REPORT

# A Path to Improve Colorectal Cancer Screening Outcomes: Faculty Roundtable Evaluation of Cost-Effectiveness and Utility

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***Note:*** *The roundtable meeting described in this article took place in November 2017. To accurately reflect the best available evidence at that time, this article includes only publications that could have informed the opinions of the meeting participants (ie, that were published before the meeting date). The only newer information included in this article is composed of updated statistics on colorectal cancer incidence and mortality and updated guideline recommendations.*

## ABSTRACT

*The American Journal of Managed Care*® and Exact Sciences Corporation hosted a roundtable meeting to discuss the impact of colorectal cancer (CRC) screening modalities on improving patient outcomes. The roundtable participants were a diverse panel of experts, including primary care, gastroenterology, and oncology providers; experts in health outcomes research and health policy; and managed care executives with commercial and public payer experience. Participants discussed CRC prevention and treatment strategies, screening modalities and adherence, molecular diagnostics, patient navigation, evaluation of large data sets, managed care, outcomes research, quality improvement, and reimbursement policies. They focused on developing better value-based medical policies and payment procedures, identifying knowledge, practice, and access deficits related to CRC screening. Participants also provided suggestions on how to improve care quality and patient outcomes through effective evidence-based approaches. They also discussed cost-effectiveness modeling for CRC screening, specifically the advantages and the real-world limitations of these models.

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For author information and disclosures, see end of text.

## Background on Colorectal Cancer

Colorectal cancer (CRC) is the second-leading cause of cancer death in the United States, accounting for an estimated 51,020 deaths in 2019.[1,2] Also, an estimated 147,950 Americans received a CRC diagnosis in 2019, making it the third most commonly diagnosed cancer in the United States.[3] The risk of CRC increases with age, and the disease is most frequently diagnosed in those aged 65 to 74 years.[2]

The stage at which CRC is detected has a substantial effect on survival. Diagnosis at stage I or II allows surgical cure in a majority of cases; the 5-year survival rate is as high as 90% in patients diagnosed with localized-stage disease.[4] However, lack of access to healthcare, underuse of CRC screening, and poor adherence to established clinical practice screening guidelines can lead to later-stage diagnosis and poor patient outcomes.[5] Only a minority of patients (39%) are diagnosed at stage I; most cases (57%) are diagnosed at later stages (III or IV), and few (4%) are diagnosed at an unknown stage.[2,4] The 5-year survival rate is lower in patients with distant CRC at diagnosis, as low as 14.2%, compared with that of patients with regional disease (71.3%), where the cancer has spread to the regional lymph nodes but has not metastasized.[2]

Most CRCs originate as adenomatous polyps.[6] Polyps are evaluated based on appearance (pedunculated [stalked] or sessile [flat]), histology, and size.[7] There is a span of approximately 10 years between the formation of most adenomatous polyps and the development of CRC.[8,9] This lengthy development time provides multiple screening

opportunities throughout the natural history of the disease. Adherent and systematic screening in eligible individuals ensures early detection and diagnosis of precancerous adenomas or early-stage CRC, when treatment is most effective, thereby improving patient health outcomes and reducing mortality rates.[6,10] Early-stage CRC is often asymptomatic, with symptoms becoming clinically evident in later stages.[4] With effective CRC screening, precancerous adenomatous polyps can be detected and surgically excised (polypectomy) before they progress to later-stage cancer.[4]

## An Economic Proposition for CRC Screening

In 2018, CRC accounted for approximately $16.6 billion in national cancer care expenditures in the United States, making it the second most expensive cancer care cost after breast cancer.[11] The total cost of care is even greater when both direct and indirect costs of screening and treatment of CRC are considered,[12] with $10.7 billion in lost productivity due to CRC-associated mortality.[11] Between 2005 and 2020, the total cost of lost productivity in the US population with CRC was predicted to reach $339 billion.[13]

Early detection and management of CRC is vital to improving patient outcomes and minimizing both short- and long-term healthcare expenses. Later-stage or metastatic CRC can present with bowel obstruction, perforation, sepsis, and complications from anemia.[14] Emergency surgery, the need for bowel diversion, and potential anastomosis to reestablish bowel continuity are all expensive sequelae in symptom-associated CRC diagnoses.

Beyond emergency surgical and medical interventions, the potential savings associated with CRC screening are proportional to disease stage at diagnosis.[15] With later-stage disease, simple operations become more complex, adjuvant therapies become more expensive, and the invariable adverse effects and potential complications of such treatments increase costs even more. The most expensive CRC treatments are those for patients with stage IV disease.[16] Effective CRC screening through CRC prevention and enhanced early-stage detection can mitigate many of these adverse events and reduce the economic burden of CRC.

## Evidence-Based Recommendations for CRC Screening and Available Screening Modalities

CRC screening guidelines in the United States are developed by multiple organizations, including the US Preventive Services Task Force (USPSTF), the American Cancer Society (ACS), and the National Comprehensive Cancer Network, among others. In general, the guidelines recommend regular screening by a variety of modalities in average-risk, asymptomatic individuals aged 50 to 75 years, although the ACS updated their recommendation in 2018 to begin screening average-risk adults at age 45.[8,17-19] Notably, nongrandfathered health insurance plans, with plan-years beginning on or after September 23, 2010, are required to provide coverage without patient cost sharing for preventive services that have a rating of A or B in the recommendations of the USPSTF.[20]

Currently, screening recommendations are based on data-informed modeling (see **Characteristics of CRC Screening Models**). Although published results of several randomized controlled trials (RCTs) demonstrate a slight reduction in CRC mortality with sigmoidoscopy and guaiac-based fecal occult blood test (gFOBT) screening, no published RCTs currently exist on the long-term impact of fecal immunochemical test (FIT) and colonoscopy on reducing CRC incidence and mortality.[21] However, several RCTs designed to answer this question with respect to colonoscopy are in progress, including COLONPREV (NCT00906997), SCREESCO (NCT02078804), US CONFIRM trials (NCT01239082), and NordICC (NCT00883792).[22-28] Roundtable participants pointed out that with increasingly younger ages at CRC diagnosis, dropping the age threshold in the ACS' CRC screening guidelines is expected to capture more cases earlier; however, the impact of this recommendation on CRC and related healthcare practices, outcomes, and finances is yet to be determined.

In contrast with its 2008 recommendations, the USPSTF did not grade specific screening modalities in the 2016 update. Instead, the USPSTF broadly recommended that maximizing participation of the eligible population by screening programs using a variety of recommended options will have the greatest effect on reducing CRC morbidity and mortality, regardless of the screening modality used.[22] As such, USPSTF assigned grade A to the overall evidence-based recommendation for CRC screening in adults aged 50 to 75 years. This recommendation was based on a systematic review of the available evidence regarding several CRC screening modalities, including reports of their harms, their ability to reduce CRC incidence and mortality, and their performance.[22] Comparative effectiveness assessments were performed using Cancer Intervention and Surveillance Modeling Network (CISNET) analyses and observational evidence on the benefits of screening when trial evidence was unavailable.[22]

In its 2016 recommendations, the USPSTF suggested that 7 recommended screening strategies provided similar benefits with respect to life-years gained, CRC deaths averted, and improvement in benefit-to-harm ratio when evaluated against colonoscopy as the control comparator (**Table 1**).[4,6,22,29-31] The USPSTF equally recommended each of these screening modalities: (1) flexible sigmoidoscopy every 5 years; (2) multitarget stool (mt-sDNA; referred to as FIT-DNA by the USPSTF) test every 1 or 3 years; (3) FIT every year; (4) gFOBT every year; (5) CT colonography every 5 years; (6) flexible sigmoidoscopy every 10 years plus FIT every year; and (7) colonoscopy every 10 years.[22] Colonoscopy and flexible sigmoidoscopy were considered invasive screening technologies, whereas noninvasive screening technologies were CT colonography, gFOBT, FIT, and mt-sDNA. The functionality,

**TABLE 1.** CRC Screening Modalities Recommended by the US Preventive Services Task Force[4,6,22,29-31a]

| Screening Modality and USPSTF-Recommended Interval | Life-Years Gained per 1000 Screened[22b] | CRC Deaths Averted per 1000 Screened[22b] | Number of Harms per 1000 Screened[22b,c] | Considerations |
|---|---|---|---|---|
| **INVASIVE** | | | | |
| **Colonoscopy**[4,30,31]<br>Allows for visualization of the entire colon and rectum, as well as for concurrent biopsies and polypectomy and diagnosis of additional diseases | | | | |
| Every 10 years | 270-275 | 22-24 | 14-15 | • Colonoscopy has both indirect and direct harms. Measure of harms and disease burden resulting from complications of colonoscopy and number of colonoscopies are commonly used as surrogate measures.<br>• Highest risk of procedural complications (bleeding and perforation)<br>› A meta-analysis of data from 39 studies demonstrated that the rate of serious morbidity from major bleedings was 0.8 per 1000 procedures, and the rate of serious morbidity from perforations was 0.07 per 1000 procedures.[30]<br>• Requirements with extended patient time commitments:<br>› Patient bowel preparation<br>› Anesthesia<br>› Chaperone to accompany patient to and from procedure<br>• Long screening intervals<br>• Screening and diagnostic follow-up of positive results can be performed in the same session. |
| **Flexible sigmoidoscopy**[4]<br>Allows for visualization of the rectum and lower third of the colon (sigmoid colon) but not much of the proximal colon | | | | |
| Every 5 years | 181-227 | 17-21 | 9-12 | • Unable to remove adenomas in the proximal colon because of limitation to distal portion of the colon<br>• Requirements:<br>› Patient bowel preparation |
| Every 10 years (plus FIT annually) | 246-270 | 22-24 | 11-12 | • Positive result requires follow-up colonoscopy for diagnosis.<br>• Availability has decreased in the United States.<br>• Strategy for patients who want endoscopy screening but not colonoscopy |

*(continued)*

limitations, and other characteristics of each screening modality are explored next.

## Invasive Screening Modalities

In 2015, the National Health Interview Survey found that 58.3% of eligible Americans had been screened by colonoscopy in the past 10 years, an increase from 46.9% in 2008.[32] Before the widespread use of colonoscopy, flexible sigmoidoscopy was a commonly used CRC screening method. This technique allows direct visualization of the rectum and sigmoid colon, but for most practitioners, it leaves more than two-thirds of a normal-length colon unvisualized. The use of flexible sigmoidoscopy in the United States has declined substantially since the widespread adoption of colonoscopy.[4]

The available USPSTF-recommended CRC screening methods have different sensitivities and specificities (**Table 2**).[4,6,29,33,34] Although all CRC tests increase survival rates, colonoscopy is most commonly used because it has the highest performance rate of all the tests. It is the preferred follow-up diagnostic strategy for all other positive CRC screening tests because of its ability to visualize, biopsy, and ablate or remove small- to moderate-sized lesions. However, colonoscopy quality can vary depending on the endoscopist, the medical facility, time of day, or quality of bowel preparation, and it still can fail to detect certain adenomas.[4]

Invasive procedures can drive the morbidity and costs associated with CRC screening. Colonoscopy is associated with the highest risk of harms compared with the other CRC screening modalities included in the 2016 USPSTF recommendations.[22] These

**TABLE 1.** *(continued)* CRC Screening Modalities Recommended by the US Preventive Services Task Force[4,6,22,29-31a]

| Screening Modality and USPSTF-Recommended Interval | Life-Years Gained per 1000 Screened[22b] | CRC Deaths Averted per 1000 Screened[22b] | Number of Harms per 1000 Screened[22b,c] | Considerations |
|---|---|---|---|---|
| **NONINVASIVE** | | | | |
| **CT colonography/virtual colonoscopy**[4,6,29]<br>Imaging procedure results in a cross-sectional, 2- or 3-dimensional view of the entire colon and rectum. | | | | |
| Every 5 years | 226-265 | 20-24 | 10-11 | • Exposure of low-dose radiation to patients carries a small risk of radiation-induced cancer.<br>• During a CT colonography, polyp removal and biopsies cannot be performed.<br>• Positive result requires follow-up colonoscopy for diagnosis.<br>• Requirements:<br>› Patient bowel preparation<br>• Does not require sedation<br>• Overdiagnosis and overtreatment of incidental extracolonic findings (40%-70% of screening examinations) that are of no importance or non–life-threatening can result in unnecessary diagnostic testing or treatment (5%-37% of these findings result in diagnostic follow-up, and about 3% require definitive treatment). |
| **gFOBT (Hemoccult Sensa, Beckman Coulter)**[4]<br>Detects blood in stool from CRC tumors and large polyps that bleed into the intestines through a chemical reaction that identifies the heme portion of hemoglobin | | | | |
| Annually | 232-261 | 20-23 | 11 | • Test is performed at home.<br>• Requirements:<br>› Dietary limits<br>› Follow-up diagnostic colonoscopy for positive results<br>› Requires multiple stool samples |
| **FIT (OC-Light S FIT, Polymedco; and InSure FIT, Enterix Inc)**[4]<br>Detects blood in stool using an antibody-based assay to identify the globin portion of hemoglobin | | | | |
| Annually | 231-260 | 20-23 | 10-11 | • Test is performed at home with a single specimen.<br>• Positive result requires follow-up colonoscopy for diagnosis. |
| **mt-sDNA (Cologuard, Exact Sciences)**[4]<br>Detects alterations in DNA released from cells shed into the intestinal tract from precancers and early- and late-stage cancers. Combines quantitative values of 11 biomarkers in an algorithm that generates a single composite result | | | | |
| Annually | 246-271 | 22-24 | 12-13 | • Test is performed at home.<br>• Positive result requires follow-up colonoscopy for diagnosis.<br>• May lead to oversurveillance |
| Every 3 years | 215-250 | 19-22 | 9-10 | |

CRC indicates colorectal cancer; CRC-SPIN, Colorectal Cancer Simulated Population model for Incidence and Natural history; CT, computed tomography; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood test; MISCAN, Microsimulation Screening Analysis; mt-sDNA, multitarget stool DNA; SimCRC, Simulation Model of Colorectal Cancer; USPSTF, United States Preventive Services Task Force.

