy demonstrating mortality reduction • Offers both early detection and prevention of CRC through polypectomy	• Risk of bowel perforation/bleeding and cardiopulmonary complications of anesthesia • Performance is dependent upon adequacy of bowel preparation, the cecal intubation rate, withdrawal time, and adenoma detection rate • Limited collection of quality data in many settings • Level of adherence to 10-y interval is unknown • Lower sensitivity for neoplasia in the proximal than the distal colon	• Requires full bowel cleansing • Requires time off work and a chaperone (if sedation is used)	• Most expensive test, but currently reimbursable for those with insurance coverage • Polypectomy and anesthesia may be subject to out-of-pocket costs
CTC	Every 5 y	• Extrapolation from RCTs of sigmoidoscopy demonstrating mortality reduction • Sensitivity and specificity for cancer and advanced adenomas comparable to colonoscopy	• Incidental extracolonic findings may require workup, with unclear benefit-burden balance • Exposure to low-dose radiation	• Requires full bowel cleansing • Colonoscopy required if test positive. If same day colonoscopy is not possible, a second bowel cleansing will be required before the follow-up colonoscopy.	• Relatively expensive and may not be covered by insurance (not covered by Medicare at this time) • Follow-up colonoscopy for positive test may be subject to out-of-pocket costs
FS	Every 5 y	• Best evidence among structural examinations for reducing mortality and incidence	• Does not examine the proximal colon • Concerns about lack of quality standards, limited availability, failure to achieve a complete examination	• Pain and discomfort • Requires enema prior to procedure • Abnormal findings require second endoscopic procedure (colonoscopy)	• Follow-up colonoscopy for positive test may be subject to out-of-pocket costs

CRC, colorectal cancer; CTC, computed tomographic colonography; FDA, US Food and Drug Administration; FIT, fecal immunochemical test; FS, flexible sigmoidoscopy; gFOBT, guaiac-based fecal occult blood test; mt-sDNA, multitarget stool DNA; RCT, randomized controlled trial. [a]The American Cancer Society considers these options as acceptable choices for CRC screening in average-risk adults. Individuals should be given information on the characteristics related to prevention potential, effectiveness, accuracy, costs, and potential harms of available and accessible tests to make an informed decision on which test to choose for CRC screening. All positive noncolonoscopy screening tests should be followed up with timely colonoscopy as a part of the screening process. Repeating positive noncolonoscopy tests is not acceptable.

in screening and lead to increased screening compared with not providing information.[79]

Trials offering a choice between a stool test and a structural examination compared with either test alone have generally demonstrated greater uptake when a choice is offered. The best evidence in the United States derives from a randomized trial in a safety-net population comparing annual gFOBT versus colonoscopy versus choice between the 2 in which it was demonstrated that choice was more effective than offering colonoscopy alone. In the first year of the study, which included patient navigation (year 1 only), the screening completion rate was 38% for patients offered colonoscopy, 66% for those offered gFOBT, and 68% for those offered a choice.[80] While uptake overall was similar in the gFOBT group versus the choice group, it is clear that a "colonoscopy-only" referral resulted in substantially lower adherence. Adherence to screening declined significantly in subsequent years, reinforcing the importance of patient navigation, reminder systems, and other support strategies in achieving sustained adherence.[80,81] A non-US prospective trial corroborated the finding that offering a choice of FIT or colonoscopy led to significantly greater adherence than offering either test alone.[82] Although providing an array of screening options may enhance uptake and allows patients to exert their autonomy, in one study, offering multiple test options was shown to create confusion and decisional conflict, potentially leading to poor adherence.[83] There clearly is a need to provide clinicians with guidance and tools to facilitate decision making that best meet patients' needs and enhance uptake of screening.

The GDG recognized that the complexity and time requirements for implementing a choice among multiple tests in the clinician-patient encounter may be burdensome. The importance of offering a choice between structural or stool-based testing is included in this guideline in recognition of the role of patient values and preferences and as a practical implementation strategy to improve adherence; clinicians who experience time pressures that conflict with this imperative should look to practice enhancements that take advantage of team-based approaches among practice personnel.[84,85] Importantly, the choice of screening test may be limited by the local availability of high-quality test options or by patient access to tests based on cost or other factors. In this instance, there is little purpose in offering tests that are not readily available and accessible. However, clinicians should be prepared to describe/offer options that are available and introduce additional options if the patient does not appear to be accepting of the tests initially presented.

The information provided on characteristics of the tests in this guideline is designed to facilitate clinician-patient encounters and patient choices consistent with preferences and thus, it is hoped, to increase utilization of CRC screening. In addition, materials to facilitate decision making in selecting a test at the point of care have been developed by the ACS to facilitate implementation of this guideline and are available online (cancer.org/colonmd).[86,87]

Follow-up of positive noncolonoscopy screening tests

Implementation of the screening options included in this guideline is premised on the requirement that the appropriate follow-up to a positive (noncolonoscopic) test is a timely colonoscopy. The follow-up colonoscopy should not be considered a "diagnostic" colonoscopy but, rather, an integral part of the screening process, which is not complete until the colonoscopy is performed. The information provided to patients to facilitate a choice among tests must include the importance of follow-up of a positive (noncolonoscopic) test with colonoscopy. *Repeating a positive stool-based test to determine whether to proceed to colonoscopy is not an appropriate screening strategy.* A retrospective cohort study involving 70,124 patients with a positive FIT result examined the relationship between time to colonoscopy after a positive FIT result and risks of any CRC and of advanced-stage disease.[88] There were no significant differences in the risk of CRC with follow-up colonoscopy performed as late as 7 to 9 months after a positive FIT. After a delay of 10 months or more, however, there was a 48% greater risk of CRC, and the risk of stage III or IV disease was double that of those who received colonoscopy in the first few months after a positive FIT. The risks were even higher when colonoscopy was delayed for 12 months or more (odds ratio, 2.25 for any cancer and 3.22 for advanced-stage disease).[88]

The proportion of patients receiving timely colonoscopy follow-up of positive stool blood test results is fair to poor in many settings. Research has documented failure to complete follow-up colonoscopy within 12 months of a positive stool occult blood test in more than one-half of patients in some settings.[89,90] One study comparing completion rates among 4 health systems in the United States reported that rates of colonoscopy follow-up at 12 months varied from 58% to 83%. In contrast, higher rates of timely colonoscopy follow-up have been documented in organized screening programs. Programmatic elements associated with higher completion rates included explicit organizational targets for time to colonoscopy after a positive stool blood test and performance monitoring with monthly reporting.[91] A recent systematic review endorses the impact of giving providers performance data and reminders and also suggests that patient navigation may increase the rate of colonoscopy completion in this circumstance.[92]

When to Stop CRC Screening

- **The ACS recommends that average-risk adults in good health who have a life expectancy of greater than 10 years continue colorectal cancer screening through the age of 75 years (*qualified recommendation*).**

- **The ACS recommends that clinicians individualize screening decisions for individuals aged 76 through 85 years, based on patient preferences, life expectancy, health status, and prior screening history (*qualified recommendation*).**
- **The ACS recommends that clinicians discourage individuals over age 85 years from continuing screening (*qualified recommendation*).**

There is evidence from RCTs to support CRC screening up to age 75 years in average-risk populations. The US-based Prostate, Lung, Colon, and Ovarian Cancer Screening (PLCO) trial of FS enrolled patients aged 50 to 74 years, and all but one of the gFOBT trials that met acceptable quality standards enrolled patients to at least age 75 years. The US-based gFOBT trial enrolled patients through age 80 years.[26,29] Each of these trials demonstrated reductions in CRC mortality, thus providing an empiric basis for recommending screening average-risk individuals in good health up to age 75 years.

