*Technical Report*

# Evaluating the Benefits and Harms of Colorectal Cancer Screening Strategies: A Collaborative Modeling Approach

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# Executive Summary

This report describes the findings of simulation modeling performed in conjunction with the 2015 colorectal cancer screening recommendations of the United States Preventive Services Task Force (USPSTF). Using three independently developed microsimulation models of colorectal cancer from the National Cancer Institute's CISNET consortium we predicted the benefits and harms associated with 204 unique colorectal cancer screening strategies. We then identified sets of screening strategies that yielded comparable benefits and provided a reasonable balance of benefits and harms.

Screening strategies were defined by the age to begin screening, age to end screening, screening modality, and screening interval. Ages to begin screening included 45, 50, and 55 and ages to end included 75, 80, and 85. Screening modalities, or combinations of modalities, included a sensitive guaiac-based fecal occult blood test (gFOBT), a fecal immunochemical test (FIT), a multi-target stool DNA test that includes a FIT (FIT-DNA), flexible sigmoidoscopy (SIG), flexible sigmoidoscopy with interval gFOBT (SIG+gFOBT), flexible sigmoidoscopy with interval FIT (SIG+FIT), computed tomographic (CT) colonography, and colonoscopy. Screening intervals varied by modality: we simulated intervals of 1, 2, and 3 years for gFOBT and FIT; 1, 3, and 5 years for FIT-DNA; 5 and 10 years for SIG and for CT colonography; and 5, 10, and 15 years for colonoscopy. For the strategies combining flexible sigmoidoscopy with interval stool testing we evaluated four sets of intervals: sigmoidoscopy every 10 years with either a 1-year or a 2-year interval for stool testing, and sigmoidoscopy every 5 years with either a 2-year or a 3-year interval for stool testing. We also simulated outcomes in the absence of colorectal cancer screening.

Estimates of test sensitivity and specificity were based primarily on a systematic evidence review performed in conjunction with this analysis by the Kaiser Permanente Research Affiliates Evidence-based Practice Center. When the models required test characteristics to be defined differently from the definitions used in the evidence review, we derived the required estimates using data from large studies included in the evidence review that were conducted in average-risk populations in the US and were of at least fair quality.

Outcomes were simulated for a hypothetical cohort of U.S. 40-year-olds born in 1975 who are at average risk for colorectal cancer. Primary outcomes included the number of life-years gained compared with no colorectal cancer screening for the benefits of screening, and the total number of colonoscopies required as a proxy for the harms and burden of screening. Other outcomes included the number of non-colonoscopy tests (by type), screening complications, colorectal cancer diagnoses, and colorectal cancer-related deaths, as well as reductions in colorectal cancer incidence and mortality.

Ideally, all 204 unique colorectal cancer screening strategies would be evaluated together on the basis of the primary measures of benefits and harms. However, doing so would provide an incomplete picture of the tradeoffs involved due to large differences in the number of non-colonoscopy tests across screening modalities. Instead, we first grouped together non-colonoscopy screening modalities with comparable burden (e.g., stool-based modalities, modalities combining flexible sigmoidoscopy and interval stool testing) to create classes of

comparable screening modalities. Using an approach similar to cost-effectiveness analysis, we then identified efficient strategies within each screening class. Finally, we selected from the sets of efficient screening strategies those that yielded comparable life-years gained and provided a reasonable ratio of harms and benefits, assuming that all strategies would have the same age to begin and end screening for ease of clinical implementation.

The models simulated nearly identical life expectancy and similar estimates of the lifetime risk of developing and of dying from colorectal cancer among unscreened 40-year-olds. Compared to no colorectal cancer screening, all screening strategies yielded sizable reductions in colorectal cancer incidence and mortality. Reductions were lowest with fecal immunochemical testing every 3 years from ages 55 to 75, with incidence reductions ranging from 24-43% and mortality reductions ranging from 50-58% across models. Reductions were highest with colonoscopy screening every 5 years from ages 45 to 85, with reductions across models ranging from 71-96% for incidence and 87-97% for mortality.

For age to begin screening we found that strategies that begin at age 45 were generally more effective and more efficient at providing additional life-years gained than strategies in which screening begins at age 50. For colonoscopy screening, two of the three models found that lowering the age to begin screening to age 45 and lengthening the screening interval to 15 years maintained the same or slightly more life-years gained as colonoscopy screening every 10 years from age 50 without increasing the lifetime number of total colonoscopies (note that both strategies involve three lifetime screening colonoscopies). The third model predicted slightly fewer life-years gained with the 15-year interval. For all other screening modalities, only one model predicted the same or more life-years gained when the age to begin screening was lowered from 50 to 45 and the screening interval was extended to the next shortest interval.