[a]No empirical data support the use of one screening method rather than another.

[b]Evidence based on CRC-SPIN, MISCAN, and SimCRC modeling analysis for the USPSTF recommendations in 2016.

[c]Harms may be caused by bowel preparation prior to the procedure (eg, dehydration and electrolyte imbalances), the sedation used during the procedure (eg, cardiovascular events), or the procedure itself (eg, infection, colonic perforations, or bleeding).

include potential complications such as colonic perforations and hemorrhage, which are more frequent when pathology is biopsied or removed.[6,35-37]

To prepare for an invasive CRC screening procedure with flexible sigmoidoscopy or colonoscopy, individuals require bowel cleansing—generally only an enema for flexible sigmoidoscopy and a more extensive preprocedure bowel cleansing for colonoscopy—and temporary dietary restrictions.[4] In up to 26.4% of individuals, bowel preparation is inadequate, which can reduce the ability to detect polyps and CRC lesions.[38,39] Such events can lead to additional testing or repeat procedures, accompanied by their own associated morbidity.[40] Unlike CRC screening with flexible

**TABLE 2.** Comparative CRC Screening Performance[4,6,29,33,34]

| Screening Method | Specificity | Sensitivity | | Detection Considerations |
|---|---|---|---|---|
| | | CRC | Adenomas >10 mm | |
| Colonoscopy (10 year)[4,6,29] | 86.0%-88.7% | 95.0% | 89.1%-94.7% | • Potential for false-negative findings of sessile adenomas or lesions that are flat or located behind a colonic fold |
| Flexible sigmoidoscopy[4,29] | 87.0% | 95.0% | 95.0% | • Limited ability to detect adenomas in the proximal colon |
| CT colonography[6,29] | 88.0% | 84.0% | 84.0% | • Potential for false-negative findings of flat lesions or lesions located behind a colonic fold<br>• A systematic literature review found that the sensitivity of CT colonography with bowel preparation for detecting larger adenomas (10 mm or larger) ranged from 66.7% to 93.5%, with a specificity of 86.0% to 97.9%. |
| gFOBT[4,29] | 92.5% | 70.0% | 23.9% | • Potential for false-negative findings<br>› Polyps that do not bleed, bleed in small amounts, or bleed intermittently may be missed. |
| FIT[33,34] | 94.9% (95% CI, 94.4%-95.3%) | 73.8% (95% CI, 61.5%-84.0%) | 23.8% (95% CI, 20.8%-27.0%) | • FIT can be based on qualitative (fixed cutoff) or quantitative (adjustable cutoff) assays, which leads to variations in test performance.<br>• Polyps that do not bleed, bleed in small amounts, or bleed intermittently may be missed.<br>› Rate of false positives: 67.2%<br>› Rate of false negatives: 35.2%<br>• Detection rate for SSPs: 5.1% |
| mt-sDNA[33] | 86.6% (95% CI, 85.9%-87.2%) | 92.3% (95% CI, 83.0%-97.5%) | 42.4% (95% CI, 38.9%-46.0%) | • mt-sDNA showed greater sensitivity for detecting colorectal cancer than FIT ($P$ = .002).<br>› Rate of false positives: 45.4%<br>› Rate of false negatives: 33.9%<br>• Detection rate for SSPs: 42.4% |

CRC indicates colorectal cancer; CT, computed tomography; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood test; mt-sDNA, multitarget stool DNA; SSP, sessile serrated polyp.

sigmoidoscopy, the colonoscopy procedure involves sedation with narcotics, hypnotics, and/or general anesthesia, requiring a chaperone to and from the procedure. Colonoscopies also are associated with work disruption during the 24 hours of bowel preparation and during the 12-hour postprocedural window.[4] On average, caregivers provide 5.3 hours of their time in support of the colonoscopy procedure.[41]

## Noninvasive Screening Modalities

CRC screening modalities classified as noninvasive include CT colonography, a direct visualization test, and 3 stool-based tests: gFOBT, FIT, and mt-sDNA.[22] CT colonography, although less invasive than colonoscopy, requires cathartic bowel preparation, insertion of an intrarectal balloon-tipped catheter, and insufflation of gas for colon distension. Intraluminal contrast is encouraged for stool tagging, with some centers preferring oral administration and others rectal administration. Some also use intravenous (IV) contrast, although this is not strictly required for the intraluminal examination.[34]

CT colonography, also known as *virtual colonoscopy*, is an imaging procedure. This procedure results in a cross-sectional, 2- or 3-dimensional view of the entire colon and rectum. Poor bowel cleansing can lead to difficulty in differentiating stool from neoplasm.[34] As with colonoscopy, the most frequently cited reasons for nonparticipation in CT colonography are the perceived unpleasantness of the exam and inconvenience of the test preparation.[42] Tube placement can be associated with bowel perforation, but rates have shown to be as low as between 0.035% and 0.040%.[37,43] As with colonoscopy, bowel preparation may precipitate electrolyte imbalances, dehydration-associated kidney failure, and even cardiovascular events such as congestive heart failure, especially in individuals with certain comorbid conditions.[31,37] The oral or rectal contrast agents, as well as any IV contrast agents, may lead to acute severe allergic reactions.[37] Although CT colonography exposes individuals

**TABLE 3.** Costs of CRC Screening by Modality[41,45-48]

| Screening Method | Direct Costs[a] | | Indirect Costs per Screened Individual or Caregiver[41] |
|---|---|---|---|
| | List Price or Price to Employer[45] | Medicare[46-48] | |
| Colonoscopy | $2300-$5100 | $1036 | • Total cost of lost time: $335.95<br>• Caregiver: $79.03<br>• Transportation: $17.46 |
| Flexible sigmoidoscopy | $1580-$1620 | $301.89 | — |
| CT colonoscopy | $1330 | $439 | |
| gFOBT | $40-$410[b] | $4.46 | |
| FIT | $130-$530[b] | $21.82 | |
| mt-sDNA | $649 | $512.43 | |

CRC indicates colorectal cancer; CT, computed tomography; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood test; mt-sDNA, multitarget stool DNA.
[a]Cost to employer/Medicare is the median cost per screening of all charges typically rendered (or reimbursed by Medicare) on the same day as the screening.
[b]The cost of FIT and gFOBT is typically small ($15-$50); however, these tests are typically performed with other tests on the same day. This is an estimated price range based on provider billing and service practices for the entire day.

to low-dose radiation, the cumulative dose and frequency produce negligible risk.[37] CT colonography has a similar effect on life-years gained as colonoscopy screening when utilized after polyp identification.[44] Nonetheless, like colonoscopy, CT colonography may fail to detect lesions that are flat or that lie behind a colonic fold, therefore producing false-negative findings.[29] Polyp removal and tissue biopsy cannot be performed during CT colonography; therefore, for a definitive diagnosis, a positive CT colonography requires either a same-day colonoscopy or a separate follow-up diagnostic colonoscopy (with bowel preparation).[4]

The 3 stool-based CRC screening modalities are the only truly noninvasive options. Screening with stool-based tests is recommended at shorter intervals than those recommended for structural examinations or invasive screening modalities with optical or radiologic endoscopic techniques. The USPSTF recommends annual screening with FIT or gFOBT.[22] The use of mt-sDNA testing is currently recommended every 3 years.[4]

Individuals who use mt-sDNA, FIT, or gFOBT for CRC screening can perform the specimen-collection portion of the tests at home without the need for bowel preparation or anesthesia. Although these screening tools may not be preferred by individuals who have an aversion to collecting stool, they are not painful, cannot damage the colon, do not require bowel preparation or anesthesia, and are less expensive than invasive methods (**Table 3**).[41,45-48] As only positive tests are followed by colonoscopy, exposure to colonoscopy-related harms is mitigated for most individuals.

Because CRC tumors and clinically significant polyps can be traumatized by the passage of stool, they frequently bleed into the large bowel and rectum. Fecal occult hemoglobin tests (gFOBT and FIT) were designed to detect such bleeding, which include the older guaiac-based tests (gFOBT) and the newer immunological assays (FIT). However, although FIT and gFOBT are included in CRC screening guidelines, they are intended only for the detection of blood, not specifically for the detection of CRC. The gFOBT detects the heme portion of hemoglobin in stool samples through a peroxidase-mediated reaction between stool hemoglobin and the phenolic compound α-guaiaconic acid.[34] However, the catalase activity in certain vegetables, as well as the hemoglobin in orally ingested red meat, can result in false positives, whereas vitamin C can cause false negatives (gFOBT).[34,49] Therefore, individuals using gFOBT are encouraged to follow certain dietary and medication restrictions to avoid erroneous results.[4] A gFOBT test typically requires 3 consecutive stool samples that are transferred onto test cards and then mailed to the healthcare provider's office or a laboratory.[4]

FIT uses an antibody-based assay to detect the presence of hemoglobin, and because it detects only human blood, it has no dietary restrictions.[4] Unlike gFOBT, FIT typically requires fewer stool samples; 1- and 2-sample FIT tests perform equally well in detecting advanced adenomas.[4,50,51] Some medications may facilitate gastrointestinal (GI) bleeding, and depending on where in the GI tract this occurs, it may cause false positives for both gFOBT and FIT.[52] Not all CRCs and/or clinically significant polyps routinely or consistently bleed into the stool; however, many of these lesions consistently shed cells that degenerate and release abnormal DNA into stool. A limitation to FIT and gFOBT is that these modalities may not be able to detect polyps that bleed small amounts, bleed intermittently, or do not bleed. For both tests, any positive test results require a follow-up diagnostic colonoscopy.[4,34]

The mt-sDNA test (Cologuard®; Exact Sciences) is the first and only FDA-approved stool DNA screening test for detecting CRC. It detects altered levels of methylated and mutated DNA (and hemoglobin) present in stool, which are associated with precancers as well as early- and late-stage cancers. The mt-sDNA test quantifies 11 biomarkers, including 10 DNA markers and fecal hemoglobin (FIT), and it generates a single composite negative or positive result using a published algorithm.[53] A healthcare provider orders the test kit, which is sent by the laboratory directly to the individual's home and includes a prepaid return address label for shipping to the laboratory.[54] To complete the mt-sDNA test, the individual passes a spontaneous stool sample into the collection container included in the test kit, takes the fecal hemoglobin sample and adds the DNA

preservative buffer, seals the collection container in the original box, and returns the completed test kit for analysis at a nationwide centralized laboratory.[54] Although sometimes provided directly by health systems or providers, mt-sDNA testing is the only USPSTF-recommended modality that also includes a nationwide 24/7 customer service and navigation system for both patients and healthcare providers, facilitating compliance and performance of the test.[54]

A highly sensitive test is one that produces few false negatives, resulting in fewer missed precancerous lesions. The specificity of a test, which involves the ability of the test to detect true-negative results, is inversely correlated with the number of false-positive results. The FIT test has greater sensitivity than gFOBT for detecting CRC and adenomas. gFOBT has greater specificity than the FIT test, but it has a lower sensitivity with a higher percentage of false negatives (Table 2).[4,6,29,33,34]