Beyond age 75 years, there is greater uncertainty about the benefit-harm tradeoff for CRC screening. On the basis of data from gFOBT randomized trials, the lag time to CRC screening benefit has been estimated to be 10 years,[93] although this benefit represents a combination of early detection (the benefit is realized sooner than 10 years) and prevention (the benefit is realized after 10 years). Thus, a screening benefit is generally believed to require a minimum 10-year life expectancy. Modeling results indicate that there is little incremental benefit in terms of LYGs for continuing screening after age 75 years in individuals who have been screened regularly from the earliest recommended starting age.[30] However, this often will not be the case, and the absence of a history of normal examinations will be of greater concern for those adults who have not been adherent to recommended screening in the years just before age 75 years. Although the current modeling analyses did not stratify by comorbidity status, previous studies have demonstrated that screening outcomes will be heavily influenced by comorbidity and functional status.[94-96] Moreover, CRC incidence and mortality continue to rise after age 75 years, thus indicating an ongoing opportunity to decrease CRC morbidity and mortality by screening individuals in this age group who are in good health (ie, are expected to live long enough to benefit and are at low risk for treatment complications). The impact of colonoscopy on preventing CRC in the elderly was recently examined in a prospective observational cohort study of Medicare beneficiaries aged 70 to 79 years who had no diagnostic or surveillance colonoscopies in the past 5 years.[97] Among adults aged 70 to 74 years, the absolute risk of CRC over 8 years was reduced by 16% in the group undergoing colonoscopy versus the no-colonoscopy group (2.19% vs 2.62%, respectively), while risk reduction was notably less in individuals aged 75 to 79 years who underwent colonoscopy versus the no-colonoscopy group (2.84% vs 2.97%, respectively).

The harms of screening and diagnostic colonoscopy, including bleeding, perforation, complications of anesthesia, and hospitalization, are greater in the elderly, particularly those older than 80 years, and the risk increases with increasing comorbidity burden.[97,98] In the Medicare cohort study mentioned above, the risk of adverse events from colonoscopy was nearly twice as high among individuals aged 75 to 79 years (10.3 per 1000) compared with individuals aged 70 to 74 years (5.6 per 1000).[97]

Given increased competing mortality risks and the increased risk of colonoscopy-associated complications with greater age, the focus of screening among individuals aged 76 to 85 years should be on healthy individuals with no or few comorbidities who are expected to live at least 10 years. The yield would be expected to be higher in those not up to date with screening.[95] If there is concern regarding colonoscopy risks, then noncolonoscopy options may be preferable. Given the paucity of evidence to inform screening decisions in this age group, patient preference should weigh heavily in the decision. A recent examination of older individuals' views suggested that patients may be receptive to a discussion with a clinician of screening cessation based on age and health status, but not emphasizing limited life expectancy.[99] There are tools that are useful for estimating life expectancy considering an individual's comorbidity and functional status.[100,101]

After age 85 years, the competing mortality risks and risks of CRC screening complications are sufficiently high that it is reasonable to conclude that the potential harms of screening outweigh the potential benefits in this age group. Consequently, health care professionals should not offer screening to individuals in this age group. There may be exceptional circumstances when screening might be considered, such as the individual in excellent health who has not been engaged in routine screening and strongly desires testing; but, in general, screening should be discouraged in individuals older than 85 years.

Options for CRC Screening
Stool-Based CRC Screening Tests

There is consistent RCT evidence to support the use of stool testing for CRC screening. The first tests shown to be effective in screening for CRC were guaiac-based tests (gFOBT), which detect peroxidase activity involving the heme portion of the hemoglobin molecule. Consequently, both low-sensitivity and high-sensitivity gFOBT are vulnerable to false-positive results from nonsteroidal anti-inflammatory drugs that can cause upper gastrointestinal (GI) bleeding, red meat, and dietary peroxidases (found in some vegetables and fruits) as well as false-negative results

from antioxidants, such as vitamin C.[102] In contrast, immunochemical tests (FITs) use antibodies that selectively detect the globin component of human hemoglobin, which provides advantages over gFOBT. Because globin is degraded by digestive enzymes found in the upper GI tract, the positivity of FIT is generally not influenced by upper GI bleeding.[102] Furthermore, because the antibody is specific to human hemoglobin, FITs are not vulnerable to interference from medications, animal hemoglobin (red meat), or peroxidases from foods, thus eliminating the need for the dietary restrictions that are recommended with gFOBT. A third stool test is the mt-sDNA test, which combines an immunochemical assay for hemoglobin, and assays for aberrantly methylated *BMP3*, *NDRG*, and *NDRG4*, mutated *K-ras*, and *β-Actin* in cells exfoliated from colonic neoplasms.[103] Currently, there is only one mt-sDNA test marketed in the United States.[104] (See the online Supporting Information for a more detailed discussion of each test.)

All manufacturers of stool tests recommend that stool collected for CRC screening should be collected at home. However, because gFOBT and FIT require the collection of only small samples of stool, some clinicians bypass the recommendation for home testing by using a single sample of stool collected during digital rectal examination. It has been demonstrated that this practice fails to detect up to 90% of cancers.[105,106] Because of this very low sensitivity for CRC and lack of validation studies, CRC screening guidelines recommend against in-office testing with stool collected during digital rectal examination. Some practices have implemented screening programs that give patients the option of testing a spontaneously passed bowel movement in a dedicated clinic bathroom.

Performance characteristics of individual gFOBT and FIT versions vary. The US Food and Drug Administration (FDA) clearance process does not require manufacturers to provide information on the sensitivity or specificity of their test for the detection of CRC or adenomatous polyps, and tests specifically are cleared only for the detection of occult blood, not for CRC screening. This approach to clearance poses a challenge to clinicians seeking to choose a stool test with high accuracy. The poor performance of nonrehydrated, low-sensitivity gFOBT means that these gFOBT variants cannot be recommended and should not be used for CRC screening, although they still are available in the marketplace. At the time of publication, the only guaiac test evaluated in a population-based study shown to meet performance standards to qualify as a high-sensitivity test (HSgFOBT) is Hemoccult II Sensa (Beckman Coulter Inc., Brea, CA), although there may be other variants that have high sensitivity. The sensitivity of HSgFOBT ranges from 62% to 79%, with specificity ranging from 87% to 96%.[26,107,108]