In consultation with the USPSTF members, we eliminated strategies with screening beginning at age 45 from consideration due to the lack of empiric evidence to support lowering the recommended age to begin screening and the modest differences in life-years gained. When these strategies were eliminated from consideration, we found that strategies with screening beginning at age 50 yielded more life-years gained and were more efficient than those with age to begin of 55. For age to end screening we found that, for persons who were adequately screened up to age 75, there was limited benefit in terms of life-years gained for extending the age to end screening to age 80 or 85. With ages to begin and end colorectal cancer screening of 50 and 75, the following screening modalities and screening intervals were efficient and yielded comparable life-years gained: colonoscopy every 10 years, annual FIT, sigmoidoscopy every 10 years with annual FIT, and CT colonography every 5 years. Because CT colonography generally requires cathartic bowel preparation comparable to that required for colonoscopy, we performed an additional analysis in which we used the number of cathartic bowel preparations as the proxy for harms and burden, rather than the number of colonoscopies. With this metric, CT colonography was not included as a recommended strategy because its efficiency ratio (i.e., $\Delta$CatharticPreps / $\Delta$LYG) exceeded that of colonoscopy.

In sensitivity analyses we considered FIT strategies with a lower threshold for positivity than in the base-case analysis and found that annual FIT screening with the higher positivity criterion continued to be the recommended strategy. We also considered best- and worst-case scenarios

for test sensitivity across recommended strategies and models; the predicted number of colonoscopies, non-colonoscopy tests, life-years gained, and colorectal cancer deaths averted varied by at most ±7% from the base-case analysis results.

Our analysis has a number of limitations. First, we assume 100% adherence with all screening, follow-up and surveillance procedures. While this level of adherence is not observed in practice, our estimates provide an indication of what is achievable in an unscreened population. With the passage of the Affordable Care Act, many of the financial barriers to screening have been removed. As a result, the percent of the US adult population that is up-to-date with colorectal cancer screening is likely to increase from the 2010 estimate of 65%.

Data from several studies suggest that colonoscopy might offer less protection from colorectal cancers in the proximal colon compared to the distal colon and rectum. The reasons for this remain unclear but likely involve a combination of biological and technical factors. Because colonoscopy is a component of all screening modalities, either as the primary screening test or as the follow-up procedure for positive results on other screening tests, we do not anticipate that the model-recommended screening test would change if, for example, we assumed colonoscopy sensitivity differed by location.

For ease of clinical implementation, we assumed that the recommended ages to begin and end screening would be fixed across screening modalities. A different set of model-recommended strategies could emerge if we had allowed the ages to begin and end to vary across tests. Finally, we use the number of colonoscopies as a proxy for the harms of colorectal cancer screening. While this metric accounts for the majority of screening-related harms, it does not account for the burden of screening, particularly for non-colonoscopy tests. As a result, direct comparison of screening strategies that utilize different screening modalities (e.g., colonoscopy screening vs. CT colonography vs. FIT) is hampered. A metric that more fully accounts for the harms and burden of screening would enable more meaningful comparisons across screening strategies.

In summary, while the three CISNET colorectal cancer models differed slightly in terms of the absolute benefits and harms of screening, they yielded consistent rankings of screening strategies. All three models found that the following screening strategies from age 50 to age 75 provide comparable life-years gained and an efficient balance of benefits and harms: colonoscopy every 10 years, annual FIT, flexible sigmoidoscopy every 10 years with annual FIT, and CT colonography every 5 years, provided the burden of cathartic bowel preparation with CT colonography is not accounted for.

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# Chapter 1. Introduction

Despite a 46 percent decline in colorectal cancer mortality rates from 1975 to 2011,[1] colorectal cancer remains the second most common cause of cancer death in the United States (US) with 49,700 deaths expected in 2015.[2] Randomized trials have demonstrated that colorectal cancer screening with fecal occult blood tests[3-6] (FOBTs) or with flexible sigmoidoscopy[7-10] reduces colorectal cancer mortality. Randomized trials of screening colonoscopy are in progress but incidence and mortality results are not anticipated for many years.[11-13] Screening is believed to act by detecting malignancies at earlier, more treatable stages, or by removing adenomatous polyps that are the primary colorectal cancer precursor. Colorectal cancer screening has become more acceptable in the general population; approximately 65% of the age-eligible population is now up to date with screening.[14]

The U.S. Preventive Services Task Force (USPSTF) first recommended colorectal cancer screening in 2002[15] on the basis of the published randomized controlled trials in the 1990s showing that the guaiac FOBT, Hemoccult II, reduced colorectal cancer mortality by 15% to 33%.[3-5] However the USPSTF stated that there was insufficient evidence to recommend an age to begin age or end screening, as well as which tests or intervals of testing to recommend.

Randomized controlled trials provide the highest quality evidence of the effectiveness of screening, but it is not feasible for trials to examine the full range of potential screening regimes. In this context, microsimulation modeling can be used to synthesize available information about colorectal cancer screening tests to provide guidance on the risks, benefits, and burden of different screening strategies to reduce colorectal cancer incidence and mortality. For their 2008 update of the 2002 recommendation the USPSTF requested a decision analysis using two of the three colorectal cancer models funded by the Cancer Intervention and Surveillance Modeling Network (CISNET) to inform the ages to begin and end screening, and intervals of screening. The decision analysis complemented the systematic evidence review because there was little direct evidence to inform such detailed recommendations. Based on the outcomes of the evidence review and decision analysis, in 2008 the USPSTF recommended routine colorectal cancer screening from age 50 through age 75. Recommended screening strategies were colonoscopy every ten years, flexible sigmoidoscopy every five years with intermittent FOBT, and annual sensitive FOBT (i.e., Hemoccult SENSA or fecal immunochemical testing (FIT)).