In its 2016 CRC screening recommendations, the USPSTF noted that mt-sDNA has superior sensitivity for detecting CRC compared with FIT alone for both cancer and precancerous lesions of all types (Table 2).[4,6,29,33,34] In a cross-sectional study of mt-sDNA in CRC screening, the numbers of individuals needed to be screened to identify 1 cancer were 154 with colonoscopy, 166 with mt-sDNA testing, and 208 with FIT.[33] Overall, the mt-sDNA test demonstrated a 92.3% sensitivity and 86.6% specificity for CRC when evaluated in direct comparison with FIT (OC FIT-CHEK; Polymedco), which demonstrated a 73.8% sensitivity and 94.9% specificity.[33] The composite 3-year specificity of FIT performed annually is theoretically similar to that of 1 mt-sDNA test used at 3-year testing intervals.[8] The potential for false-positive results leading to unnecessary diagnostic colonoscopies is theoretically equivalent with FIT and mt-sDNA, assuming 100% compliance.[8] However, test performance reflects a balance between sensitivity and specificity. One roundtable participant noted that a provider chooses mt-sDNA as a screening tool because of its high sensitivity and still excellent specificity. Requiring a few negative colonoscopies was deemed acceptable in order not to miss a life-threatening cancer. In addition, the mt-sDNA test is more effective than FIT in detecting sessile serrated polyps[33]; these predominantly occur in the cecum and ascending colon, may be missed with colonoscopy, and may account for 20% to 30% of CRCs.[4,55]

## Current CRC Screening Adherence Rates

The adherence to CRC screening guidelines among eligible Americans aged 50 to 75 years has failed to reach recommended targets (either the 80% established by the National Colorectal Cancer Roundtable or the 70.5% targeted by the US government's *Healthy People 2020*).[56,57] The latest data indicate the CRC screening rate for the eligible American population was 66% in 2018, with screening utilization and prevalence ranging from 58% to 77% depending on the US state.[4]

In 2016, the USPSTF concluded that CRC screening in adults aged 50 to 75 years will have the greatest effect on CRC mortality reduction, independent of the CRC screening modality.[22] This recommendation was driven by the substantial underutilization of CRC screening as a preventive health strategy in the United States and by the goal of maximizing the number of Americans screened for CRC.[22]

### Real-World Longitudinal Adherence to CRC Screening

The results of real-world longitudinal studies indicate that adherence rates vary by target population and screening modality (**Table 4**).[58-65] Documentation of CRC screening using a large, national administrative claims database demonstrated a real-world CRC screening adherence of 64.3% over a 10-year period.[63] Investigators conducted a retrospective analysis of claims data from 2000 to 2004 to examine adherence with the USPSTF CRC screening recommendations among 151,638 average-risk adults aged 50 years; reports were followed for 10 years. Of the 97,518 adherent individuals, 99.6% had completed at least 1 screening with colonoscopy, 2.0% (n = 1946) had completed flexible sigmoidoscopy at least twice, and 0.6% (n = 614) had completed flexible sigmoidoscopy at least once with FIT or gFOBT tests every year for at least 5 years. The adherence rates for FIT or gFOBT were the lowest and were substantially lower than for CRC screening overall in the total adherent population; only 0.3% (n = 268) adhered to annual CRC screening recommendations for FIT or gFOBT over the 10-year period.[63] Furthermore, nearly half of the inadequately screened individuals (46%) had a single annual FIT or gFOBT over 10 years, with a mean of 2.6 annual FIT or gFOBT tests over the study period among inadequately screened subjects.[63] Larger studies confirm similarly low longer-term adherence with gFOBT.[59]

CRC screening increases when participants are given a choice of CRC screening modality. Results from an RCT of individuals aged 50 to 79 years and at average risk for CRC were randomized to gFOBT annually, colonoscopy, or choice between the 2 modalities.[58] The proportion of subjects who completed CRC screening within the 12 months following recommendation was significantly higher for individuals who chose their CRC screening modality (colonoscopy or gFOBT) compared with those who had a colonoscopy ordered by their provider (68.8% vs 38.2%; $P < .001$).[58]

Ultimately, for individuals who receive multiple negative CRC screening test results, adherence decreases over time, resulting in a phenomenon called *screening fatigue*.[66] This response indicates the need for additional engagement with the target population in order to encourage regular screening. gFOBT is especially vulnerable to nonadherence, as it requires an annual testing frequency. In a 3-year follow-up study of patients who chose gFOBT, 38% were adherent in year 1, 18% in year 2, and 12% in year 3.[59] In an additional US Department of Veterans Affairs study, adherence rates for

**TABLE 4.** Real-World Longitudinal Adherence to CRC Screening and Factors in Compliance[58-65]

| Study | Outcomes |
|---|---|
| Inadomi, 2012; and Liang, 2016[58,59] | • RCT of patients aged 50-79 years and at average risk for CRC (n = 997) randomized to gFOBT annually, colonoscopy, or choice between the 2 modalities for first year and 3-year follow-up<br>**Year 1**: › gFOBT: 67% › Choice of gFOBT: 38%<br>**Year 2**: › gFOBT: 27% › Choice of gFOBT: 18%<br>**Year 3**: › gFOBT: 14% › Choice of gFOBT: 12% |
| Schroy, 2016[60] | • RCT of patients aged 50-75 years who were at average risk for CRC and eligible for CRC screening in a 2-year period completed a web-based education module on all recommended CRC screening modalities to aid in decision making. It included discussion of the importance of CRC screening as well as descriptions of each test.<br>› Patients who had their preferred test ordered, compared with those who had a different test ordered, were significantly more likely to report satisfaction with the shared decision-making process ($P$ <.001) and to have an intention to complete the screening test ordered ($P$ <.001).<br>› Patients who had their preferred test ordered were more likely to complete screening within 6 months of the order ($P$ = .004) compared with patients whose preferred test was not ordered (37% vs 14%). |
| Finney Rutten, 2017[61] | • High compliance with the mt-sDNA test<br>› 80.8% of patients with a positive mt-sDNA screening test result followed up within 3 months<br>› 89.7% followed up with a colonoscopy within approximately 1 year |
| Prince, 2017[62] | • 12-month study of previously noncompliant Medicare patients (ie, they were previously noncompliant with a provider recommendation for colonoscopy or gFOBT screening; n = 393). They were at average risk for CRC and were seen by 77 primary care providers in the USMD Health System in Texas, who ordered mt-sDNA tests for them.<br>› 88.0% intent-to-screen compliance with mt-sDNA<br>› 96.1% compliance following positive mt-sDNA finding (ie, completed the required follow-up with diagnostic colonoscopy) |
| Cyhanuik, 2016[63] | • Retrospective claims analysis over 10-year period in patients 50 years and older (n = 151,638)<br>› 0.3% were adherent with annual CRC screening with FIT or gFOBT |
| Fenton, 2010[64] | • Washington State health plan members aged 52-78 years who were previously screened with gFOBT<br>› 44.4% adherence to repeat gFOBT screening during 2-year observation period |
| Gellad, 2011[65] | • Records of 1 million patients aged 50-75 years seen at Veterans Health Administration medical centers<br>› 14.1% of men and 13.7% of women completed a minimum of 4 gFOBTs in the study's 5-year period |

CRC indicates colorectal cancer; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood test; mt-sDNA, multitarget stool DNA; RCT, randomized controlled trial.

consecutive annual gFOBT over a 4- to 5-year period were low, with only 14.0% of men and 13.7% of women successfully completing annual gFOBT.[65]

FIT appeared to have higher adherence compared with gFOBT in several longitudinal studies. One of these studies, performed by Jensen and colleagues, retrospectively evaluated 323,349 adults aged 50 to 70 years in California's Kaiser Permanente system and found that 48.2% of enrollees completed planned FIT screening within the first year. Of those who completed FIT in the first year, adherence rates over the next 3 years ranged from 75.3% to 86.1%.[67] These rates were higher than those found in a European study by van der Vlugt and colleagues. Study results indicated that of 23,339 randomly selected, asymptomatic adults aged 50 to 74 years, adherence rates for participants over 4 consecutive rounds of biennial FIT screening ranged from 60% to 63%.[68]

## Insurance Coverage of CRC Screening

Insurance plan coverage and benefit design (ie, level of member out-of-pocket expenses) are important for CRC screening conversations, compliance, and adherence.

### Medicare/Medicaid

In 2018, the Affordable Care Act (ACA) required that Medicare cover CRC screening tests as preventive services[69]; it removed the requirement for Medicare Part B deductibles and coinsurance for routine screenings recommended by the USPSTF with an A or B rating.[70] As a result, beneficiaries aged 50 to 85 years at average risk of CRC do not pay a Medicare Part B deductible or coinsurance for a CRC screening procedure (including FIT and gFOBT every year, mt-sDNA testing every 3 years, flexible sigmoidoscopy every 4 years, and colonoscopy every 10 years). However, a 20%

coinsurance is required by Medicare for a screening colonoscopy if, during the screening procedure, polyp(s) is/are removed or a biopsy is necessary.[22,69,70] Separately, under current Medicare policies, a colonoscopy performed as a result of a positive gFOBT, FIT, or mt-sDNA test result is considered a diagnostic procedure, not a screening procedure, and beneficiaries are required to pay the Medicare Part B deductible and the 20% coinsurance for this procedure, even when no abnormality is found.[69,70]

Although ACS now recommends starting CRC screening at age 45 years, insurers are not currently required by federal law to cover the cost of CRC screening for patients under age 50 years.[19,69] Many states have mandates that require fully insured plans in their states to follow the ACS screening guidelines. Whereas the ACA, CMS, and most commercial plans follow USPSTF screening guidelines, insured plans in those states that follow the ACS guidelines may choose not to follow USPSTF. This is likely to create confusion among providers, payers, and patients as to whether screening beginning at age 45 years will be covered and reimbursed. Roundtable participants advised that it would be best for all-around screening success if the guidelines were consistent.

Federal law does not require state Medicaid programs to cover the costs of CRC screening in asymptomatic individuals.[69] Like other aspects of the Medicaid program, the services covered vary by state. Some state Medicaid plans cover only gFOBT, and overall coverage may depend on the beneficiary's Medicaid managed care plan. Some state plans cover the costs of only those screening tests that are deemed medically necessary by a provider. Both potentialities may limit patient choice in screening.

### Private or Commercial Insurance

CRC screening coverage varies among commercial or private health plans. When screening colonoscopies identify polyps, some payers classify the service as preventive screening, whereas others consider the service a diagnostic procedure. Similar to Medicare beneficiaries, patients may face higher out-of-pocket costs when the classification is as a diagnostic procedure.[69]

Noncolonoscopy screening is usually covered with no out-of-pocket expenses, but the follow-up diagnostic colonoscopy may be subject to additional costs. Reimbursement can depend on whether an invasive or structural examination or a screening procedure was coded by the healthcare provider for screening or diagnostic purposes.

### High-Deductible Plans

Individuals with high-deductible health plans must pay the full price of their healthcare expenditures until their deductible is met.[71] Because of the need to directly pay for healthcare services, some individuals delay or do not schedule follow-up tests because they cannot afford the costs of meeting their deductible.[71] As discussed previously, although the initial preventive screening is covered, follow-up testing costs that are associated with a positive initial preventive screening result can create barriers with access challenges for members. The follow-up colonoscopy after a positive noninvasive test result is an integral part of the screening continuum, as CRC screening is not considered complete without this element.

### Implications of Insurance Coverage

Any out-of-pocket expenses for medical plan enrollees deter guidelines-based CRC screening adherence. Screening by stool-based testing is relatively inexpensive compared with colonoscopy, and individuals may value the advantages of these noninvasive options. However, in the event of a positive stool-based test result, cost sharing for the subsequent diagnostic colonoscopy may create a financial barrier that prevents completion of the screening process, or it may even prevent the choice of a stool-based test for first-line screening.[70] This could result in patients avoiding any form of CRC screening. Additionally, patients may be liable for ancillary procedure-related costs, including those of pre-exam consultation, bowel preparation kits, anesthesia or sedation, pathology, and facility fees included in initial screening colonoscopies.[69]

Individuals with no out-of-pocket costs for CRC screening tests, but whose policy does not include full coverage of a subsequent diagnostic colonoscopy, have barriers that may limit the value of the initial CRC screening.[70] The ACA established new requirements in 2018 that eliminated cost sharing for USPSTF-recommended CRC screening modalities for privately insured individuals, which required nongrandfathered group health plans and individual policies to provide first-dollar coverage for CRC screening in adults 50 years and older. Specifically, Section 2713 of the Public Health Service Act (the ACA) requires nongrandfathered health plans to cover, without cost sharing, items or services that receive a rating of A or B in a USPSTF recommendation, beginning with plan years starting 1 year after the recommendation.[20] Notably, nongrandfathered health plans are required to cover, without cost sharing, at least 1 form of *each method* of preventive service that is specified in the applicable USPSTF recommendation. Although it is notable that Section 2713 does not require insurance plans to cover out-of-network costs, if no in-network provider offers a covered service, the plan must cover the service as in-network, without cost sharing. Even in instances when the ACA does not apply, such as the case involving a grandfathered plan, individual state laws might still require some plans to cover CRC screening.

## Real-World Barriers to CRC Screening Compliance and Adherence to Guidelines

Experts from the roundtable panel described the difficulty of creating awareness and outreach to individuals eligible for CRC screening.