FITs consistently demonstrate superior sensitivity for cancer and advanced neoplasia and slightly lower specificity compared with low-sensitivity gFOBT. Compared with HSgFOBT, the sensitivity and specificity of FIT tend to be similar or superior. Sensitivity for single-sample FIT ranges from 73% to 92%, and specificity ranges from 91% to 97%.[102,109-112] However, most brands of FIT have limited evidence demonstrating their accuracy for detection of CRC. Daly et al found published data from colonoscopy-confirmed studies of FIT performance for only 6 of the 26 versions of FIT sold in the United States.[113] Because studies have shown variable performance of different FITs across studies in which individuals undergo multiple tests to compare outcomes,[114-116] it should not be assumed that versions of FIT that lack published data have suitable performance characteristics.[117]

The original, low-sensitivity guaiac tests have largely been superseded by HSgFOBT and FIT in organized screening programs around the world, and a similar shift is underway in the United States.[102,118-120] National surveys of CRC screening test utilization do not distinguish between FIT and gFOBT, but overall use of stool testing in the United States is low. In 2015, 7.2% of US adults aged 50 years and older reported having completed a take-home stool-based test (FIT or gFOBT) within the past year.[65] The effectiveness of annual testing depends upon program sensitivity, which depends on multiple, annual opportunities for detection before a cancer or an advanced lesion becomes symptomatic.[121]

In the 2018 MISCAN modeling analysis for the general population under the increased-risk scenario, in which all stool tests were grouped in the same class, annual FIT from ages 45 to 75 years yielded 94% of the LYGs compared with the benchmark strategy (colonoscopy every 10 years from ages 45 to 75 years) and was found to be a model-recommendable strategy.[34] In contrast, annual HSgFOBT from ages 45 to 75 years was not among the model-recommendable strategies (Table 2).[34] Although annual HSgFOBT and FIT from ages 45 to 75 years achieved the same LYGs (403 LYGs), HSgFOBT was less efficient; for a given number of colonoscopies, more LYGs were achievable with FIT compared with HSgFOBT, because the higher false-positive rate of HSgFOBT led to more colonoscopies.

There are no direct harms of CRC screening associated with HSgFOBT and FIT. Harms are associated with injury to the colon or other complications related to colonoscopy performed after a positive HSgFOBT[29] (see Colonoscopy section, below).

In the guideline update, HSgFOBT (eg, Hemoccult II Sensa) remains an option for CRC screening, because it has high sensitivity approaching that of FIT and because of its

lower costs compared with FIT, making it an attractive option in low-resource settings where FIT may not be affordable.

The best evidence for the performance of mt-sDNA testing comes from a large, manufacturer-funded, multicenter, comparative trial of mt-sDNA and FIT testing in average-risk individuals using colonoscopy as the reference standard.[103] The sensitivity of mt-sDNA for CRC was 92.3%, compared with 73.8% for FIT. When the specificity of FIT was matched to that of mt-sDNA (86.6%), its sensitivity to detect CRC improved to 77% but remained significantly below that of mt-sDNA. The sensitivity for advanced adenomas and sessile serrated polyps also was higher for mt-sDNA compared with FIT (42.4% vs 23.8%). One significant advantage of mt-sDNA compared with FIT was its higher detection rate of serrated sessile polyps >1 cm (sensitivity was 42.4% for mt-sDNA and 5.1% for FIT). The specificity of mt-sDNA was significantly lower than that for FIT: 89.8% versus 96.4%, respectively, for participants with a negative colonoscopy, indicating a higher false-positive rate with mt-sDNA.

Like other stool-based tests, the harms of mt-sDNA are associated with the harms of colonoscopy performed for the follow-up of positive tests (see Colonoscopy section below). However, an issue unique to mt-sDNA compared with FIT and HSgFOBT is the uncertainty about the interpretation of a negative follow-up colonoscopy after a positive finding on mt-sDNA. Reported results from the mt-sDNA test currently available in the United States do not indicate which component of the test (FIT or DNA) yielded the positive result. A positive stool DNA test followed by a negative colonoscopy may be caused by failure to detect a visible lesion, neoplastic changes that are not yet visible, or the presence of noncolonic aerodigestive or supracolonic neoplasms. Patients with positive mt-sDNA results and a negative follow-up colonoscopy may undergo more aggressive short-term surveillance because of heightened concerns related to unresolved false-positive findings. In 2 follow-up studies of patients with false-positive results on mt-sDNA with median follow-up of approximately 4 years, no excess rates of CRC or aero-digestive malignancies were identified.[122,123] In a more recent study by Cooper et al that included follow-up mt-sDNA, colonoscopy and upper endoscopy among 12 patients who had prior positive mt-sDNA results and a negative colonoscopy, 7 patients had negative stool tests and colonoscopies, whereas 3 among the remaining 5 patients had positive findings on their follow-up colonoscopy (2 advanced and 1 nonadvanced adenoma).[124] Longer term follow-up will be required to provide greater reassurance and guide management, but the findings from Cooper et al are a reminder that high-quality colonoscopy is critically important, especially in the proximal colon, when following up positive findings on an mt-sDNA test.

In the general population modeling analysis conducted for this guideline update, mt-sDNA was not shown to be a model-recommendable test. Annual mt-sDNA was found to be inefficient within the class of stool tests because of the higher number of colonoscopies required per LYG (Table 2).[34] Mt-sDNA every 3 years (the screening frequency on which FDA clearance was based) yielded 88% of the LYGs from colonoscopy every 10 years (less than the a priori criterion of 90%) and 93% of the LYGs compared with annual FIT testing (Fig. 5).[34]

The GDG concluded that mt-sDNA warrants inclusion among test options based on its sensitivity for detecting CRC, its improved advanced adenoma and serrated sessile polyp detection compared with FIT, and evidence indicating that some adults would choose screening with mt-sDNA over other CRC screening tests.[125]

Options for CRC Structural (Visual) Examinations

Structural (visual) examinations used for CRC screening are procedures that allow the examiner a visual inspection of the bowel. These include endoscopic examinations (FS and colonoscopy) and a radiologic examination (CTC). One feature that distinguishes structural examinations from stool testing is the longer recommended screening interval (*see Supporting Information for a more detailed discussion of each test*).

Structural examinations place more demands on patients than stool testing. All structural examinations require bowel cleansing before the examination: for FS, bowel cleansing rectal enemas are recommended and, for colonoscopy and CTC, the most common bowel cleansing preparation involves ingestion of polyethylene glycol oral laxatives, and patients are usually advised to replace solid foods with a liquid diet the day before bowel cleansing. In a recent systematic review of the effectiveness of various bowel cleansing protocols, the USMSTF noted that the length of time between the last dose of preparation and the initiation of colonoscopy is correlated with the quality of cleansing in the proximal colon. When bowel cleansing is split between the day before and the day of colonoscopy, the data consistently demonstrate superior bowel cleansing performance.[126] On the basis of these findings, the USMSTF strongly recommends use of a split-dose bowel cleansing regimen for elective colonoscopy (strong recommendation, high-quality evidence) and, alternatively, a same-day regimen for patients undergoing an afternoon examination (strong recommendation, high-quality evidence).[126] Colonoscopy usually is performed with sedation, thus requiring a day away from work and a chaperone to provide transportation. FS and CTC usually are performed without sedation, entailing less time commitment than colonoscopy.

The adequacy of bowel preparation and expertise of clinicians performing structural examinations are critical to the effectiveness of CRC screening with structural examinations. Primary care clinicians should ascertain the degree to which recommended quality-assurance programs[127-131] are in place and, in particular, whether the practice is monitoring performance metrics, including the adenoma detection rate.