Since the 2008 USPSTF recommendations, new colorectal cancer screening tests have been developed (e.g., a multi-target stool DNA test[16]) and existing tests have been further studied (e.g., computed tomographic (CT) colonography[17-23] and fecal immunochemical tests[16,18,24-31]). For the 2015 update of the USPSTF colorectal cancer screening recommendations, the CISNET Colorectal Cancer Working Group has again provided estimates of the benefits, harms, and burden of various colorectal cancer screening strategies for the general population.

# Chapter 2. Methods

We used three independently-developed microsimulation models of colorectal cancer that are funded by the National Cancer Institute's CISNET consortium – Simulation Model of Colorectal Cancer (SimCRC), Microsimulation Screening Analysis (MISCAN) for Colorectal Cancer, and Colorectal Cancer Simulated Population model for Incidence and Natural history (CRC-SPIN) – to predict life years gained, colorectal cancer incidence and mortality, number of screening tests required, and complications of screening for over 200 colorectal cancer screening strategies. The strategies varied by screening modality, age to begin screening, age to end screening and screening interval. Using an approach similar to cost-effectiveness analysis,[32-33] we identified efficient strategies within each screening modality or combination of screening modalities, with the burden and harms of colorectal cancer screening represented by the number of colonoscopies required and the benefits of screening represented by the number of life-years gained relative to a base scenario with no screening for colorectal cancer.

## Microsimulation Models

The three microsimulation models used for this analysis have a long history of use in collaborative modeling analyses, including analyses to inform colorectal cancer screening National Coverage Determinations for the Centers for Medicare and Medicaid Services,[34-37] as well as to guide screening programs in South Carolina.[38] Each model consists of a natural history component and a screening component. These components are described in detail in the sections that follow.

### Natural History Component of CISNET Colorectal Cancer Models

All three microsimulation models describe the natural history of colorectal cancer in an unscreened population, based on the adenoma-carcinoma sequence.[39-41] Simulated persons begin in a disease-free "no lesion" state and may progressively transition to an adenoma state, a preclinical colorectal cancer state, and a clinically detected colorectal cancer state, from which they may die from colorectal cancer (**Figure 1**). Persons may die from other causes at any time. While the models have a similar natural history framework, they differ in the implementation of the framework. **Table 1** provides a comparison of the structure of the natural history components of the three models, and key components are described below.

#### Adenoma Risk

In all three models, adenoma risk varies stochastically across individuals and by age and sex, although they use different distributions to describe risk. All models allow multiple adenomas within individuals, although they use different mechanisms to generate the number of adenomas within an individual. None of the models allow detectable adenomas in individuals younger than 20 years of age. The risk of having an adenoma is derived to match the prevalence of adenomas by age from autopsy studies. None of the models allow regression of adenomas, nor do they simulate the serrated polyp pathway.[42-43]

Simulated adenoma prevalence among an unscreened population ranges from 11-13% at age 40, 26-36% at age 60, and 43-50% at age 80, with higher prevalence at younger ages in MISCAN and higher at older ages with SimCRC (**Figure 2**). In MISCAN, adenoma prevalence after age 80 decreases with age. This is the result of a substantial decrease in the model-predicted onset of adenomas after age 80 and of adenomas progressing to (preclinical) colorectal cancer.

**Distribution of Adenomas in the Colon and Rectum**

All three models assign adenomas a location in the large intestine based on a multinomial distribution. SimCRC and CRC-SPIN inform these distributions using data on the location of adenomas from autopsy studies;[44-53] MISCAN assumes that the distribution of adenomas in the colon and rectum is the same as the distribution of clinically-detected colorectal cancer.[54] Consequently, the models differ in the distribution of adenomas by location within the colon and rectum (**Figure 3**). The proportion of adenomas in the distal colon (i.e., descending or sigmoid colon) or rectum ranged from 38% to 63%, with a higher proportion in MISCAN compared with SimCRC and CRC-SPIN. This difference has implications for the simulated effectiveness of flexible sigmoidoscopy – a test that only visualizes the distal colon and rectum.

**Adenoma Growth**

All models allow adenoma growth to vary stochastically across individuals, and across adenomas within individuals, though the models use different distributions to describe variability in growth. None of the models specify correlation of adenoma growth within individuals. MISCAN and SimCRC define adenoma size categorically (≤5 mm, 6-9 mm, ≥10 mm) and do not explicitly specify a minimum or maximum size. CRC-SPIN simulates adenoma growth continuously, with a minimum detectable size of 1 mm and maximum size of 50 mm. Adenoma growth depends on location in the SimCRC and CRC-SPIN models, with SimCRC distinguishing between adenomas in the proximal colon, distal colon, and rectum, and CRC-SPIN distinguishing between adenomas in the colon and rectum.