**TABLE 5.** Factors Influencing CRC Screening Choice and Common Reported Barriers to CRC Screening[4,34,59,60,73-75]

| Test Characteristics | Disparities Among Racial Groups | Limited Resources | Fear and Apprehension | Awareness and Education |
|---|---|---|---|---|
| • Level of invasiveness<br>• Bowel preparation and diet/medication restrictions<br>• Cost<br>• In-home privacy<br>• Risk of complications or infection<br>• Test frequency interval<br>• Test accuracy<br>• Patients and providers placing different values on various test characteristics | • Hispanic patients have more barriers, less awareness/education of screening options, and fewer provider recommendations.<br>• Populations in lower socioeconomic groups are more likely to be uninsured or have other cost barriers.<br>• African Americans report lack of education, fatalism, fear of diagnosis and procedure, insufficient provider-patient communication, lack of access to care, and prioritizing family obligations over self-care. | • Inadequate or no health insurance coverage<br>• Out-of-pocket costs<br>• Limited access to certain tests (due to health plan restrictions)<br>• Lack of transportation for procedure/appointment<br>• Cannot afford to leave work for appointment<br>• Not enough time; scheduling difficulties | • Fear of test results, cancer, and burden on family<br>• Fear of invasive procedure and complications<br>• Bowel preparation<br>• Discomfort and pain<br>• Embarrassment | • Lack of knowledge of different screening options and scope of test<br>• Lack of provider recommendation for CRC screening<br>• Lack of choice of screening test<br>• No symptoms or family history of CRC<br>• Unaware of CRC screening importance<br>• Unaware of the need for colonoscopy<br>• Confusion about insurance coverage for tests |

CRC indicates colorectal cancer.

In its early stages, CRC is often asymptomatic, and without exhibiting signs or symptoms, patients might not think to get screened.

## Factors Influencing CRC Screening Uptake and Compliance

Some populations face substantial economic barriers to CRC screening. Further, differences in incidence and mortality rates, socioeconomic status, education, and inherent CRC risk may all contribute to lower screening rates.[4,72] For example, in the Medicare population, key barriers include issues regarding health literacy, psychosocial function, and socioeconomic barriers.[72] The roundtable participants suggested the development of appropriate population health management tools to address these issues, which are described in detail later in this manuscript.

Two concerning reasons for CRC underscreening are a widespread devaluing of its importance and a lack of provider referral and follow-up (**Table 5**).[4,34,59,60,73-75] Even with screening recommendations from a healthcare provider, limited patient awareness of the breadth of available screening modalities can decrease compliance. Certain aspects or characteristics of each modality may disincentivize certain individuals to engage in screening, emphasizing the importance of shared decision making between patients and providers. Individuals may be afraid of bowel preparation or have a personal or cultural aversion to transanal instrumentation. Others may have distaste for any procedure that involves collecting stool. An individual's preference should be considered by the healthcare provider because these preferences can have a profound influence on screening behavior.[76] Education on the noninvasive screening options that are available, walking an individual through the steps of various procedures, and involving them in the decision-making process may increase the rates of both initial and follow-up CRC screening.[77]

Additionally, costs and inadequate insurance are reported as barriers to CRC screening.[73] The recent USPSTF grade A recommendation for CRC screening for stool-based testing, and the increasing insurance coverage for these modalities, can ameliorate such concerns. However, actively educating the at-risk population on the noninvasive screening tests covered by insurance might increase overall awareness and adoption of these screening modalities.

## Opportunities for Real-World Improvements in CRC Screening Rates

Strategies that focus on population health, patient navigation, and shared decision making aim to improve screening rates, with varying levels of success.

## Population Health Strategies

Population health strategies can be used to overcome barriers and support provider recommendations for screening by identifying patients who are at risk for nonadherence. Roundtable participants agreed that although the recommendation from a physician

(or physician assistant or nurse practitioner) helps persuade patients to get screened, there needs to be greater understanding of the screening barriers for nonadherent patients. Discussions can focus on proactively identifying the at-risk population, rather than waiting until patients appear in a healthcare provider's office for a wellness visit. Although participants remarked that repeatedly reminding a screening-eligible patient about their need for screening seems effective based on the current screening adherence rates, they highlighted results from a recent study in which evidence-based screening interventions were evaluated in North Carolina.[78] Using public and private claims data, the investigators developed a cost-effectiveness model based on a Microsimulation Screening Analysis (MISCAN)-Colon model of 4 simulated CRC screening interventions. The 2 most effective interventions were (1) the combination of a monthlong annual mass media campaign (television, print, and radio advertisements communicating the importance of CRC screening) and (2) mailed reminders to all Medicaid enrollees turning 50 that outlined the importance of CRC screening, recommended screening guidelines, information on available screening options, and instructions for scheduling a screening test or requesting additional information. The cost per additional life-year was lowest (<$15) for mailed reminders.[78]

Payers can share data on comparative care gaps to incentivize providers to achieve better performance. Several roundtable participants suggested holding health plans and providers accountable for CRC screening by providing incentives for both patients and providers. For example, incentives for providers could include improvement in National Committee for Quality Assurance's Healthcare Effectiveness Data and Information Set (HEDIS) quality measures or the Medicare Star Ratings System. Payers want to be involved because screening is economically favorable irrespective of the costs of the screening test and because of the impact of HEDIS, Medicare Advantage, and the Star Ratings System on payer income.

Member outreach programs can increase CRC screening rates, as well, especially when health plans and health systems work together. Several health plans, including Kaiser Permanente and Cigna, have implemented outreach and educational approaches to improve CRC screening rates through population health strategies.[57] Roundtable participants agreed that payers, accountable care organizations (ACOs), and large medical organizations need to engage in outreach programs. Payers can prioritize investments in evidence-based outreach interventions to improve rates of CRC screening by providing providers with information on unmet prevention needs. Participants suggested engaging predictive analytics by using data on demographics, as well as using population health management tools to optimize how adults are identified for screening. Payers could stratify and differentiate among the types of outreach—letters, phone calls, fax or emails, social media messaging, etc—to identify the most effective method for particular individuals.

## Patient Navigation

Patient navigation is particularly important for individuals who face high barriers to screening and need care management, such as screening-naïve populations who are eligible for screening but have not received education about the process or a provider recommendation. Patient navigators work to eliminate barriers to healthcare services generally and to CRC screening specifically (**Table 6**).[59,79-82] Patient navigation is associated with increased compliance with both gFOBT and colonoscopy screening.[59,82] FIT and gFOBT are commonly offered for programmatic CRC screening. However, health systems and medical groups often lack the infrastructure and resources required to achieve desired compliance rates annually.

The effect of a statewide patient navigation program for colonoscopy was evaluated by comparing a group of participants who received support from a patient navigator for a screening or surveillance colonoscopy at a single community health center (n = 131) with a group of participants who were not enrolled in the patient navigation program (n = 75). Participants with patient navigation support were 11.2 times more likely to complete colonoscopy screening and nearly 6 times more likely to complete the bowel preparation procedure correctly compared with participants without this support. Additionally, none of the participants with navigation support missed screening appointments.[82]

The total cost of planning and implementing a patient navigation program can be substantial. For example, participant support costs accounted for 18% of the total cost of the CRC Screening Demonstration Program developed by the CDC (average of $316 per person). Clinical services accounted for 41% of the total program cost, with an average cost of $695 per person.[83]

Despite the total costs of participant support, navigation programs may be cost-effective, increase life expectancy, and increase adherence to CRC screening guidelines.[84] Investigators on an RCT assigned participants to 1 of 4 arms: usual care with provider reminders; automated intervention (a letter and pamphlet offering education on screening choices such as gFOBT, flexible sigmoidoscopy, or colonoscopy); assisted intervention (a call from a medical assistant asking about screening preferences); or navigation support from a nurse. More participants assigned to interventions than to usual care were compliant with CRC screening at the 2-year follow-up. Moreover, the patient navigation intervention was most cost-effective, but savings with interventions compared with usual care costs ranged from $36 to $159 (defined as the value of resources used to implement and operate the screening promotion interventions over the 2-year trial period).[85]

Of the screening modalities recommended in the 2016 USPSTF guidelines, only mt-sDNA testing encourages compliance by virtue of an embedded patient navigation system that offers support 24 hours a day, 7 days a week for every mt-sDNA test order. This system also includes a welcome call, reminder phone calls and

**TABLE 6.** Patient Navigation to Improve Adherence and Quality of Screening[59,79-82]

| | |
|---|---|
| Potential patient barriers | • Patient failure to make or keep appointments<br>• Misunderstanding of provider direction for screening<br>• Language barrier<br>• Lack of insurance or miscomprehension of insurance paperwork<br>• Travel expenses and transportation |
| Solutions to barriers by patient navigators | • Have a reminder call system for the initial screening test and follow up on missed appointments<br>• Educate patients about techniques for at-home tests or bowel preparation for colonoscopy<br>• Ensure patient understanding and completion of testing<br>• Address patient barriers (eg, arrange an escort, translator, or transportation)<br>• Ensure that the patient receives test results from the provider promptly<br>• Schedule and prepare the patient for follow-up procedures<br>• Identify treatment resources and support networks when needed |
| Evidence supporting patient navigation | • In an RCT including patients aged 50-75 years not current with recommended CRC screenings who were enrolled in 2 community health centers (n = 265), more patients who received patient navigation in combination with a patient decision aid intervention completed CRC screening with gFOBT, FIT, or colonoscopy within 6 months compared with patients receiving usual care (68% vs 27%, respectively).<br>• In a 3-year longitudinal trial, withdrawal of patient navigation after the first year of enrollment was associated with a reduction in screening with colonoscopy and gFOBT in the second and third years of follow-up. gFOBT had the lowest compliance rates without patient navigation support; this was likely due to the lack of research assistants helping with patient navigation in years 2 and 3 because of low funding.<br>• Patients with patient navigation support were 11.2 times more likely to complete colonoscopy screening and nearly 6 times more likely to complete the bowel preparation procedure correctly compared with patients without this support. No patients with navigation support missed screening appointments. |

CRC indicates colorectal cancer; FIT, fecal immunochemical test; gFOBT, guaiac-based fecal occult blood test; RCT, randomized clinical trial.

letter, and contacts to customers regarding when their healthcare provider has ordered the test and when to expect the kit's arrival. The patient navigation system associated with the mt-sDNA test has enabled previously noncompliant Medicare beneficiaries to achieve CRC screening completion with mt-sDNA testing and to achieve an 88.3% intent-to-screen compliance rate over 12 months.[62]

At the meeting, roundtable participants indicated that the availability of a patient navigation program accompanying a screening test that is necessary every 3 years (as opposed to yearly) has the potential to influence provider recommendation. Increased cost-effectiveness may result from integrating both patient navigation and population health management with the mt-sDNA test. A population health management approach involves the provider and their electronic health record system, and ensures that the patient has communicated with the medical home within a reasonable amount of time. For patient navigation to be most cost-effective, it should involve one-on-one interventions with patients who need the barrier reduction.

## Shared Decision Making and Provider Recommendations

Another potentially effective approach is shared decision making between the individual eligible for screening and their provider to overcome barriers to CRC screening and to increase screening compliance. The importance of shared decision making is highlighted in the 2016 USPSTF CRC screening recommendation statement, which declares, "The best screening test is the one that gets done."[22] Participants from the roundtable panel suggested that increasing awareness and education about the prevalence, complications, and survival rates of CRC and about the available screening options might also give individuals the incentive to comply with CRC screening and to adhere to guideline recommendations on screening frequency. Many state Medicaid programs partner with departments of public health, and the population health strategies they can create are avenues by which Medicaid programs can engage with payers, providers, and patients to increase awareness of and educate on screening eligible populations.