Colonoscopy

Colonoscopy is the most frequently used CRC screening modality in the United States.[65] It allows direct visual inspection of the entire colon and same-session detection, biopsy, and removal of polyps. Colonoscopy also is used for further evaluation of patients who have had a positive test result on a noncolonoscopy CRC screening examination. The best direct evidence of effectiveness comes from a large, prospective, observational cohort study[132] in which the authors reported a hazard ratio (HR) for CRC mortality of 0.32 (95% confidence interval [95% CI], 0.24-0.45) comparing 1 or more colonoscopy versus no colonoscopy over 24 years, with better results for distal cancers (HR, 0.18; 95% CI, 0.10-0.31) than for proximal cancers (HR, 0.47; 95% CI, 0.29-0.76). Incidence reduction was demonstrated for individuals who had a negative colonoscopy, with an HR of 0.53 (95% CI, 0.40-0.71).[132] In the systematic evidence review, colonoscopy sensitivity for detecting adenomas ≥6 mm (using CTC as the comparator) ranged from 75% to 93%, with a specificity of 94%, and sensitivity for adenomas ≥1 cm ranged from 89% to 98%, with a specificity of 89%.[29]

The 3 CISNET models that informed the USPSTF's 2016 CRC screening recommendation statement[44] estimated that colonoscopy screening every 10 years from ages 50 through 75 years would reduce CRC incidence by 62% to 88% and mortality by 79% to 90%, averting 22 to 24 deaths from CRC per 1000 individuals screened. The median LYGs (270) was superior to that of other testing options.[30] In the general-population MISCAN modeling conducted for the ACS using updated incidence data, colonoscopy every 10 years from ages 45 through 75 years provides a greater reduction in the lifetime risk of CRC and somewhat more LYGs and CRC deaths averted than other recommendable strategies (Fig. 5),[34] although it requires more than twice the number of lifetime colonoscopies as stool-based testing (Table 2).[34]

There is a risk of overdetection and removal of small polyps that have low likelihood of progressing to cancer, increasing the risks associated with polypectomy and potentially leading to unnecessary recommendations for short-term surveillance. Colonoscopy is significantly more likely to miss sessile serrated polyps than typical adenomas.[133,134]

The primary harms from screening colonoscopy include perforation and bleeding, which occur more commonly if polypectomy is performed. The USPSTF evidence synthesis estimated that the risk of perforation is approximately 4 per 10,000 colonoscopies, and the risk of major bleeding is approximately 8 events per 10,000 colonoscopies.[29] The complication rate of colonoscopies performed to follow up positive noncolonoscopy screening tests is significantly higher than that for primary screening colonoscopies.[26,40] Importantly, the harms of colonoscopy rise significantly and nonlinearly with age and comorbidity burden.[135] In a population-based study of 1.6 million Californians undergoing colonoscopy that was published after the USPSTF evidence review, the rate of lower GI bleeding was 5 per 10,000 among those not undergoing biopsy and 36 per 10,000 among those undergoing biopsy or other intervention. The comparable perforation rates were 3 per 10,000 and 6 per 10,000, respectively. Thirty-day non-GI complications were reassuringly low in that study; the risk of myocardial infarction was 2.5 per 10,000 for colonoscopy without biopsy and 4 of 10,000 with biopsy, which was lower than that for comparator procedures (joint aspiration/injection and lithotripsy).[41]

Computed tomography colonography

CTC, sometimes referred to as "virtual colonoscopy," involves the acquisition of thin-slice computed tomography images that can be evaluated as 2-dimensional images or reconstructed into 3-dimensional images of the colorectal lumen, creating views previously available only through a colonoscope. In the 2 largest and highest quality studies of CTC, CRC detection rates with CTC were essentially identical to those achieved with optical colonoscopy.[136,137] A systematic review and meta-analysis of 49 studies using colonoscopy as the reference standard estimated that the sensitivity of CTC for cancer detection was 96.1%, and the sensitivity for adenomas >6 mm ranged from 73% to 98% with a specificity of 89% to 91%.[138]

Screening every 5 years with CTC from aged 50 through 75 years was considered a model-recommendable strategy in the 2016 analyses conducted for the USPSTF.[30,31] The general-population modeling analysis commissioned for the ACS, using updated incidence data, also found that CTC every 5 years from ages 45 through 75 years was a model-recommendable strategy (Table 2).[34]

Adverse events associated with CTC include those associated with bowel preparation, such as abdominal pain, examination related pain, and vasovagal syncope or presyncope. Potentially more serious harms, although very rare, include perforation and the possibility of an induced cancer associated with radiation exposure from single or multiple examinations. A more common occurrence, which may or may not be beneficial, is the identification of extracolonic findings.

Perforation, mostly due to insufflation, is very rare and is estimated to occur in less than 2 per 10,000 procedures.[29] As with any imaging test, radiation exposure commonly is raised as a potential harm, although new screening protocols have resulted in substantial dose reductions, with average doses ranging from <1 to 2 millisieverts (mSv) in recent reports,[139,140] which is less than the 3-mSv-per-year estimate of average background radiation exposure in the United States.[141] This low level of exposure every 5 years has been judged to be a negligible harm when considered in the context of the potential LYGs from avoiding a premature CRC death.[142]

The detection of incidental extracolonic findings with CTC screening is an area of concern. The USPSTF evidence report concluded that, based on empiric evidence, it remains unclear whether extracolonic findings represent a net benefit or harm.[26] In their review of 21 studies ranging in size from 75 to 10,286 patients, Lin et al observed that E4 findings, which are potentially important findings that are judged to require further follow-up, ranged from 1.7% to 12%.[26]

Patients with polyps of significant size will require follow-up colonoscopy to remove the polyps. While same-day colonoscopy for polyp removal can be offered without the need for additional preparation, this requires coordination between medical specialists (radiologists and endoscopists) and facilities (radiology departments and endoscopy suites).[143] If this coordination is not in place, patients who have abnormalities detected at CTC must be scheduled for follow-up colonoscopy in the future, necessitating a repeat of the cathartic bowel preparation and additional time commitment.

Flexible sigmoidoscopy

FS, the first visual inspection examination demonstrated to be effective for CRC screening,[144,145] is an endoscopic procedure that examines the lower half of the colorectal lumen. It is typically performed without sedation and with a more limited bowel preparation than the other structural examinations, usually 1 or 2 enemas. CRC incidence and mortality reductions have been demonstrated by 4 RCTs of FS with 1 or 2 screening examinations (at intervals of every 3-5 years).[145-148] In the pooled analysis conducted for the USPSTF,[26,29] CRC mortality was reduced by 27% over 11 or 12 years of follow-up (relative risk, 0.73; 95% CI, 0.66-0.82). Mortality reduction was significant for distal CRC, but not proximal CRC. CRC incidence was reduced by 21%. PLCO investigators reported significant reductions in the incidence of both distal and proximal cancers.[29] A recent 17-year follow-up of the UK Flexible Sigmoidoscopy Screening Trial reported a 26% reduction in the incidence of CRC and a 30% reduction in mortality. As in the pooled analysis, the overall effectiveness of screening in the UK trial

derived from the detection of distal lesions, as there was no significant reduction in incidence or mortality for proximal cancers.[149] A recent pooled analysis of 3 of the 4 trials (PLCO, SCORE, and Norwegian Colorectal Cancer Prevention [NORCCAP]) with a median of 10 to 12 years of follow-up reported an overall 21% reduction in CRC incidence and a 27% reduction in mortality with screening FS.[150] However, neither incidence nor mortality was lowered by FS in women aged 60 years or older, primarily because of the poorer performance of FS in detecting proximal colon cancers, which disproportionately affected older women.