The models also differ in the distribution of the size of the most advanced adenoma (**Figure 4**). Compared with MISCAN and CRC-SPIN, persons with adenomas in SimCRC were less likely to have 1-5 mm adenoma(s) as the largest adenoma, while persons in CRC-SPIN were more likely to have 10+ mm adenoma(s) as the largest adenoma(s). For all models the percentage of adenomas that are ≥10 mm increases with increasing age.

**Progression to Preclinical Colorectal Cancer**

All three models allow multiple preclinical cancers and allow the time from adenoma onset to progression to preclinical disease to vary stochastically across individuals and across adenomas within individuals, although the models use different distributions to describe variability in adenoma progression. None of the models specify correlation of adenoma progression rates within individuals. MISCAN and SimCRC do not allow progression to preclinical cancer in adenomas that are less than 6mm. CRC-SPIN simulates progression rates that are a function of continuous size, with a very small (but non-zero) probability of progression to preclinical cancer in adenomas less than 6mm.

In MISCAN and CRC-SPIN, the probability that an adenoma progresses to preclinical cancer depends on age at adenoma initiation. In the SimCRC and CRC-SPIN models, adenoma progression depends on location in the colon or rectum. MISCAN specifies two types of adenomas: non-progressive adenomas, which have no potential of becoming cancerous, and progressive adenomas, which have this potential. The SimCRC and CRC-SPIN models do not explicitly model non-progressive adenomas; these models simulate slow-growing adenomas that would not progress, even for individuals living more than 100 years after adenoma initiation.

**Progression to Clinically-Detected Colorectal Cancer (Sojourn Time)**

All models allow sojourn time (i.e., the time from preclinical cancer to cancer detection) to vary stochastically across individuals, although the models use different distributions to describe variability in sojourn times. The SimCRC and MISCAN models have a longer average sojourn time than CRC-SPIN and therefore SimCRC and MISCAN have a higher prevalence of preclinical disease than CRC-SPIN. The simulated prevalence of preclinical cancer is low at all ages, never exceeding 4% (**Figure 5**).

All models assume that when one preclinical cancer is detected (either by symptoms or by screening), all are detected. Currently, none of the models explicitly simulate metachronous primary colorectal cancer after colorectal cancer detection. The impact of metachronous primary colorectal cancer is incorporated in the overall colorectal cancer relative survival after diagnosis.

Prior to age 75, the models reproduced age-specific colorectal cancer incidence rates from the Surveillance, Epidemiology, and End Results Program (SEER) from 1975-1979 – a period with little to no colorectal cancer screening (**Figure 6**). At older ages SimCRC and CRC-SPIN predicted incidence rates that were higher than those observed in SEER. For comparison, **Figure 6** also shows colorectal cancer incidence rates from more recent SEER data (2007-2011), which are considerably lower than those from 1975-1979. However, the rates in the recent period are among a population in which many (55-59%) of those eligible for colorectal cancer screening are up-to-date with current guidelines.[55] Incidence in an unscreened population would be higher than those currently reported in SEER.

The models generally replicated the stage distribution observed in SEER among a largely unscreened population, although the proportion of cases diagnosed at stage IV was lower with CRC-SPIN (19% of cases vs. 25% of cases in SEER) (**Figure 7**).

**Colorectal Cancer Death**

All three models stochastically assign colorectal cancer death using survival probabilities based on Cox proportional hazards models for relative survival applied to SEER survival data for cases diagnosed from 1/1/1975 to 12/31/2003 with follow-up through 12/31/2010.[56] Time to colorectal cancer death depends on year at diagnosis, stage, location (colon or rectum), age at diagnosis, sex, and (optionally) race. None of the models allow colorectal cancer death during the lead time (i.e., the time between a screen-detected cancer and the time that the person would have been clinically detected).

### Non-Colorectal Cancer Death

All three models stochastically assign non-colorectal cancer death using the 2009 US life tables from the National Center for Health Statistics.[57]

## Screening Component of CISNET Colorectal Cancer Models

All models have a screening component that allows the adenoma carcinoma sequence to be interrupted through detection and removal of preclinical lesions. Screening is overlaid on the same population, so that the impact of screening on each individual life history is known. In other words we know for every individual in the model what happens with screening and in the absence of screening. The effectiveness of a screening strategy is modeled through a test's ability to detect lesions (that is, adenomas or preclinical colorectal cancer) (**Figure 1**). Once screening is introduced, a simulated person who has an underlying lesion has a chance of having it detected during a screening round depending on the sensitivity of the test for that lesion and, for endoscopic tests, whether the lesion is within the reach of the scope. Screened persons without an underlying lesion can have a false-positive test result and undergo unnecessary follow-up colonoscopy. Non-adenomatous polyps are not modeled explicitly, but their detection is reflected in false-positive rates of the screening tests. The models incorporate the risk for fatal complications associated with perforation during endoscopy. The impact of screening depends on the test performed, its associated estimates of sensitivity and specificity for detecting adenomas (by size) and cancer at each testing, and how frequently the test is repeated over time.