Several studies have investigated the role of shared decision making to identify a preferred screening test and its association with improved CRC screening outcomes. A prospective RCT enrolled individuals at average risk of CRC who were aged 50 to 75 years and eligible for CRC screening between 2012 and 2014. Individuals completed a web-based education module on all recommended CRC screening modalities to aid in decision making; it described the importance of CRC screening and included descriptions of each test. Those who had their preferred test ordered were significantly more likely to report satisfaction with the shared decision-making process ($P < .001$), have an intention to complete the screening test ordered ($P < .001$), and complete screening within 6 months of the order ($P = .004$) compared with individuals whose preferred test was not ordered.[60]

Provider recommendation can increase compliance and encourage shared decision making to increase CRC screening uptake. The importance of provider recommendations was highlighted in a

**TABLE 7.** Strategies and Management Tools for Health Plans to Generate Successful CRC Screening[57]

| Payer Strategies to Influence Providers and Members | |
|---|---|
| **Members** | **Providers** |
| • Member education<br>› Education on CRC prevalence, complications, and survival<br>› Education on available CRC screening modalities and their pros and cons<br>• Outreach<br>› Member reminders<br>› Mass media campaigns<br>› Partnerships with vendors to identify patients who need CRC screening<br>• Patient navigation<br>• Financial barrier removal<br>› Removal of out-of-pocket expenses for CRC screening<br>› Waived cost sharing<br>› Member incentives | • Provide financial incentives<br>› Performance-based financial incentives<br>› Provider incentives<br>• Strategic use of data and performance data<br>› Using quality assurance metrics to assess the process<br>› Removal of systemic barriers (eg, lack of coordination among departments)<br>• Strategies that combine leadership responsibilities to achieve CRC screening goals<br>• Education and outreach<br>• Community partnerships<br>› CRC screening reminders by telephone, email, and mail<br>• Screening recommendations for patients<br>› Shared decision making<br>› EHR prompts |

CRC indicates colorectal cancer; EHR, electronic health record.

study of 197 screening-eligible individuals, the majority of whom reported that they had never received a provider recommendation for CRC screening and fewer than 30% of whom were adherent to USPSTF recommendations. Individuals who received a provider recommendation for CRC screening were significantly more likely to complete CRC screening compared with those who did not receive a recommendation ($P < .05$).[74]

Roundtable participants indicated that primary care providers should involve their patients in shared decision making and provide education on the available CRC screening modalities, which may influence choice and increase screening adherence.[58] Many patients may have an idea of which test they prefer ahead of the visit with their healthcare provider, but many may also be unsure of which test to choose, particularly when all tests are indicated as appropriate. Providers need to be able to discuss with their patients how each test aligns with the patient's needs in terms of value, costs, risk, and personal preference.

## Incentives to Increase Screening Rates

Incentives to increase screening rates can take many forms, from incentivizing the health plans and providers to providing incentives for the health plan members themselves.

### Incentivizing Health Plans and Providers

Adherence to CRC screening schedules reduces long-term healthcare expenses, but organizations may need additional motivation to promote guideline-adherent CRC screening.[15] **Table 7** includes strategies and management tools for health plans and payers to use in implementing successful CRC screening.[57] Experts from the roundtable panel encouraged payers to completely cover diagnostic colonoscopies after positive noninvasive screening test results because diagnostic testing is an integral part of the CRC screening continuum. Roundtable participants suggested that health plans and payers waive cost sharing for all screening-related colonoscopies, including guidelines-based surveillance colonoscopies and those that follow positive stool tests.

Some roundtable participants suggested removing the cost barriers for both diagnostic testing and follow-up treatment because the barrier to testing could be the consideration of potential follow-up treatment costs. This highlights the importance of alignment from both the patient and payer perspective. From a patient's perspective, if the routine screening is free but the diagnostic screening colonoscopy is not, it may be cheaper to simply get the colonoscopy. Not only is this inefficient from the payer's perspective, but it creates a high possibility of value misalignment. Health insurance policies could include colonoscopy for polyp removal or biopsy in the definition of CRC screening, which would reduce the cost-sharing burden of follow-up testing for a positive screening test result.[70]

According to some roundtable participants, health plans may be reluctant to cover CRC screening out of concern that the investment may not be cost-effective. The transience of health insurance, particularly as individuals age onto Medicare, means that a health plan may not pay for screening because it would not be the payer that saves long-term expenses from reduced treatment costs. Furthermore, at the primary care level, providers may question how improving screening to satisfy the health plan is going to bring

**TABLE 8.** Real-World Case Studies of Provider and Member Incentives for Increased CRC Screening Rates by Select Health Plan[57]

| | |
|---|---|
| **BCBS of Massachusetts (Employer-Sponsored, Individual, Medicare)** | |
| **Approach** | • AQCs with providers<br>• Risk-sharing alternative to traditional fee-for-service contracts<br>• Eighty-five percent of provider network participates in the AQC.<br>• Educated on how to appropriately code and bill colonoscopies that follow positive stool tests<br>• Providers are incentivized for both absolute performance and evidence of improvement. |
| **Incentives** | *Provider*<br>• Performance compared with the network across 64 quality measures, many based on HEDIS measures and patient satisfaction scores<br>• Providers' reimbursement is directly related to their performance on quality measures.<br>• Providers earn quality bonus dollars if they perform at least at the 50th percentile; incentives are awarded across a continuum of improvement.<br><br>*Member*<br>• Waives cost sharing for all screening procedures, including colonoscopies that follow positive stool tests<br>• Educated their provider network about how to appropriately code and bill these procedures |
| **Outcomes** | • CRC screening rate with this approach: 84%<br>• Giving providers assessment and feedback is a well-established, evidence-based, recommended intervention for CRC screening.<br>• Support providers with actionable and comparative data<br>• Providers want to improve their performance when shown comparative successes in other groups. |
| **Wellmark BCBS (employer-sponsored, individual, Medicare)** | |
| **Approach** | • Commercial health plan ACO<br>• Educate providers about proper coding of colonoscopies as preventive services to avoid out-of-pocket cost for preventive screening.<br>• Share data with ACOs; provide incentives and a monthly dashboard of quality indicators. |
| **Incentives** | *Provider*<br>• Providers receive financial incentives that are tied to their overall value index scores; CRC screening is 1 component of that score. |
| **Outcomes** | • CRC screening rate: 71% |

*(continued)*

money to their practice. Therefore, health plans are encouraged to link substantial payments to providers with high CRC screening rates and measures of quality. For example, the Meridian Incentive Program, developed by the business incentives company Meridian Loyalty, is a pay-for-performance incentivized program that rewards providers for delivering CRC screening services aligned with HEDIS measures. Meridian rewards providers with $20 for completion of CRC screening for each individual enrolled in a Medicare Advantage or combined Medicare and Medicaid plan.[86] Additional real-world case studies demonstrate that a wide range of plan types have implemented both member and provider incentives with different strategies designed to influence CRC screening rates (**Table 8**).[57]

Preferred modalities in a given health plan or group may be biased by certain relationships with vendors or a history of referral patterns for a specific screening modality. Care must be taken to help health plans and organizations make the best choices regarding modalities. In 2016, the National Committee for Quality Assurance (NCQA) announced that the 2017 HEDIS measures would be expanded to include all USPSTF-recommended screening modalities during the measurement year or the previous 2 years.[87] Because of the incentives, payers and some ACOs may be more engaged in doing their own outreach and getting the kind of results that they need, explained the roundtable participants.

One roundtable participant shared that in the current environment with ACOs and value-based contracting, some institutions are looking at shared risk. Payers and providers are looking into population health management models that evaluate the cost-effectiveness of a technology to help achieve better outcomes because the benefits from that technology might outweigh the increased cost. For example, it was important that NCQA HEDIS measures were updated in 2017 to include all modalities recommended by USPSTF. The inclusion of mt-sDNA testing gives payers,

**TABLE 8.** *(continued)* Real-World Case Studies of Provider and Member Incentives for Increased CRC Screening Rates by Select Health Plan[57]

| | |
|---|---|
| **Gateway Health (Managed Care Organization, Medicare/Medicaid, Special-Needs Plans, Medicare)** | |
| **Approach** | • Provide member education about what a positive FIT means and why, even it proves to be a false positive, it's important to get a colonoscopy as the next step.<br>• Invest in computer member profile system to note members who are due for screening.<br>• Provide a *care gap* button in the system that prompts staff members to remind patients about overdue screenings.<br>• Trained staff helps members overcome barriers; staff works with members and providers to schedule appointments and help with community referrals with nonmedical needs. |
| **Incentives** | *Provider*<br>• Providers' pay-for-performance incentive program<br>• Offers face-to-face visits with providers; shares dashboards and lists of members who are due for screening<br>• Webinars about current guidelines, requirements of the incentive program, and information about the importance of their recommendation<br>*Member*<br>• Eliminated cost sharing for all screening colonoscopies (including after FIT test)<br>• No co-payments or deductibles for screening or diagnostic colonoscopies |
| **Outcomes** | • CRC screening rates increased by 15% in 5 years in the Medicare population aged 50-75 years.<br>• FIT mailings achieved a 22% return rate, with 8% having abnormal results requiring follow-up. This contributed to a 15% increase in their HEDIS measure for Medicare members. |
| **Community Health Plan of Washington [State] (Medicare, Medicaid, Individual/Marketplace)** | |
| **Approach** | • MORE program identifies gaps in care with claims data. |
| **Incentives** | *Provider*<br>• Providers receive incentives based on their performance on 12 clinical quality measures that are based on HEDIS measures and aligned with Uniform Data System.<br>*Member*<br>• Members receive IVR calls, text messages, or mailings, which help them schedule their service.<br>• Repeated communications are focused on up to 2 gaps in care every 90 days as long as the gaps persist.<br>• Incentive: $15 gift card in the mail 6-8 weeks after patient has completed a service; members receive a separate gift card for each service completed |
| **Outcomes** | • Improved screening rates for its Medicare members, rising from 52% in 2013 to 66% in 2016<br>• Ten percent of members with IVR calls complete the service being incentivized. |
| **Care N' Care, Texas (PPO and HMO Medicare Advantage)** | |
| **Approach** | • Coordinated care outreach partner with Quest Diagnostics (Quest 360 program) for FIT orders |
| **Incentives** | *Member*<br>• Call-outreach reminders every 30, 60, and 90 days to return FIT kits<br>• Healthcare concierges assist members with finding a physician and scheduling appointments; they also answer plan and benefit questions and help with claims and billing resolutions and prescription drugs. |
| **Outcomes** | • Seventy-seven percent CRC screening rate in 2014; Medicare 5-Star rating in 2014 and 2015 |

ACO indicates accountable care organization; AQC, alternative quality contract; BCBS, Blue Cross Blue Shield; CRC, colorectal cancer; FIT, fecal immunochemical test; HEDIS, Healthcare Effectiveness Data and Information Set; HMO, health maintenance organization; IVR, interactive voice response; MORE, member outreach reminder and engagement; PPO, preferred provider organization.

health systems, and providers the opportunity to receive 3 years of credit, with a 2-year look-back, for providing CRC screening through financial reimbursements for mt-sDNA tests. This type of incentive can encourage payers to offer mt-sDNA testing in outreach programs and prescribe mt-sDNA testing to increase quality measure ratings.

## Incentivizing Members

Principles of behavioral economics, such as offering member-level financial incentives, can be leveraged to encourage CRC screening. Health systems may have the opportunity to incentivize members by providing monetary rewards for completion of CRC screening.

**TABLE 9.** CISNET Models Verified Theoretical Model Outputs for USPSTF-Recommended CRC Screening Modalities[10,29a]

| Screening Approach (50-75 years) | Reduction in Mortality Compared with No Screening[b] | Complications[b,c] | Colonoscopy Burden[d] | Life-Years Gained Compared with No Screening |
|---|---|---|---|---|
| Colonoscopy (10 years) | 78.8%-89.9% | 14-15 | 4007-4100 | 248-275 |
| Sigmoidoscopy (10 years) + FIT (annual) | 77.4%-85.2% | 11-12 | 2248-2490 | 246-270 |
| CT colonoscopy (5 years) | 71.5%-84.6% | 10-11 | 1654-1927 | 226-265 |
| FIT (annually) | 71.8%-81.3% | 10-11 | 1739-1899 | 231-260 |
| mt-sDNA[b] (3 years) | 67.5%-78.0% | 9-10 | 1701-1827 | 215-250 |

CISNET indicates Cancer Intervention and Surveillance Modeling Network; CRC, colorectal cancer; CRC-SPIN, Colorectal Cancer Simulated Population model for Incidence and Natural history; CT, computed tomography; FIT, fecal immunochemical test; MISCAN, Microsimulation Screening Analysis; mt-sDNA, multitarget stool DNA; SimCRC, Simulation Model of Colorectal Cancer; USPSTF, United States Preventive Services Task Force.
[a]Data from SimCRC, MISCAN, CRC-SPIN; assumed 100% adherence, per 1000 40-year-olds.
[b]Assuming 100% recommended adherence beginning at age 50 years (3 colonoscopies; 3 sigmoidoscopies and 26 FITs; 6 CT colonoscopies; 26 FITs; and 9 mt-sDNA tests).
[c]mt-sDNA screening had the least number of harms from screening, as measured by the number of complications from colonoscopy: serious gastrointestinal events (perforations, gastrointestinal bleeding, or transfusions), gastrointestinal events (paralytic ileus, nausea and vomiting, dehydration, or abdominal pain), and cardiovascular events (myocardial infarction or angina, arrhythmias, congestive heart failure, cardiac or respiratory arrest, syncope, hypotension, or shock).
[d]Colonoscopy burden indicates the number of colonoscopies required, including screening, follow-up, surveillance, and diagnosis, as a measure of the overall burden.