In the MISCAN modeling analyses adjusted for increased incidence, FS every 5 years from ages 45 through 75 years was a model-recommended strategy. In contrast, assuming stable incidence, in the CISNET analysis conducted for the USPSTF 2016 update, FS alone every 5 years or 10 years in adults aged 50 to 75 years was not a model-recommended strategy.[30] The greater efficiency of FS in the updated model is likely attributable to the observation that most of the increased incidence is confined to the rectum and distal colon (Fig. 5).[34]

The use of FS as a CRC screening test has declined markedly over the past several decades in the United States, having been replaced by colonoscopy as the primary structural examination. As of 2010, only 2.5% of adults aged 50 to 75 years reported having an FS in the recommended interval, compared with 60% for colonoscopy.[151]

Despite evidence for the efficacy of FS as a CRC screening test in expert settings, the low level of utilization of FS in the United States raises questions as to whether community-based clinicians have received adequate training or perform a sufficient number of procedures to maintain proficiency. Standards, including depth of insertion, adenoma detection rate, and adequacy of preparation, have been proposed,[130] but rigorous quality standards are not currently in place in the United States. Despite the robust body of RCT evidence demonstrating the effectiveness of FS, low utilization rates coupled with quality concerns led the GDG to consider removing FS as a recommended test. The decision was made to retain it based primarily on the foundation of evidence it provides of a mortality reduction benefit from screening with structural examinations. In addition, there was an acknowledgment that FS might be the primary structural examination available in some geographic areas.

Emerging Technologies Not Currently Recommended for Routine Screening

The following tests are not among the list of recommended CRC screening options but have been cleared by the FDA for use in special circumstances.

Methylated Sept9 DNA

The FDA recently cleared a blood test to detect circulating methylated Septin 9 DNA (m*SEPT9*), a molecular CRC biomarker shed by the tumor into the circulation, as a test for average-risk individuals who have repeatedly refused other forms of CRC screening.[152] According to the FDA, all tests that are available and recommended in the USPSTF CRC screening guidelines should be offered and declined before offering the mSept9 test. Because patients with a positive mSept9 test should be referred for colonoscopy, they must be prepared to undergo a follow-up test that they previously had rejected for screening.

Most studies of mSept9 have been tandem studies comparing advanced neoplasia detection rates with a conventional CRC screening test. The USPSTF evidence report included one prospective study of mSept9 that showed a sensitivity and specificity of 48% and 91%, respectively, for detecting CRC in an average-risk population scheduled to undergo colonoscopy.[29,153] Since the USPSTF review, a retesting of samples from the same prospective cohort using a newer version of the test yielded an improved sensitivity for cancer and advanced adenomas of 68% but a lower specificity of 80%.[154] A second study using the newer version of the test involving US subjects undergoing screening colonoscopy reported similar sensitivity and specificity for screen-detected CRC (73% and 82%, respectively).[155]

Although these studies demonstrate improving test sensitivity, concerns remain about poor specificity compared with recommended screening options and the limited base of evidence in asymptomatic, screening populations. In addition, there has been no microsimulation modeling of the newer version of the test to estimate its benefit, a benefit-harm ratio, or a screening interval for regular testing, which also has not been established by the manufacturer. In addition, mSept9 is a novel blood test for CRC early detection with no comparable screening tests from which to infer a benefit in terms of critical outcomes (CRC mortality or incidence reduction), as there are for the included screening test options. Importantly, the test has not been cleared by the FDA for unrestricted use in general routine screening. Going forward, the performance of plasma DNA tests should be monitored. An accurate blood test would have obvious value in the repertoire of screening options, and even a test with somewhat poorer performance would likely make a contribution in adults persistently nonadherent to screening recommendations. In both instances, adherence would likely be high. However, based on the limitations noted above, at this time, mSept9 is not included in this guideline as an option for routine CRC screening for average-risk adults.

Capsule endoscopy

Early versions of capsule endoscopy, also known as capsule colonoscopy, principally were used to evaluate the small bowel, but interest has grown in the past decade to apply this technology to CRC screening. The device incorporates a camera on both sides of an ingestible capsule that captures images of the colon and rectum as it passes through the GI tract. The images are recorded and stored in an external device worn by the patient and later analyzed by a clinician. The test is complete when the capsule is passed in the stool.[156]

In a systematic review[157] of the diagnostic accuracy and safety of colon capsule endoscopy for the detection of colorectal polyps in persons with signs or symptoms of CRC or at high risk for the disease, the reported pooled sensitivity and specificity of capsule endoscopy were 87% (95% CI, 77%-93%) and 76% (95% CI, 60%-87%), respectively, for the detection of a colorectal polyps $\geq$6 mm. The results showed improved test performance for larger polyps (at least 10 mm), with pooled sensitivity of 89% (95% CI, 77%-95%) and specificity at 91% (95% CI, 86%-95%).[157] Adverse events associated with capsule endoscopy were reported in <4% of patients, which mostly included nausea, vomiting, abdominal pain, and fatigue from the required bowel preparation.[157] Capsule retention is the most serious reported problem and occurred in 0.8% of patients (95% CI, 0.2%-2.4%). Like other endoscopic procedures, capsule endoscopy requires adequate cleansing of the colon and, if polyps are found, a colonoscopy may be needed to further investigate and remove precancerous polyps.

In 2014, the FDA cleared the capsule endoscopy system "for use only in patients who had an incomplete optical colonoscopy with adequate preparation, and a complete evaluation of the colon was not technically possible"[158] and, in 2016, capsule endoscopy was cleared for identifying the location of colon polyps in patients suffering from lower GI bleeding.[159] Capsule endoscopy does not have FDA clearance for CRC screening.

Decision Making and Clinical Considerations

Clinician roles in decision making

This update of the ACS CRC guideline emphasizes the importance of patient preferences and choice to improve uptake and adherence to CRC screening (see Choice of Screening Test, above). Health care professionals and the systems in which they work have a vital role in implementing the ACS recommendation that adults undergo regular screening with either a structural (visual) examination or a high-sensitivity stool-based test, depending on patient preference and test availability. In most settings, either an FIT or an HSgFOBT will be available through the practice and, depending on the patient's insurance coverage, mt-sDNA may be an option. Colonoscopy is the most commonly available structural examination. In a growing number of settings, CTC will be available and, for non-Medicare

beneficiaries, may be covered by the patient's insurance. In some settings, FS may be the most readily available structural examination. From a practical implementation standpoint, the choice offered will usually be among 1 or 2 stool-based tests and 1 or 2 structural examinations. The offering of a choice applies primarily to the *uptake* of screening by individuals who are initiating screening or have failed to adhere to prior recommendations for screening; for these patients, exploring test preferences may be particularly effective to improve adherence to screening. For individuals who have been adherent to screening, it is reasonable for clinicians to continue ordering the same previously completed test without offering new options, unless the patient raises specific concerns. The ACS recognizes that, in some settings (eg, rural or low-resource settings), there may be only one high-quality screening option available for many patients, in which case, discussing a menu of unavailable options is not useful.