# Model Calibration

Because the natural history of colorectal cancer is largely unobserved, there are limited data to directly inform the parameters of the natural history components of the models. Model parameters values for the natural history components were derived by calibration. Model calibration is the process of selecting parameters so that model predictions closely match data from observational studies ("calibration data").[58]

All three natural history models are calibrated to SEER colorectal cancer incidence rates in 1975-1979 because this period represents colorectal cancer incidence in the US when there was little or no screening for the disease. All models incorporate information about adenoma prevalence from autopsy studies.[44-53] The MISCAN and SimCRC models are calibrated using findings from each study. The CRC-SPIN model incorporates this information by specifying prior distributions for adenoma risk parameters that are based on a meta-analysis of autopsy studies.[59] Each model includes additional calibration data.

SimCRC was calibrated to outcomes from autopsy studies that report size distribution of adenomas[44-46,48-53] and the prevalence of preclinical colorectal cancer[44-45,48-53,60] (by age group and sex, when reported). MISCAN was calibrated to adenoma size distributions from colonoscopy studies,[61-63] stage-specific screen-detected and interval cancers from three large randomized FOBT trials,[64] and incidence reduction from the United Kingdom Flexible Sigmoidoscopy Screening (UKFSS) Trial.[7] CRC-SPIN was calibrated to adenoma prevalence,[65]

adenoma size,[62,66] and prevalence of preclinical colorectal cancer[61] reported in screening studies, and the proportion of adenomas that included colorectal cancer from two clinical series that reported adenoma-level data from drawn from pathology records.[67-68]

## Model Validation

It is difficult to trace how differences in model assumptions and implementation of assumptions lead to differences in model output. Because of this the three modeling groups have carried out a series of model comparisons (cross-validation) to better understand differences in model predictions. In our first comparison, we showed that although the natural history models predicted similar adenoma prevalence, lifetime cancer incidence, and stage distribution, they predicted very different mean time between adenoma formation and clinical colorectal cancer detection ('dwell time'). Mean predictions ranged from 11 years with MISCAN (prior to the recalibration described below) to 25 years with SimCRC and 26 years with CRC-SPIN.[69]

In our next comparison, we simulated a hypothetical one-time "perfect" screening test that detects and removes all adenomas and diagnoses all preclinical colorectal cancers.[70] We then recorded the model-predicted incidence of colorectal cancer following this hypothetical screening intervention and compared it to the incidence in the absence of screening (i.e., the background incidence); we refer to this comparison as the maximal clinical incidence reduction (MCLIR) (**Figure 8**). We found that with SimCRC and CRC-SPIN, colorectal cancer incidence does not return to the background age-specific incidence rate within a typical lifetime following a perfect screen at age 65. With MISCAN, the incidence rate following the hypothetical perfect screening intervention quickly approached that of the background incidence.

Together, these two analyses demonstrate the importance of dwell time on the model-predicted effectiveness of screening. All else equal, models with a shorter mean dwell time predict lower effectiveness of screening, while models with longer mean dwell times support greater benefit from earlier ages to begin screening and little harm from longer screening intervals. Unfortunately, dwell times are unobservable.

Since these two comparisons were performed, the MISCAN model has been recalibrated using UKFSS Trial data, resulting in longer mean dwell times.[71] The recalibrated MISCAN model (first published in 2014[71]) has a mean dwell time from adenoma incidence to cancer diagnosis of 17 years (an increase of seven years), which remains shorter than the mean dwell times predicted by SimCRC and CRC-SPIN. The change in mean dwell time has had a significant impact on the predicted impact of screening with MISCAN. **Figure 8** shows the MCLIR from SimCRC, CRC-SPIN, and both the original (first published in 2006[72]) and recalibrated versions of MISCAN. Compared with the original model, the recalibrated MISCAN model (i.e., the version used for the analysis described in this report) predicts a much longer protective effect from the hypothetical screening intervention, although the duration of this effect remains shorter than that predicted by SimCRC and CRC-SPIN.

## Other Calibration, Validation, and Goodness of Fit Evaluation

The modeling groups have also carried out separate model evaluations and validations.

The duration of the preclinical cancer phase in the MISCAN model was calibrated to match the incidence of interval and screen-detected cancer observed in the Minnesota, Nottingham, and Funen randomized trials of FOBT.[64] The MISCAN group has also validated the model-predicted short-term impact of sigmoidoscopy screening against the findings of the Norwegian Colorectal Cancer Prevention (NORCAPP) sigmoidoscopy study.