Wellness programs among commercial and self-insured employers commonly include incentives for completing certain preventive screenings, such as a premium reduction or a gift card. CRC screening is 1 component of a wellness program. For example, Medica offers its Medicare and Medicaid members $15 Visa rewards cards when they complete CRC screening.[57] Recently, several real-world investigations have been made into this approach to encourage screening uptake. Compared with individuals given access to a direct line for scheduling screening, the rates of preventive colonoscopy screening completion more than doubled when individuals were offered a $100 gift card incentive to complete a colonoscopy within 3 months. However, this incentive may be limited to large employers with financial ability to encourage screening this way and not feasible for many individual insurance plans or safety net health systems.[88]

## Characteristics of CRC Screening Models

The USPSTF, CMS, and other health organizations use modeling to evaluate the effectiveness and characteristics of different screening strategies to complement existing empirical data.[89] These models complement empirical research by evaluating data from multiple sources—demographic and epidemiological data, screening participation, tumor detection rates, and more—to identify important gaps in currently available knowledge and to quantify the impact of those gaps.[90] Simulation allows for the identification of key assumptions and questioning those related to CRC screening in a consistent, reproducible manner.[90]

CRC screening microsimulation models can generate important clinical outcomes and cost-effectiveness evidence for medical policy decisions. Prospective RCTs are the gold standard for evidence-based validation of effective screening approaches.[91] However, for assessing the long-term effectiveness or cost-effectiveness of all potential CRC screening regimens, microsimulation modeling is better suited than are RCTs.[10] The data from these models can allow payers and providers to monitor trends across diseases and types of interventions.

### Available Theoretical Models

Three CISNET CRC screening models are within CISNET, which are recognized by the USPSTF: MISCAN, Simulation Model of Colorectal Cancer, and the CRC Simulated Population Model for Incidence and Natural History. **Table 9** includes a summary of CISNET modeled cost-effectiveness data.[10,29]

Two other prominent models have been used to evaluate CRC screening characteristics (**Table 10**).[84,92] One of these, the Archimedes cost-effectiveness model, was used to generate evidence to support the inclusion of mt-sDNA testing in CRC screening guidelines by anticipating its impact on CRC incidence and mortality.[92] This model has been validated against several large studies, including the Cancer Prevention II study; it contains screening and treatment components that allow simulation of the detection and removal of polyps, and it generates information on prognosis and survival.[92] The model compared the clinical effectiveness of mt-sDNA testing at 1, 3, and 5 years with colonoscopy performed at 10-year intervals with no screening during a 30-year period. At an assumed average price of $600 per test and an assumed average cost of $1500 per colonoscopy following a positive test, 3-year mt-sDNA screening had an incremental cost-effectiveness ratio of $11,313 per quality-adjusted life-year (QALY) compared with no screening. Modeling results demonstrated that mt-sDNA is cost-effective with a willingness-to-pay threshold of $25,000 per QALY.[92]

A lifetime natural history Markov model was used to determine the cost-effectiveness of screening with mt-sDNA compared with FIT and colonoscopy (Table 10).[84,92] This model accounted for

**TABLE 10**. Archimedes and Markov Model Outputs: Clinical Effectiveness and Cost-Effectiveness by CRC Screening Approach[84,92]

| Markov Model[84] | | | | |
|---|---|---|---|---|
| Screening Approach | CRC Cases per 100,000 | CRC Deaths per 100,000 | QALYs/person | Cost-Effectiveness Ratio ($/QALY) Compared with No Screening |
| Outcomes for hypothetical 100,000-person cohorts with optimal participation of patients aged 50-80 years | | | | |
| No screening | 5927 | 2316 | 18.6687 | N/A |
| Colonoscopy every 10 years | 1597 | 445 | 18.7455 | $15,000 |
| FIT annually | 2334 | 519 | 18.747 | FIT was more effective and less costly. |
| mt-sDNA every 3 years | 2627 | 628 | 18.7423 | $29,500 |
| mt-sDNA annually | N/A | N/A | 18.7479 | $66,500 |
| Outcomes for hypothetical 100,000-person cohorts with high participation of patients aged 50-80 years[a] | | | | |
| No screening | 5927 | 2316 | 18.6687 | N/A |
| FIT annually | 3464 | 1054 | 18.7236 | $14,300 |
| mt-sDNA every 3 years | 3714 | 1173 | 18.7181 | $27,500 |

| Archimedes Model[92] | | | | |
|---|---|---|---|---|
| Screening Approach | Decrease in CRC Incidence (%) | Decrease in CRC Mortality (%) | QALYs Gained Compared with No Screening | Cost-Effectiveness Ratio ($/QALY) |
| No screening | 0 | 0 | 0 | $0 |
| Colonoscopy every 10 years | 65 | 73 | 0.133 | N/A |
| mt-sDNA annually | 63 | 72 | 0.129 | $20,178 |
| mt-sDNA every 3 years | 57 | 67 | 0.116 | $11,313 |

CRC indicates colorectal cancer; FIT, fecal immunochemical test; mt-sDNA, multitarget stool DNA; N/A, not applicable; QALY, quality-adjusted life-year.
[a]Based on the screening behavior assumption of 50% consistent screeners, 27% intermittent screeners, and 23% never screeners with an additional $153 for patient support per patient per testing cycle for FIT.

longitudinal screening participation behaviors in a US population and the natural history of CRC from development to progression for predictions of clinical and economic outcomes.[84] All CRC screening modalities that the USPSTF recommended show that CRC screening is cost-effective, meaning that screening is less costly and more effective than no screening. However, these analyses assume 100% adherence, which can significantly influence the calculated effectiveness and reduction in mortality.[93]

## Challenges Associated With Modeling

In general, the variables underlying the models can be subdivided into 2 categories: those focused on lesion detection and those that assess harms, and both come with unique challenges.

### Model Assumptions

Each model uses slightly different assumptions about the natural history of CRC and about test performance to predict screening outcomes such as QALYs gained, CRC incidence and mortality, and screening intervals and frequency.[10] However, the design and assumptions of various microsimulation models have limitations that may reduce their ability to predict the real-world clinical utility and value of a given screening modality. Some members noted that at this time, void of available clinical or study data, the models work relatively well.

Each CISNET model makes similar assumptions about carcinogenesis but assumes different levels of risk of adenoma development, sojourn time, and anatomical location.[94] The average dwell time (from polyp formation to CRC development) is assumed and calibrated to CRC incidence rates from 1975-1979 National Cancer Institute Surveillance, Epidemiology, and End Results data because the population included in this database from this period had largely been unscreened. In this way, the baseline CRC incidence rates used in the model are higher than those currently observed.[10,94]

CRC screening microsimulation models also factor in the sensitivity and specificity of each screening test according to reports in the published literature.[10] However, test performance values do not account for multiyear screenings and are based on the assumption of no false-negative results. Existing CRC screening models do not

include a differentiation for sessile serrated adenomas/polyps and treat all polyps as equal regardless of size.[10]

To predict the maximum achievable benefit for each screening modality, most CRC screening models assume 100% adherence rates for each procedure (including all screening modalities, as well as diagnostic and surveillance colonoscopies). These rates do not reflect real-world compliance rates.[10] Furthermore, these models do not account for a variety of risk factors, underlying health issues, and personal preferences, which are all likely to affect screening adherence and compliance.[10] Colonoscopies are used as the screening standard, against which other screening evaluations are judged. The models assume that the burden of each test is comparable; however, real-world evidence suggests that the relative burden of each test will vary by individual preference and circumstance. In addition, the measures of burdens and harms used in these models do not take into account a variance in quality-of-life outcomes.[10]

### Use of Microsimulation Model Data by Decision Makers

Payers often prefer to use empiric practice pattern evidence rather than microsimulation models to support decision making. Unequivocal evidence of benefit is an important consideration for payers. Most clinical decisions are made by a committee of senior physicians in large payer organizations. Therefore, the focus of the review is often on the clinical Level 1 evidence, which consists of either high-quality, adequately powered, prospective cohort studies or systematic review of these studies.[95]

In a study of representatives of 18 US health plans and health-system organizations, 89% of respondents agreed that organizations should be willing to make healthcare decisions based on RCTs as well as observational studies.[96] Payers may view empiric results as more useful than analyses generated with hypothetical models because the assumptions made in models might not reflect real-world conditions. There is an absence of RCTs and empiric outcome analyses of several currently used CRC screening modalities. Direct comparative evaluation of several CRC screening methods is limited. Therefore, the cost-effectiveness data preferred for payer decision making may simply be unavailable. In many diagnostic tests, the clinical utility of a test has not yet been established or has been established in a sample of people who are believers in the study already, which does not prove generalizability.[97]

The advantage of models in general is that they can simulate conditions under which it would be unethical or financially unmanageable to conduct RCTs. However, varying degrees of transparency exist among microsimulation models with respect to publishing model parameters, calibration data, and validation results.[98] Although numerous challenges to model transparency exist, including overcoming substantial financial investment and technical challenges with describing and evaluating the model, model transparency is considered essential if model outcomes are to influence healthcare policy.[98]

## Recommendations for Improving Evaluations of CRC Screening Modalities

At the roundtable meeting, participants stated that decision makers need specific data when assessing CRC screening modalities, including the assumptions made in theoretical models regarding the sensitivity and specificity of each modality. The expert panel recommended that model developers emphasize absolute transparency, including reporting the factors used to design studies and describing the analyses that led to comparative cost-effectiveness findings among modalities.

Roundtable participants recognized that real-world study data are necessary to earn payer trust. For example, they favored a collaborative approach to develop a cost-effectiveness model that reflects variability in population characteristics, screening volume, and screening modality price. They called for the publication of CRC screening data that address this limitation. They noted that empiric cost-effectiveness analyses are more useful for payers than are hypothetical models because the data can be used for indirect comparative analyses where no head-to-head comparisons are available. Meta-analyses of real-world data may lead to actionable insights.

Another recommendation from the expert panel was to evaluate screening modalities in populations who are not perfectly adherent. Because perfect adherence does not exist, different modalities might be optimal or better in different circumstances. An adherence-adjusted model that uses reasonable adherence rates, which has been demonstrated in a CISNET model of lung cancer,[93] could highlight key differences among the screening modalities.

Roundtable participants stated that evidence demonstrating the clinical utility of CRC screening modalities in highly regarded, peer-reviewed journals, with a focus on individual preference and uptake, is critical to creating a budget impact model that could influence stakeholder decisions about adopting and promoting CRC screening strategies. They highlighted the need for high-quality evidence of effective strategies to increase compliance, and they suggested that payers may be less likely to trust budget impact models that overwhelmingly favor 1 particular screening method.

The participants also highlighted the reputational and economic importance of improved quality ratings associated with increased CRC screening. One area of cost-effectiveness modeling that has shown promise is the cost per additional person to screen. A number of stakeholders care about getting their populations up-to-date. Their quality ratings depend on up-to-date screenings, or there are linked incentives at the provider level. Using models to determine the most cost-effective way to increase adherence could help move this forward.

## Health Economic Value Proposition for CRC Screening: The Accountable Care Model

ACOs, formed by the ACA, are groups of healthcare providers (including physicians and hospitals) that are held jointly accountable for improving quality of care and population health and for lowering costs for delivering care to beneficiaries.[99] ACO enrollment was associated with positive changes in CRC screening rates in a claims analysis of Medicare beneficiary data collected from 2006 to 2013.[100] ACO enrollment in the Medicare Shared Savings Program was associated with a 0.24% increase in CRC screening rates relative to before ACO enrollment in the total population of Medicare beneficiaries 65 years or older ($P = .03$). In the population 75 years and younger, ACO enrollment was associated with a 3% increase compared with CRC screening rates before ACO enrollment.[100] Although other literature has demonstrated challenges to increase screening compliance, this outcome has been observed in other studies that deployed screening interventions (ie, media campaigns or patient navigation programs) to increase screening rates.[78,81]

ACOs are structured appropriately to support member outreach, disease management, wellness programs, and population health. Evidence from cost-benefit analyses can be used to implement CRC screening guidelines and pathways for ACOs, which would expect their providers to follow these guidelines and pathways by prescribing the agreed-on CRC screening modalities. Physicians in the ACO can decide what pathway or what guidelines they expect their providers to follow. Therefore, the availability of a cost-benefit analysis that provided information on which made the most sense for their institution would allow stakeholders to set guidelines and pathways accordingly. That would then be the approach they would expect their providers to follow.