Resources for clinicians and patients

This guideline provides a list of options for CRC screening along with considerations for decision making to assist health professionals and patients in selecting the option most likely to be completed (Table 3). In addition, a clinicians' guide and decision support materials have been developed to accompany this guideline to facilitate the decision-making process.[86] It is anticipated that these materials will help both uptake of and adherence to CRC screening by better aligning the selected screening test with patient preferences. The materials can be found online at cancer.org/colonmd.[87]

Patient considerations of cost and reimbursement

There are several important issues for clinicians and patients to keep in mind with regard to the costs of CRC screening. There is wide variation in the costs of screening, depending on which test is chosen, with guaiac and fecal immunochemical tests at the low end ($20-$30),[160] colonoscopy usually priced between $1000 and several thousand dollars,[161] and other testing methods falling between these 2 extremes. Patient out-of-pocket costs for each of these tests may also vary, depending on a variety of factors, including insurance status (insured vs uninsured), type of insurance (ie, low-deductible vs high-deductible plans), and site of service (eg, hospital vs free-standing endoscopy center and within-network vs out-of-network). Insurance policy and interpretation of coding rules may also impact patient costs for CRC screening.

A stipulation in the Patient Protection and Affordable Care Act (ACA) requires provision of preventive services that receive an "A" or "B" recommendation from the USPSTF, including CRC screening, with no copay or deductible for beneficiaries. This provision applies to Medicare and to most commercial insurance plans, and there is evidence that the ACA's elimination of cost-sharing contributed to increases in CRC screening among low-income Medicare beneficiaries.[162] This waiver of cost-sharing is required only for screening examinations. Many patients choosing colonoscopy as their initial screening test will have the procedure with no out-of-pocket costs, but patients covered by Medicare currently incur costs if a polyp is removed, and patients with commercial insurance may still be charged inappropriately for polyp removal during an examination initiated for screening (see below). Furthermore, ACA provisions have been interpreted differently by some insurers; some insurers have judged a personal history of cancer, polyps, or a family history as defining all subsequent colonoscopies as diagnostic, especially if they are performed at shorter intervals than were recommended by the USPSTF for average-risk adults, thus resulting in charges to the patient. Furthermore, if a patient is first screened with a stool test or any other noncolonoscopy examination, then most insurers interpret a colonoscopy performed to follow up a positive initial screen as a diagnostic procedure, meaning that the patient becomes responsible for cost-sharing.[163] A small number of insurers, recognizing that this policy encourages some patients to choose colonoscopy to avoid possible out-of-pocket costs, have opted to treat the colonoscopy after a positive stool test as a continuation of the screening process; legislation in Oregon requires insurers that sell products in that state to treat the follow-up colonoscopy in this manner.[164] Patients living in states that do not have this provision should be informed that, if they choose a noncolonoscopy option as their initial screening test and have an abnormal result, then they may be responsible for some of the costs of colonoscopy. This ACS guideline update strongly recommends that follow-up colonoscopy should be regarded as a part of the continuum of the screening process rather than a diagnostic procedure.

A second policy issue that may impact patient cost also relates to the operational definition of a screening colonoscopy. During implementation of the ACA, many insurers used a narrow classification of screening colonoscopy to guide application of the "no cost-sharing" provision. If a lesion was biopsied or removed during a procedure that had originally been scheduled as a screening colonoscopy, the procedure would often be recoded as a diagnostic examination and thus belatedly and unexpectedly become subject to patient cost-sharing. In 2013 the US Departments of Labor, Health and Human Services, and the Treasury clarified that this was not the intent of the ACA provision on preventive services, issuing guidance to insurers stating that, "polyp removal is an integral part of a colonoscopy" and indicating that commercial plans "may not impose cost-sharing with

respect to a polyp removal during a colonoscopy performed as a screening procedure."[165] Subsequent communications to insurers clarified that anesthesia and pathology services and bowel preparation medications provided in conjunction with a screening colonoscopy must also be covered without cost-sharing.[166-168] Unfortunately, these rule clarifications do not currently apply to the Medicare program; Medicare beneficiaries frequently experience unexpected out-of-pocket liabilities for "screening" colonoscopy if tissue is sampled during the procedure. A recent modeling analysis showed that waiving copays would have a favorable impact on health improvements and costs.[169] Changing the implementation of this element of the ACA in the Medicare program will require federal legislative action.

Insurance coverage policies related to CRC screening are largely driven by the linkage of the ACA's preventive services provisions to USPSTF recommendations. The current USPSTF recommendation to begin CRC screening at age 50 years sets a minimal threshold for insurers; there is no prohibition against coverage for screening at an earlier age. However, it is likely that, in the near term, many individuals aged 45 to 49 years will experience challenges with insurance coverage for their screening examinations and may experience out-of-pocket costs if they seek to begin screening. The ACS and other organizations are working aggressively to educate insurers and policymakers on the rising rates of CRC among younger individuals, the evidence in support of screening for individuals aged 45 to 49 years, and the importance of expanding screening coverage to this group.

Interventions to increase utilization and adherence

Poor utilization of and adherence to CRC screening is a major contributor to avoidable CRC mortality in the United States and has been a persistent challenge since the earliest prospective studies of CRC screening were conducted. A systematic review of 100 prospective studies of participation after first-time invitation found that overall adherence was 47% for gFOBT, 42% for FIT, 35% for FS, 28% for colonoscopy, and 22% for CTC.[170] Only 62.4% of adults older than 50 years in the United States report recent CRC screening consistent with guideline recommendations, with lower rates among American Indians and Alaska Natives (48.4%), Hispanics (27.4%), and the uninsured (25.1%).[171] As noted above, screening rates vary by age (only 45.3% of adults aged 50-54 years report recent CRC screening vs 57.9% of adults aged 50-64 years and 71.8% for adults aged 65-75 years), by education (only 46.7% of adults with less than a high school education report recent CRC screening vs 70.7% of college graduates), and by insurance status (only 25.1% of uninsured adults report recent CRC screening vs 65.6% of insured adults).[171]

Optimizing adherence to CRC screening will require a multipronged approach that addresses the barriers to screening at the individual, provider, organizational, and policy levels with evidence-based interventions. Multicomponent interventions to reduce structural barriers have been found to have greater effects on utilization of colonoscopy and FOBT than when single interventions were used.[172]

One of the most powerful factors for increasing adherence to CRC screening is clinician recommendation. A systematic review reported overwhelming evidence that provider recommendation significantly improves screening rates.[173] Furthermore, as noted above, it has been demonstrated that offering patients a choice of CRC screening tests rather than recommending a single test improves adherence to screening and likely conveys to patients the importance of the recommendation.