Both the SimCRC and MISCAN models have been shown to replicate the observed colorectal cancer SEER incidence and mortality rates from 1975 to 2000 after accounting for trends in risk factor prevalence, the dissemination of screening, and the utilization of chemotherapy.[72-74] CRC-SPIN has been externally validated to two colonoscopy studies.[75] In the first validation analysis, the model predicted somewhat fewer adenomas than observed among subjects who had a colonoscopy approximately five years after an initial negative screening colonoscopy (i.e., colonoscopy with no cancers or adenomas found). In the second validation analysis, the model predicted greater protection from colorectal cancer than observed among subjects in the first nine years following a negative colonoscopy, similar protection in the years 10-19, and less protection more than 20 years after a negative colonoscopy.

# Colorectal Cancer Screening Strategies

In consultation with the USPSTF, we included the following screening modalities: no screening, fecal occult blood testing with a high-sensitivity guaiac-based test (e.g., Hemoccult SENSA), fecal occult blood testing with an immunochemical test, multi-target stool-DNA testing, flexible sigmoidoscopy, flexible sigmoidoscopy with interval guaiac-based fecal occult blood testing, flexible sigmoidoscopy with interval fecal immunochemical testing, colonoscopy, and CT colonography (**Table 2**). We excluded from our analysis the blood test for circulating methylated septin 9 gene DNA because it has not been FDA-approved for colorectal cancer screening, as well as magnetic resonance colonography and capsule endoscopy due to limited evidence for their performance in screening populations.[76] We also excluded older colorectal cancer screening modalities that were not included in the 2008 USPSTF recommendations (e.g., low-sensitivity fecal occult blood tests, barium enema).

For each modality (other than no screening), we evaluated multiple screening intervals. Screening intervals refer to the timing between subsequent screening tests for persons with a negative test result. Intervals were 1, 2, and 3 years for the fecal occult blood tests; 1, 3, and 5 years for the multi-target stool DNA test; 5 or 10 years for flexible sigmoidoscopy and for CT colonography; and 5, 10 or 15 years for colonoscopy. For the screening modalities that use flexible sigmoidoscopy and interval FOBT, we simulated sigmoidoscopy at a 5-year interval with FOBT at either a 2- or 3-year interval, and sigmoidoscopy at a 10-year interval with FOBT at either a 1- or 2-year interval.

For each combination of screening modality and interval, we considered ages to begin screening

of 45, 50, and 55 and ages to end screening of 75, 80, and 85. These ages were chosen to provide narrow ranges around the recommended ages to begin (age 50) and end (age 75) screening from the 2008 USPSTF recommendations. The age at the last screening test for a particular strategy is not necessarily equal to the age to end screening, but rather a function of the age to begin and the screening interval. For example, colonoscopy every 10 years for age to begin 50 and age to end 75 results in three screening colonoscopies at ages 50, 60, and 70. We assume no screening occurs after the stopping age, but that colonoscopy surveillance of persons with a history of adenoma(s) is continued through at least age 85 (see below for more details).

In all, we evaluated 204 unique screening strategies (**Table 2**). Including duplicate strategies (e.g., "COL 50-80, 10" and "COL 50-85, 10", both of which have screening colonoscopies at ages 50, 60, 70, and 80), the total number was 217.

# Implementation of Screening

We made a number of assumptions about the implementation of screening and management of persons with various findings, as described below.

## Follow-Up of Positive Screening Tests With Colonoscopy

We assume that all people with a positive (non-colonoscopy) screening test subsequently undergo a follow-up (i.e., diagnostic) colonoscopy. Based on the test characteristics of colonoscopy, the person may be found to (correctly or incorrectly) have no adenomas, one or more adenomas, which would be removed via polypectomy, or colorectal cancer. It is also possible to detect non-adenomatous polyps, which would be removed via polypectomy, but would still be considered a negative colonoscopy test result (assuming no adenomas or colorectal cancer are detected). Patient management following cancer detection is not explicitly simulated.

## Patient Management of False-Positive Screening Tests

Simulated persons who have a positive screening test but have no adenomas or cancer at the diagnostic colonoscopy return to their original screening modality and schedule ten years after their negative diagnostic colonoscopy. Persons with adenomas detected enter surveillance (see below).

## Surveillance

Patients with a history of adenomas of any size are assumed to undergo surveillance with colonoscopy. The time to the next surveillance colonoscopy is simulated based on findings at the last exam: three years when an adenoma 10 mm or larger was detected or when three or more adenomas of any size were detected, or five years if no more than two adenomas that were both smaller than 10 mm were detected.[77] Surveillance colonoscopy is assumed to continue through age 85, provided no adenomas or colorectal cancer are detected at the last surveillance colonoscopy. Otherwise we continue surveillance according to the clinical findings at the last

colonoscopy until no adenomas are detected.

## Adherence

We assume 100% adherence to all screening and surveillance procedures, reflecting the goal of estimating the impact of screening among an average risk US population that is willing to be screened for colorectal cancer.

A comparison of the 2015 and 2008 CISNET colorectal cancer screening analyses is presented in **Table 3**.