## Conclusions

Participants from the roundtable meeting discussed the need to increase CRC screening rates to reduce CRC-related morbidity and mortality. They reviewed the USPSTF recommendations on CRC screening and acknowledged the suboptimal adherence to these recommendations. They identified real-world barriers to CRC screening compliance, cost implications of CRC screening, and factors that influence screening compliance. A discussion of the health economic value proposition for CRC screening addressed insurance coverage for CRC screening and coverage gaps. Roundtable participants stressed the importance of collecting and modeling real-world data that reflect actual practice variations and that acknowledge imperfect patient adherence. They felt it important to recognize the varied implications of different types of colorectal polyps and better take into account the particular biology of each. Participants discussed recommendations for increasing CRC screening rates through evidence-based strategies, such as patient navigation, reminders, education, and awareness. They noted the importance of shared decision making between providers and potential screening participants. Finally, participants recognized the importance of CRC screening recommendations from healthcare providers and the strategies payers might employ to increase screening rates. These would include the removal of financial barriers, outreach efforts to identify beneficiaries who need CRC screening, and targeted incentives to increase screening rates. ■

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## REFERENCES

1. Tests to detect colorectal cancer and polyps: what is colorectal cancer? National Cancer Institute website. cancer.gov/types/colorectal/screening-fact-sheet#what-is-colorectal-cancer. Updated July 7, 2016. Accessed February 20, 2020.
2. Cancer stat facts: colorectal cancer. Surveillance, Epidemiology, and End Results Program website. seer.cancer.gov/statfacts/html/colorect.html. Published 2019. Accessed March 16, 2020.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin.* 2020;70(1):7-30. doi: 10.3322/caac.21590.
4. Colorectal cancer facts & figures 2020-2022. American Cancer Society website. cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/colorectal-cancer-facts-and-figures/colorectal-cancer-facts-and-figures-2020-2022.pdf. Published January 8, 2020. Accessed March 11, 2020.
5. Ward E, Halpern M, Schrag N, et al. Association of insurance with cancer care utilization and outcomes. *CA Cancer J Clin.* 2008;58(1):9-31. doi: 10.3322/CA.2007.0011.

6. Lin JS, Piper MA, Perdue LA, et al. *Screening for Colorectal Cancer: A Systematic Review for the U.S. Preventive Services Task Force.* Evidence Syntheses, No. 135. AHRQ Publication No. 14-05203-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2016.
7. Aarons CB, Shanmugan S, Bleier JI. Management of malignant colon polyps: current status and controversies. *World J Gastroenterol*. 2014;20(43):16178-16183. doi: 10.3748/wjg.v20.i43.16178.
8. Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: recommendations for physicians and patients from the U.S. Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol*. 2017;112(7):1016-1030. doi: 10.1038/ajg.2017.174.
9. Brenner H, Hoffmeister M, Stegmaier C, Brenner G, Altenhofen L, Haug U. Risk of progression of advanced adenomas to colorectal cancer by age and sex: estimates based on 840,149 screening colonoscopies. *Gut.* 2007;56(11):1585-1589. doi: 10.1136/gut.2007.122739.
10. Zauber A, Knudsen A, Rutter CM, Lansdorp-Vogelaar I, Kuntz KM. *Evaluating the Benefits and Harms of Colorectal Cancer Screening Strategies: A Collaborative Modeling Approach*. Rockville, MD: Agency for Healthcare Research and Quality; 2015.
11. Cancer trends progress report: financial burden of cancer care. National Cancer Institute website. progressreport.cancer.gov/after/economic_burden. Updated February 2019. Accessed February 12, 2020.
12. Subramanian S, Tangka FKL, Hoover S, Royalty J, Degroff A, Joseph D. Costs of colorectal cancer screening provision in CDC's Colorectal Cancer Control Program: comparisons of colonoscopy and FOBT/FIT based screening. *Eval Program Plann*. 2017;62:73-80. doi: 10.1016/j.evalprogplan.2017.02.007.
13. Bradley CJ, Lansdorp-Vogelaar I, Yabroff R, et al. Productivity savings from colorectal cancer prevention and control strategies. *Am J Prev Med.* 2011;41(2):e5-e14. doi: 10.1016/j.amepre.2011.04.088.
14. Rodriguez-Bigas MA, Lin EH, Crane CH. Colorectal cancer management. In: Kufe DW, Pollock RE, Weichselbaum RR, et al. *Holland-Frei Cancer Medicine*. 6th ed. Hamilton, ON: BC Decker; 2003:1-2.
15. Goede SL, Kuntz KM, van Ballegooijen M, et al. Cost-savings to Medicare from pre-Medicare colorectal cancer screening. *Med Care*. 2015;53(7):630-638. doi: 10.1097/MLR.0000000000000380.
16. Cancer care spending in California: what Medicare data say. California Healthcare Foundation website. chcf.org/wp-content/uploads/2017/12/PDF-CancerCareSpendingMedicare.pdf. Published August 2015. Accessed August 30, 2019.
17. NCCN Clinical Practice Guidelines in Oncology. Colorectal Cancer Screening, version 2.2020. National Comprehensive Cancer Network website. nccn.org/professionals/physician_gls/pdf/colon.pdf. Published February 2020. Accessed March 12, 2020.
18. Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM; American College of Gastroenterology. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol.* 2009;104(3):739-750. doi: 10.1038/ajg.2009.104.
19. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250-281. doi: 10.3322/caac.21457.
20. Patient Protection and Affordable Care Act, 42 USC §18001 (2010). Coverage of certain preventive services under the Affordable Care Act: a rule by the Internal Revenue Service, the Employee Benefits Security Administration, and the Health and Human Services Department. *Federal Register* website. federalregister.gov/documents/2015/07/14/2015-17076/coverage-of-certain-preventive-services-under-the-affordable-care-act. Published July 14, 2015. Accessed April 16, 2020.
21. Jodal HC, Helsingen LM, Anderson JC, Lytvyn L, Vandvik PO, Emilsson L. Colorectal cancer screening with faecal testing, sigmoidoscopy or colonoscopy: a systematic review and network meta-analysis. *BMJ Open*. 2019;9(10):e032773. doi: 10.1136/bmjopen-2019-032773.
22. US Preventive Services Task Force; Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement [published corrections appear in *JAMA*. 2016;316(5):545. doi: 10.1001/jama.2016.9943; *JAMA*. 2017;317(21):2239. doi: 10.1001/jama.2017.5918]. *JAMA.* 2016;315(23):2564-2575. doi: 10.1001/jama.2016.5989.
23. Colorectal Cancer Screening in Average-risk Population: Immunochemical Fecal Occult Blood Testing Versus Colonoscopy. clinicaltrials.gov/ct2/show/NCT00906997. Updated April 1, 2015. Accessed March 18, 2020.
24. Colonoscopy and FIT as Colorectal Cancer Screening Test in the Average Risk Population. clinicaltrials.gov/ct2/show/NCT02078804. Updated February 19, 2020. Accessed March 18, 2020.
25. Colonoscopy Versus Fecal Immunochemical Test in Reducing Mortality From Colorectal Cancer (CONFIRM). clinicaltrials.gov/ct2/show/NCT01239082. Updated November 22, 2019. Accessed March 18, 2020.
26. The Northern-European Initiative on Colorectal Cancer (NordICC). clinicaltrials.gov/ct2/show/NCT00883792. Published June 19, 2017. Accessed March 18, 2020.
27. Kaminski MF, Bretthauer M, Zauber AG, et al. The NordICC study: rationale and design of a randomized trial on colonoscopy screening for colorectal cancer. *Endoscopy*. 2012;44(7):695-702. doi: 10.1055/s-0032-1306895.
28. Quintero E, Castells A, Bujanda L, et al; COLONPREV Study Investigators. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. *N Engl J Med*. 2012;366(8):697-708. doi: 10.1056/NEJMoa1108895.
29. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of benefits, burden, and harms of colorectal cancer screening strategies: modeling study for the US Preventive Services Task Force. *JAMA*. 2016;315(23):2595-2609. doi: 10.1001/jama.2016.6828.
30. Vermeer NC, Snijders HS, Holman FA, et al. Colorectal cancer screening: systematic review of screen-related morbidity and mortality. *Cancer Treat Rev*. 2017;54:87-98. doi: 10.1016/j.ctrv.2017.02.002.
31. Warren JL, Klabunde CN, Mariotto AB, et al. Adverse events after outpatient colonoscopy in the Medicare population. *Ann Intern Med*. 2009;150(12):849-857,W152. doi: 10.7326/0003-4819-150-12-200906160-00008.
32. de Moor JS, Cohen RA, Shapiro JA, et al. Colorectal cancer screening in the United States: trends from 2008 to 2015 and variation by health insurance coverage. *Prev Med*. 2018;112:199-206. doi: 10.1016/j.ypmed.2018.05.001.
33. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitargeted stool DNA testing for colorectal-cancer screening. *N Engl J Med.* 2014;370(14):1287-1297. doi: 10.1056/NEJMoa1311194.
34. Levin B, Lieberman DA, McFarland B, et al; American Cancer Society Colorectal Cancer Advisory Group; US Multi-Society Task Force; American College of Radiology Colon Cancer Committee. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *Gastroenterology*. 2008;134(5):1570-1595. doi: 10.1053/j.gastro.2008.02.002.
35. Ranasinghe I, Parzynski CS, Searfoss R, et al. Differences in colonoscopy quality among facilities: development of a post-colonoscopy risk-standardized rate of unplanned hospital visits. *Gastroenterology*. 2016;150(1):103-113. doi: 10.1053/j.gastro.2015.09.009.
36. Ko CW, Riffle S, Michaels L, et al. Serious complications within 30 days of screening and surveillance colonoscopy are uncommon. *Clin Gastroenterol Hepatol*. 2010;8(2):166-173. doi: 10.1016/j.cgh.2009.10.007.
37. Pendsé DA, Taylor SA. Complications of CT colonography: a review. *Eur J Radiol.* 2013;82(8):1159-1165. doi: 10.1016/j.ejrad.2012.04.011.
38. Froehlich F, Wietlisbach V, Gonvers JJ, Burnand B, Vader JP. Impact of colonic cleansing on quality and diagnostic yield of colonoscopy: the European Panel of Appropriateness of Gastrointestinal Endoscopy European multicenter study. *Gastrointest Endosc*. 2005;61(3):378-384. doi: 10.1016/s0016-5107(04)02776-2.
39. Harewood GC, Sharma VK, de Garmo P. Impact of colonoscopy preparation quality on detection of suspected colonic neoplasia. *Gastrointest Endosc*. 2003;58(1):76-79. doi: 10.1067/mge.2003.294.
40. Lebwohl B, Kastrinos F, Glick M, Rosenbaum AJ, Wang T, Neugut AI. The impact of suboptimal bowel preparation on adenoma miss rates and the factors associated with early repeat colonoscopy. *Gastrointest Endosc.* 2011;73(6):1207-1214. doi: 10.1016/j.gie.2011.01.051.
41. Hoover S, Subramanian S, Tangka FKL, et al. Patients and caregivers costs for colonoscopy-based colorectal cancer screening: experience of low-income individuals undergoing free colonoscopies. *Eval Program Plann.* 2017;62:81-86. doi: 10.1016/j.evalprogplan.2017.01.002.
42. de Wijkerslooth TR, de Haan MC, Stoop EM, et al. Reasons for participation and nonparticipation in colorectal cancer screening: a randomized trial of colonoscopy and CT colonography. *Am J Gastroenterol.* 2012;107(12):1777-1783. doi: 10.1038/ajg.2012.140.
43. Bellini D, Rengo M, De Cecco CN, Iafrate F, Hassan C, Laghi A. Perforation rate in CT colonography: a systematic review of the literature and meta-analysis. *Eur Radiol.* 2014;24(7):1487-1496. doi: 10.1007/s00330-014-3190-1.
44. Lansdorp-Vogelaar I, van Ballegooijen M, Zauber AG, Boer R, Wilschut J, Habbema JD. At what costs will screening with CT colonography be competitive? a cost-effectiveness approach. *Int J Cancer*. 2009;124(5):1161-1168. doi: 10.1002/ijc.24025.
45. Moyer A. Comparing your options for colorectal cancer screening. The Alliance website. the-alliance.org/blog/comparing-your-options-for-colorectal-cancer-screening. Published August 17, 2016. Accessed December 15, 2017.
46. Pyenson B, Pickhardt PJ, Sawhney TG, Berrios M. Medicare cost of colorectal cancer screening: CT colonography vs. optical colonoscopy. *Abdom Imaging*. 2015;40(8):2966-2976. doi: 10.1007/s00261-015-0538-1.
47. CMS. 2017 Alpha-Numeric HCPCS [Healthcare Common Procedure Coding System] File. cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/Alpha-Numeric-HCPCS-Items/2017-Alpha-Numeric-HCPCS-File. Updated November 17, 2016. Accessed April 16, 2020.
48. CMS. 17CLAB [clinical laboratory fee schedule). cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Clinical-Laboratory-Fee-Schedule-Files-Items/17CLAB. Updated January 2017. Accessed April 16, 2020.
49. Young GP, Symonds EL, Allison JE, et al. Advances in fecal occult blood tests: the FIT revolution. *Dig Dis Sci.* 2015;60(3):609-622. doi: 10.1007/s10620-014-3445-3.
50. van Roon AH, Wilschut JA, Hol L, et al. Diagnostic yield improves with collection of 2 samples in fecal immunochemical test screening without affecting attendance. *Clin Gastroenterol Hepatol*. 2011;9(4):333-339. doi: 10.1016/j.cgh.2010.12.012.
51. Allison JE, Fraser CG, Halloran SP, Young GP. Population screening for colorectal cancer means getting FIT: the past, present, and future of colorectal cancer screening using the fecal immunochemical test for hemoglobin (FIT). *Gut Liver*. 2014;8(2):117-130. doi: 10.5009/gnl.2014.8.2.117.
52. Mathews B, Ratcliffe T, Sehgal R, Abraham J, Monash B. Fecal occult blood testing in hospitalized patients with upper gastrointestinal bleeding. *J Hosp Med*. 2017;12(7):567-569. doi: 10.12788/jhm.2773.
53. Pickhardt PJ. Emerging stool-based and blood-based non-invasive DNA tests for colorectal cancer screening: the importance of cancer prevention in addition to cancer detection. *Abdom Radiol (NY).* 2016;41(8):1441-1444. doi: 10.1007/s00261-016-0798-4.
54. Cologuard physician brochure. Madison, WI: Exact Sciences Corp. https://cdn2.hubspot.net/hubfs/377740/LBL-0260 Rev 2 FINAL.pdf. Accessed March 12, 2020.
55. East JE, Vieth M, Rex DK. Serrated lesions in colorectal cancer screening: detection, resection, pathology and surveillance. *Gut*. 2015;64(6):991-1000. doi: 10.1136/gutjnl-2014-309041.
56. White A, Thompson TD, White MC, et al. Cancer screening test use – United States, 2015. *MMWR Morb Mortal Wkly Rep.* 2017;66(8):201-206. doi: 10.15585/mmwr.mm6608a1.
57. Colorectal cancer screening: best practices handbook for health plans. National Colorectal Cancer Roundtable website. nccrt.org/wp-content/uploads/NCCRT-Health-Plan-Handbook-Draft-07c.pdf. Published March 2017. Accessed November 12, 2019.
58. Inadomi JM, Vijan S, Janz NK, et al. Adherence to colorectal cancer screening: a randomized clinical trial of competing strategies. *Arch Intern Med.* 2012;172(7):575-582. doi: 10.1001/archinternmed.2012.332.
59. Liang PS, Wheat CL, Abhat A, et al. Adherence to competing strategies for colorectal cancer screening over 3 years. *Am J Gastroenterol.* 2016;111(1):105-114. doi: 10.1038/ajg.2015.367.
60. Schroy PC III, Duhovic E, Chen CA, et al. Risk stratification and shared decision making for colorectal cancer screening: a randomized controlled trial. *Med Decis Making*. 2016;36(4):526-535. doi: 10.1177/0272989X1562562.
61. Finney Rutten LJ, Jacobson RM, Wilson PM. Early adoption of a multitarget stool DNA test for colorectal cancer screening. *Mayo Clin Proc*. 2017;92(5):726-733. doi: 10.1016/j.mayocp.2017.01.019.
62. Prince M, Lester L, Chiniwala R, Berger B. Multitarget stool DNA tests increases colorectal cancer screening among previously noncompliant Medicare patients. *World J Gastroenterol.* 2017;23(3):464-471. doi: 10.3748/wjg.v23.i3.464.
63. Cyhaniuk A, Coombes ME. Longitudinal adherence to colorectal cancer screening guidelines. *Am J Manag Care.* 2016;22(2):105-111.
64. Fenton JJ, Elmore JG, Buist DS, Reid RJ, Tancredi DJ, Baldwin LM. Longitudinal adherence with fecal occult blood test screening in community practice. *Ann Fam Med*. 2010;8(5):397-401. doi: 10.1370/afm.1133.
65. Gellad ZF, Stechuchak KM, Fisher DA, et al. Longitudinal adherence to fecal occult blood testing impacts colorectal cancer screening quality. *Am J Gastroenterol.* 2011;106(6):1125-1134. doi: 10.1038/ajg.2011.11.