Several visit-based strategies have been shown to be effective in improving screening rates within practices and integrated systems, especially reminder systems to help care teams identify patients who are due for screening.[46,174,175] Other effective visit-based strategies include "opportunistic screening" or "in-reach" methods, including offering screening during nurse-driven influenza vaccination clinics.[176-178]

Evidence examining the impact of decision aids on CRC screening adherence is mixed. Several systematic reviews have found that, whereas decision aids increase screening knowledge and modestly increase screening, there were no significant differences in screening interest or behavior among individuals who were exposed to decision aids compared with those who were given general information about CRC screening.[46,79] A study examining the impact of combining a decision aid with patient navigation in a diverse, vulnerable patient population did demonstrate a strong impact on screening completion but was unable to separate the effects of the decision aid from patient navigation.[179] A recent study incorporating an iPad-based CRC decision aid with test-ordering capability into the office visit demonstrated a doubling of CRC screening completion from 15% to 30% among vulnerable primary care patients who were randomized to the intervention.[180]

Nonoffice-based strategies, including "outreach" strategies whereby patients receive invitations to screening via mail, have shown a 5% to 15% increase in adherence rates. Mailed reminders with or without FIT kits/gFOBT cards timed to a scheduled clinic appointment can increase screening.[174,176,181-187] Open-access endoscopy has not been demonstrated to increase scheduling of screening endoscopy, although it is associated with higher procedure completion rates.[188]

RCTs have shown that patient navigation is an effective intervention for implementing stool-based and colonoscopy-based screening programs. Navigation is particularly helpful

in increasing CRC screening in vulnerable populations.[189-198] Investigators have offered helpful guidance on key considerations when designing a successful navigation program.[199,200] Tailored patient navigation that allows the patient's care team to address specific patient barriers to screening, including language, has been shown to be more effective than standard navigation.[195,196,201] Personal invitation letters, preferably signed by the care provider, and reminders mailed to all nonattendees are also highly effective in enhancing CRC screening acceptance.[202]

Multifaceted interventions that target multiple levels of care and consider factors outside the individual clinician's control represent the most effective strategies to enhance CRC screening uptake and adherence, particularly in populations that have multiple barriers to CRC screening (eg, financial barriers, lack of health insurance, low income, low educational attainment, and language barriers). For example, the ACA's elimination of cost-sharing was associated with an increase in utilization of CRC screening in adults with low socioeconomic status likely because of the removal of financial barriers.[162] In community health center settings, Baker et al found that, compared with usual care (computerized reminders, standing orders for home FIT distribution by medical assistants, and clinician feedback on CRC screening rates), patients in an intervention group that also received a mailed reminder letter, a free FIT with low-literacy instructions, a postage-paid return envelope, and automated follow-up telephone and text messages were much more likely than those in usual care to complete screening with a stool test (82.2% vs 37.3%; $P < .001$).[203] After 2 years of follow-up, 71.6% of the intervention group remained fully up to date with CRC screening.[204] Several organizations have compiled valuable resources to facilitate the implementation of multifaceted interventions to increase uptake of and adherence to CRC screening (see Supporting Information).

Discussion

Changes From the Previous Guideline

The most notable change from the 2008 ACS guideline is the recommendation for all average-risk adults to initiate screening for CRC at age 45 years. In addition, the 2018 update provides more specific guidance regarding when to discontinue CRC screening, which was not specifically addressed in the previous guideline. The 2008 guideline stated that CRC prevention should be the primary goal of screening and that tests that detect both early cancer and adenomatous polyps should be encouraged if resources are available and the patient is willing to undergo an invasive test. Although this update places value on both CRC incidence and mortality reduction, the GDG chose not to prioritize among screening tests, emphasizing instead that

screening utilization and adherence could be improved and the benefits of screening more fully achieved by offering a choice of tests. This guideline includes 6 test options for CRC screening: specifically, annual FIT or HSgFOBT, mt-sDNA every 3 years, colonoscopy every 10 years, CTC every 5 years, and FS every 5 years. Recommended screening intervals remain unchanged since 2008. Double-contrast barium enema is no longer included as an acceptable screening option (see Supporting Information Table 1).

Considerations in Lowering the Starting Age to 45 Years

The overall quality of the evidence and the balance of benefits and harms were judged to support a strong recommendation for CRC screening in adults aged 50 years and older with any of the included test options. Because until now the recommended age to start has been 50 years, there is very limited direct evidence to support a younger starting age other than the 3 RCTs of gFOBT that started enrollment at age 45 years, although no age-specific results have been published.[205-207] As soon as screening begins to occur regularly in the group aged 45 to 49 years, observational evidence on the performance and outcomes of screening will accrue. The GDG relied on disease burden data and modeling studies to address the question of optimal starting age. Thus, the starting age of 45 years has been designated as a qualified recommendation given the limitations of the evidence base.[38] An absolute mortality benefit in younger age groups will be lower than for older adults and, as some of our reviewers have noted, there will be some increased patient burden associated with a younger starting age. However, the recommendation places a high value on the potential years of life saved, addresses anticipated rising incidence going forward, and is expected to contribute to the reduction in disparities in incidence before age 50 years in some racial groups.[33,34]

In addition to the potential early detection and prevention benefit for adults aged 45 to 49 years, lowering the starting age to 45 years also is likely to have a favorable impact on CRC incidence and incidence-based mortality in the group ages 50 to 54 years. Incidence in this age group is currently increasing, in contrast to the declining incidence in all age groups after age 54 years.[3]

Implementation

The GDG acknowledged the implementation challenges posed by lowering the starting age. First, changing the age to begin screening—a key component of recommendations that heretofore have achieved broad consensus—may contribute to confusion and uncertainty among clinicians and patients as to the best course of action. The ACS will seek to mitigate the impact of conflicting recommendations

through clear communication of its recommendation and rationale, including provider and patient support materials (cancer.org/colonmd).[86] Second, there will likely be a lag between the publication of this recommendation and insurance coverage by all providers of CRC screening starting at age 45 years. The 2010 ACA requires that nongrandfathered commercial insurance plans fully cover USPSTF-recommended screening tests; these are minimum coverage standards for an ACA-qualified health plan, and plans are not restricted from extending CRC screening coverage to individuals aged 45 to 49 years. Third, some have expressed concerns that the US health care infrastructure will be unduly strained by lowering the starting age to 45 years and that efforts should focus instead on increasing screening rates in adults aged 50 years and older. The ACS remains fully committed to increasing screening rates; both expanding the screening to include adults aged 45 to 49 years and increasing screening rates in the population aged 50 years and older can be achieved within the current health care infrastructure. A study that combined results from the 2012 Survey of Endoscopic Capacity with a modeling analysis indicated that increasing screening rates to 80% (with any combination of screening modalities) can be accommodated with current excess capacity.[76] In addition, this guideline places increased emphasis on choice of screening options (not limited to colonoscopy) for those initiating CRC screening.