# Model Input Parameters

## Operating Characteristics of Screening Tests

Test characteristics are based primarily on estimates from a systematic evidence review conducted by Lin et al. for the USPSTF.[76] When the models required test characteristics to be defined differently from the definitions used in the evidence review, we derived the required estimates using data from large studies included in the evidence review that were conducted in average-risk populations in the US and were deemed by Lin et al.[76] to be of at least fair quality.

The sensitivity for structural tests (colonoscopy, flexible sigmoidoscopy, and CT colonography) is often reported on both a per-lesion and a per-person basis, whereas sensitivity estimates for stool-based tests are always per person. All three models specify lesion-level sensitivity for structural tests so that simulated persons with multiple adenomas have a greater likelihood of a positive test than persons with only one adenoma. For stool-based tests, CRC-SPIN specifies person-level sensitivity. SimCRC and MISCAN specify lesion-specific sensitivity values that are calibrated so that sensitivity estimates on a person-level match those observed in the selected studies.

For all tests other than CT colonography, specificity in the models is defined as the probability of a negative test result among persons who do not have adenomas or colorectal cancer. For CT colonography, we use a different definition for specificity to match the purpose of CT colonography for detecting adenomas 6 mm and larger (see below for details). The lack of specificity with endoscopy reflects the detection of non-adenomatous lesions, which, in the case of sigmoidoscopy, leads to referral to diagnostic colonoscopy.

Our estimates for sensitivity and specificity for each test are provided in **Table 4**.

### Colonoscopy

Lin et al.[76] identified four studies of the diagnostic accuracy of CT colonography in screening populations that also reported the sensitivity for colonoscopy. These fair- to good-quality studies[19-20,22,66] included a large number of endoscopists and were therefore deemed to be more likely than studies with fewer endoscopists to represent test performance in community practice.

Three of the four studies reported the sensitivity of colonoscopy for colorectal cancer. Estimates ranged from 50% to 100% with wide confidence intervals due to the small number of cancers detected in each study.[19-20,66] The per-lesion sensitivity of colonoscopy for an adenoma ≥10 mm ranged from 89.8% to 97.6% across the four studies. None of the studies reported the sensitivity for a 6-9 mm adenoma as required by the models. Two studies reported the sensitivity for an adenoma ≥6 mm, with estimates ranging from 75.8% to 90.4%. Given that CT colonography does not report lesions < 6 mm, no studies reported the sensitivity for an adenoma < 6 mm (also required by the models), nor did they report the sensitivity for any adenoma.

Our estimates for the sensitivity of colonoscopy for adenomas by size (**Table 4**) were based on a meta-analysis of tandem colonoscopy studies.[78] We used these estimates rather than those from the four studies identified by Lin et al.[76] because the latter estimates were not reported using the size categories required by the models, as noted above. Our estimate for the sensitivity for the detection of an adenoma ≥10 mm of 95% is within the range across the four studies. We assumed the sensitivity of colonoscopy for colorectal cancer is the same as the sensitivity for large adenomas (95%).

Only one of the four studies reported the specificity of colonoscopy.[22] However, the reported estimates were for persons with adenomas ≥10 mm (88.7%) and with adenomas ≥6 mm (94.2%), whereas the models require specificity defined in terms of any adenoma. We therefore used the specificity for colonoscopy from a screening study of colonoscopy in the general population of the Boston University catchment area.[79]

### Flexible Sigmoidoscopy

Lin et al.[76] found no studies evaluating the test performance of flexible sigmoidoscopy that met their inclusion criteria. We assumed that flexible sigmoidoscopy had the same sensitivity as colonoscopy *within the reach of the endoscope* (**Table 4**). We assumed that neither biopsies nor polypectomy would be performed during flexible sigmoidoscopy and that persons with any lesion visualized at sigmoidoscopy were deemed positive and referred for diagnostic colonoscopy. This is similar to the sigmoidoscopy approach used in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial in which biopsy and polypectomy were not routinely performed.[80]

Our estimate for the specificity for sigmoidoscopy is based on the PLCO Trial.[80] In this trial, 23.4% of subjects had a positive baseline flexible sigmoidoscopy (i.e., one or more polyp was visualized), and in 52.2%, an adenoma or a cancer was detected at the diagnostic colonoscopy, indicating that 11.1% of screened individuals had a false-positive sigmoidoscopy [i.e., (1 – 0.522) * 0.234 = 0.111]. This amounts to a lack of specificity of 12.7% for persons in whom no adenomas or cancers were detected [i.e., 0.111 / (1 – 0.234 * 0.522) = 0.127].