66. Greuter MJ, Berkhof J, Canfell K, Lew JB, Dekker E, Coupé VM. Resilience of a FIT screening programme against screening fatigue: a modelling study. *BMC Public Health.* 2016;16(1):1009. doi: 10.1186/s12889-016-3667-8.
67. Jensen CD, Corley DA, Quinn VP, et al. Fecal immunochemical test program performance over 4 rounds of annual screening: a retrospective cohort study. *Ann Intern Med.* 2016;164(7):456-463. doi: 10.7326/M15-0983.
68. van der Vlugt M, Grobbee EJ, Bossuyt PM, et al. Adherence to colorectal cancer screening: four rounds of faecal immunochemical test-based screening. *Br J Cancer*. 2017;116(1):44-49. doi: 10.1038/bjc.2016.399.
69. Insurance coverage for colorectal cancer screening. American Cancer Society website. cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/screening-coverage-laws.html#written_by. Updated May 30, 2018. Accessed April 16, 2020.
70. Flowers L, Noel-Miller C, Okrent D. Colonoscopy screening after the Affordable Care Act: cost barriers persist for Medicare beneficiaries. AARP website. aarp.org/content/dam/aarp/research/public_policy_institute/health/2013/colonoscopy-screening-after-aca-insight-AARP-ppi-health.pdf. Published December 2013. Accessed December 18, 2017.
71. The costs of cancer: addressing patient costs. American Cancer Society Cancer Action Network website. fightcancer.org/sites/default/files/Costs%20of%20Cancer%20-%20Final%20Web.pdf. Published April 2017. Accessed September 30, 2019.
72. Klabunde CN, Schenck AP, Davis WW. Barriers to colorectal cancer screening among Medicare consumers. *Am J Prev Med.* 2006;30(4):313-319. doi: 10.1016/j.amepre.2005.11.006.
73. Jones RM, Devers KJ, Kuzel AJ, Woolf SH. Patient-reported barriers to colorectal cancer screening: a mixed-methods analysis. *Am J Prev Med.* 2010;38(5):508-516. doi: 10.1016/j.amepre.2010.01.021.
74. Nagelhout E, Comarell K, Samadder NJ, Wu YP. Barriers to colorectal cancer screening in a racially diverse population served by a safety-net clinic. *J Community Health*. 2017;42(4):791-796. doi: 10.1007/s10900-mu017-0319-6.
75. Sly JR, Edwards T, Shelton RC, Jandorf L. Identifying barriers to colonoscopy screening for nonadherent African American participants in a patient navigation intervention. *Health Educ Behav.* 2013;40(4):449-457. doi: 10.1177/1090198112459514.
76. Marshall DA, Johnson FR, Kulin NA, et al. How do physician assessments of patient preferences for colorectal cancer screening tests differ from actual preferences? a comparison in Canada and the United States using a stated-choice survey. *Health Econ*. 2009;18(12):1420-1439. doi: 10.1002/hec.1437.
77. Cole D, Mai E, Gaebler J, et al. Preferences for colorectal screening tests among a previously unscreened population. Presented at: American College of Gastroenterology Annual Scientific Meeting; October 16-21, 2015; Honolulu, HI.
78. Hassmiller Lich K, Cornejo DA, Mayorga ME, et al. Cost-effectiveness analysis of four simulated colorectal cancer screening interventions, North Carolina. *Prev Chronic Dis*. 2017;14:E18. doi: 10.5888/pcd14.160158.
79. Wender R. Screening for colorectal cancer: optimizing quality. primary care version: part 2: delivering high-quality stool blood testing in primary care. CDC website. cdc.gov/cancer/colorectal/quality/crc_screening_optimizing_quality_primary_care2.pdf. Reviewed February 10, 2020. Accessed February 12, 2020.
80. Paying for colorectal cancer screening navigation toolkit: strategies for payment and sustainability. National Colorectal Cancer Roundtable website. nccrt.org/wp-content/uploads/v.22016_paying_pntoolkit_full_final.pdf. Published February 2016. Accessed September 30, 2019.
81. Reuland DS, Brenner AT, Hoffman R, et al. Effect of combined patient decision aid and patient navigation vs usual care for colorectal cancer screening in a vulnerable patient population: a randomized clinical trial. *JAMA Intern Med*. 2017;177(7):967-974. doi: 10.1001/jamainternmed.2017.1294.
82. Rice K, Gressard L, DeGroff A, et al. Increasing colonoscopy screening in disparate populations: results from an evaluation of patient navigation in the New Hampshire Colorectal Cancer Screening Program. *Cancer.* 2017;123(17):3356-3366. doi: 10.1002/cncr.30761.
83. Subramanian S, Tangka FK, Hoover S, et al. Costs of planning and implementing the CDC's Colorectal Cancer Screening Demonstration Program. *Cancer.* 2013;119(suppl 15):2855-2862. doi: 10.1002/cncr.28158.
84. Ladabaum U, Mannalithara A. Comparative effectiveness and cost effectiveness of a multitarget stool DNA test to screen for colorectal neoplasia. *Gastroenterology.* 2016;151(3):427-439.e6. doi: 10.1053/j.gastro.2016.06.003.
85. Meenan RT, Anderson ML, Chubak J, et al. An economic evaluation of colorectal cancer screening in primary care practice. *Am J Prev Med.* 2015;48(6):714-721. doi: 10.1016/j.amepre.2014.12.016.
86. Meridian incentive program. Meridian website. corp.mhplan.com/ContentDocuments/default.aspx?x=ZotNbWg5i0Ry4caZb1ziFsA6EPEH5WOMBBhhoHOA7Og7c1NU6mIe+CtnpLmJ1r5RfK3n6N0YXwLdsU/7o1IHmQ==. Published January 1, 2018. Accessed April 4, 2018.
87. 2017 HEDIS for the quality rating system: technical update. National Committee for Quality Assurance website. ncqa.org/wp-content/uploads/2018/08/20161003_-HEDIS_Quality_Rating-System_Technical_Specifications_Update.pdf. Published October 3, 2016. Accessed April 4, 2018.
88. Mehta SJ, Feingold J, Vandertuyn M, et al. Active choice and financial incentives to increase rates of screening colonoscopy – a randomized controlled trial. *Gastroenterology*. 2017;153(5):1227-1229.e2. doi: 10.1053/j.gastro.2017.07.015.
89. Sainfort F, Kuntz KM, Gregory S, et al. Adding decision models to systematic reviews: informing a framework for deciding when and how to do so. *Value Health.* 2013;16(1):133-139. doi: 10.1016/j.jval.2012.09.009.
90. van Ballegooijen M, Boer R, Zauber AG. Simulation of colorectal cancer screening: what we do and do not know and does it matter. *Best Pract Res Clin Gastroenterol.* 2010;24(4):427-437. doi: 10.1016/j.bpg.2010.07.001.
91. Devereaux PJ, Yusuf S. The evolution of the randomized controlled trial and its role in evidence-based decision making. *J Intern Med.* 2003;254(2):105-113. doi: 10.1046/j.1365-2796.2003.01201.x.
92. Berger BM, Schroy PC III, Dinh TA. Screening for colorectal cancer using a multitarget stool DNA test: modeling the effect of the interest interval on clinical effectiveness. *Clin Colorectal Cancer.* 2016;15(3):e65-e74. doi: 10.1016/j.clcc.2015.12.003.
93. Han SS, Erdogan SA, Toumazis I, Leung A, Plevritis SK. Evaluating the impact of varied compliance to lung cancer screening recommendations using a microsimulation model. *Cancer Causes Control*. 2017;28(9):947-958. doi: 10.1007/s10552-017-0907-x.
94. Rutter CM, Knudsen AB, March TL, et al. Validation of models used to inform colorectal cancer screening guidelines: accuracy and implications. *Med Decis Making.* 2016;36(5):604-614. doi: 10.1177/0272989X15622642.
95. Burns PB, Rohrich RJ, Chung KC. The levels of evidence and their role in evidence-based medicine. *Plast Reconstr Surg*. 2011;128(1):305-310. doi: 10.1097/PRS.0b013e318219c171.
96. Malone DC, Brown M, Hurwitz JT, Peters L, Graff JS. Real-world evidence: useful in the real world of US payer decision making? how? when? and what studies? *Value Health.* 2018;21(3):326-333. doi: 10.1016/j.jval.2017.08.3013.
97. Neumann PJ, Tunis SR. Medicare and medical technology—the growing demand for relevant outcomes. *N Engl J Med*. 2010;362(5):377-379. doi: 10.1056/NEJMp0912062.
98. Rutter CM, Zaslavsky AM, Feuer EJ. Dynamic microsimulation models for health outcomes: a review. *Med Decis Making*. 2011;31(1):10-18. doi: 10.1177/0272989X10369005.
99. Accountable Care Organizations (ACOs). CMS website. cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ACO. Updated February 11, 2020. Accessed March 18, 2020.
100. Resnick MJ, Graves AJ, Thapa S, et al. Medicare accountable care organization enrollment and appropriateness of cancer screening. *JAMA Intern Med*. 2018;178(5):648-654. doi: 10.1001/jamainternmed.2017.8087.