Patient Choice and Decision Making

Whereas past CRC screening guidelines have prioritized specific tests or specific outcomes (ie, prevention), in this update, the GDG chose to prioritize the opportunity for patients to select either a structural (visual) examination or a high-sensitivity stool-based test, depending on their preference and test availability. This decision does not discount the argument that clinicians and the target population also desire expert advice. However, too many adults who are advised to undergo CRC screening with colonoscopy do not adhere to the advice from the referring provider, and the opportunity to be adherent with CRC screening is missed because of multiple factors, including the failure to ascertain the patient's willingness to undergo an invasive procedure. Health professionals should be prepared to describe and offer options for a structural examination and a stool test and to discuss additional options if the patient does not appear to be accepting of the tests initially presented. As detailed in Table 3, the screening options differ in several ways that influence patient choice. The information provided is designed to facilitate clinician-patient encounters and patient choices consistent with their preferences and thus increase utilization of CRC screening. In addition, materials to facilitate test selection at the point of care have been developed by the ACS.[86,87]

Comparison With Other Guidelines

The USPSTF updated their CRC screening guideline in 2016.[44] CRC screening from ages 50 through 75 years with any of 7 screening strategies was given an "A" recommendation (comparable to a strong recommendation using GRADE criteria), which largely overlaps with the 2018 ACS recommendations. The primary differences are as follows: ACS recommends beginning screening at age 45 years, while the USPSTF recommends beginning at age 50 years and the USPSTF recommends FS every 10 years combined with annual FIT, which is not included in the ACS list of testing options. The ACS GDG relied upon RCT evidence supporting a 5-year screening interval for FS alone, as well as the results of modeling commissioned for this guideline, and concluded that the FS-only option at a 5-year interval should be maintained. The modeling data suggested that any incremental benefit conferred by the combined strategy would be small compared with model-recommended strategies for either test alone, and there also would be the complexity of integrating 2 test schedules. Finally, the GDG expressed concerns about even continuing to endorse FS, given the low availability and utilization in the United States (see Supporting Information Table 1).

In 2017 the USMSTF preferentially recommended screening with colonoscopy every 10 years, annual FIT for individuals declining colonoscopy, and, as second-tier tests, CTC every 5 years, mt-sDNA every 3 years, and FS every 5 to 10 years.[57] The USMSTF recommended that African Americans initiate screening at age 45 years and that average-risk adults belonging to other racial/ethnic groups begin screening at age 50 years. For individuals with no adenomatous findings or CRC at prior screening, the USMSTF recommended discontinuing screening at age 75 years or when life expectancy is less than 10 years; and they recommended continuing screening to age 85 years for those not previously screened, depending on comorbidities (see Supporting Information Table 1).

Screening in Individuals at Increased or High Risk for CRC

This guideline update focuses on CRC screening in average-risk adults and does not address screening or surveillance in persons at increased or high risk for developing CRC. These include individuals with history of adenomatous polyps, a personal history of CRC, a family history of CRC or adenomatous polyps diagnosed in a relative before age 60 years, a personal history of inflammatory bowel disease, a confirmed or suspected hereditary CRC syndrome, or a history of abdominal or pelvic radiation for a previous cancer.[18-21] Updated screening and surveillance recommendations for these groups have been developed by other organizations.[208-211] Identification of candidates for

differential screening requires adequate collection and updating of family history information and appropriate referral for genetic counseling and testing of individuals at increased risk for hereditary syndromes.

Limitations

The recommendation to initiate screening at age 45 years is based on limited empirical data related to outcomes in average-risk individuals who initiate screening between ages 45 and 49 years. The decision to begin screening in average-risk adults at aged 50 years, in both clinical practice and research, has been largely based on expert opinion about an appropriate threshold for the burden of disease, and this practice understandably has limited the available evidence on screening outcomes in adults aged 45 to 49 years. However, the increasing CRC incidence in successive birth cohorts and subsequent, recent increases in mortality in the group ages 50 to 54 years suggest an opportunity to address a well recognized trend and mitigate future increased incidence and mortality. In the presence of the changing epidemiology of CRC, it is important to acknowledge that the desired empirical evidence (ie, prospective data on screening outcomes in adults aged 45-49 years), conservatively, would be a decade or more away even if a large study were launched this year. In the 5 years before the conventionally accepted age to begin screening, there is little evidence to suggest that screening would be less effective in detecting occult blood or advanced neoplasia, apart from the lower but increasing prevalence of disease.

The modeling analysis that supported the recommendation for an earlier starting age did not examine the use of alternating modalities or of combination or hybrid screening strategies. Hybrid strategies have been proposed as a means of decreasing the burden of screening from either an individual or a societal perspective.[96] For example, switching from colonoscopy to a stool-based test or CTC at older ages could theoretically reduce exposure to the higher complication risk associated with colonoscopy with advancing age. With greater confidence about the influence of prior findings on future risk, CRC screening test choice, interval, and stopping age might be tailored based on prior results. This is an area in need of further research, both to determine which hybrid strategies would be most effective and acceptable to the target population and to address the challenge of implementing different hybrid strategies in the primary care setting.

Conclusions

Since the last update of the ACS CRC screening guideline a decade ago, there have been numerous developments in the field of CRC screening that have informed this update.

Although the 6 screening options presented in this guideline have not fundamentally changed, the accrual of experimental, observational, and modeling data has served to validate their role in CRC screening and further reinforce the conclusion that the benefits of regular screening with any of the tests in terms of CRC mortality and incidence reduction significantly outweigh the risks and burdens they confer.

One of the most significant and disturbing developments in CRC is the marked increase in CRC incidence—particularly rectal cancer—among younger individuals. While the causes of this increase are not understood, it has been observed in all adult age groups below the age when screening has historically been offered and is contributing significantly to the burden of suffering imposed by premature CRC mortality. Incorporating this epidemiological shift into contemporary modeling of CRC screening demonstrated that the benefit-burden balance is improved by lowering the age to initiate CRC screening to 45 years. Lowering the starting age is expected to benefit not only the segments of the population who suffer disproportionately from CRC—blacks, Alaska Natives, and American Indians—but also those individuals otherwise considered to be at average risk. Moreover, epidemiological trends in cohorts as young as those born in 1990 suggest that the higher risk of developing CRC will be a persistent concern for decades to come.

As outlined in this guideline, there have been substantive advances in our understanding of strategies to overcome barriers to CRC screening through interventions at the patient, provider, office, and system levels that serve to increase uptake of and adherence to screening. Yet, with almost 40% of eligible adults not up to date with CRC screening, it is clear that these interventions too often are not being implemented. Reaching the full potential of CRC screening in the United States will require multifaceted approaches tailored to the individual patient and practice setting. These approaches vary in intensity and resource utilization, but even an intervention as simple as offering a choice of screening test to improve uptake—as emphasized in this guideline—is expected to further the goal of improving screening rates and reducing the burden of suffering from CRC.

In conclusion, the ACS recommends that all US adults at average risk of CRC undergo regular screening with any of the 6 options outlined in this guideline, beginning at age 45 years. Adults in good health should continue screening until age 75 years, beyond which the decision to continue screening should be individualized based on patient preferences, health status, life expectancy, and screening history. Ascribing to the adage that the best CRC screening test is the one that gets done, and done

well, the ACS recommends that patients initiating screening or previously nonadherent with screening be offered a choice of tests based on availability of high-quality options. It is our hope that widespread adoption of this guideline will have a major impact on the incidence, suffering, and mortality caused by CRC. ■

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