### CT Colonography

The systematic evidence review reported pooled estimates of the per-person sensitivity and specificity of CT colonography for adenomas by size. However, due to the large statistical heterogeneity around the estimates, Lin et al.[76] issued a caution about their interpretability. Due

to this caution and the fact that the pooled estimates are provided for different size categorizations than required by the models, we did not use these estimates for test performance. Instead we used test performance data from the American College of Radiology Imaging Network National CT Colonography (ACRIN) Trial.[19] This US study is the largest of the nine trials[17-18,20-22,66,81-82] of CT colonography with cathartic bowel preparation included in the systematic evidence review. It also included many more readers (15) than the other studies (range 1-6 readers), which may imply greater applicability to CT colonography performance in community practice. We used the sensitivity per adenoma ≥ 10 mm and per-person specificity for adenomas ≥ 6 mm reported by Johnson et al. The sensitivity per 6-9 mm adenoma was derived from the sensitivity and number of adenomas by size category (i.e., ≥6 mm and ≥10 mm) reported by Johnson et al. We assumed that the sensitivity of CT colonography for colorectal cancer was the same as the sensitivity for large adenomas (**Table 4**).

### Sensitive Guaiac-Based Fecal Occult Blood Test (gFOBT)

Lin et al.[76] identified two studies, one study in the US[83] and one in Israel,[84] reporting the diagnostic accuracy of the sensitive guaiac FOBT, Hemoccult SENSA. Both studies were deemed 'fair-quality'. One additional study in the US reported diagnostic accuracy, but only for lesions in the distal colon.[85] Sensitivity for colorectal cancer in the US study[83] and the Israeli study[84] were 79.4% and 61.5%, respectively. Due to small numbers of cancers, the 95% confidence intervals were wide and overlapped across the studies. Sensitivity for adenomas was not reported in either study. Per person specificity estimates for colorectal cancer were 86.7% and 96.4%, respectively, although we note that the models require specificity for any adenoma or colorectal cancer. Since neither study provided sensitivity for adenomas, nor the specificity for any adenoma or colorectal cancer, we used the test characteristics for gFOBT from our 2008 analysis for the USPSTF (**Table 4**).[86] CRC-SPIN used these per-person estimates of sensitivity directly, while SimCRC and MISCAN calibrated per-lesion estimates (assuming 1-5 mm adenomas do not bleed, see **Appendix Table 1**) to match the per-person estimates. Our estimate for the sensitivity for colorectal cancer of 70% is within the confidence intervals of both the US and Israeli studies.

### Fecal Immunochemical Tests (FITs)

Lin et al.[76] identified 14 studies of FITs that performed colonoscopy in all subjects regardless of FIT finding.[16] They did not pool the estimates due to differences across studies in cutoff for positivity, number of samples used per test, and patient populations. We used the study by Imperiale et al.,[16] the largest of the US studies, for our estimates of FIT sensitivity and specificity. This study used the OC FIT-CHEK® (Polymedco) test, which is one of the FIT tests cleared by the Food and Drug Administration and available for use in the US.[87] It has a fixed cutoff of 100 ng of hemoglobin per ml of buffer (i.e., 20 µg of hemoglobin per g of feces), which we use for our base-case analysis of FIT (a lower cutoff is explored in a sensitivity analysis). The study did not distinguish adenoma findings by size, but rather by whether the person had advanced vs. non-advanced adenomas, with advanced adenomas defined as an adenoma ≥ 10 mm in size or an adenoma containing high-grade dysplasia or villous histology. Since our colorectal cancer models do not simulate histology, we used the sensitivity for advanced adenomas as a proxy for sensitivity for adenomas ≥10 mm, and sensitivity for non-advanced

adenomas as a proxy for sensitivity for 6-9 mm and 1-5 mm adenomas combined. The CRC-SPIN model used estimates from Imperiale et al.[16] directly, simulating FIT detection of adenomas at the person-level based on the most advanced lesion (e.g., <10 mm, ≥10 mm, or preclinical cancer as shown in **Table 4**). The SimCRC and MISCAN models used calibration to select per-lesion sensitivity to match these per-person estimates, with the additional assumption that 1-5 mm adenomas are only found through chance. The calibrated per-lesion sensitivity estimates for the MISCAN and SimCRC models to match these per-person level estimates can be found in **Appendix Table 1**. In all models, specificity was set equal to the estimate for specificity for any adenomas or cancer at 96.4%.

### Multi-Target Stool DNA Test (FIT-DNA)

We used the test parameters for the multi-target stool DNA test reported in the study by Imperiale et al.[16] described above. As with FIT, the sensitivity of FIT-DNA was reported for colorectal cancer, for advanced adenomas, and for non-advanced adenomas. We used the reported sensitivities for advanced adenomas and non-advanced adenomas as proxies for the sensitivities for adenomas ≥10 mm and 1-9 mm adenomas, respectively. As with FIT (described above), CRC-SPIN used these per-person sensitivities directly, while SimCRC and MISCAN calibrated to derive per-lesion sensitivities that match these lesion-level sensitivities, assuming that 1-5 mm adenomas do not bleed or shed DNA (**Table 4**). The calibrated per-lesion FIT-DNA sensitivity estimates for the SimCRC and MISCAN models are shown in **Appendix Table 1**. In all models, specificity was set equal to the estimate for specificity for any adenomas or cancer at 89.8%.

## Endoscopy Reach Assumptions

We assume that 5% of persons undergoing colonoscopy require two procedures to achieve complete visualization and that the cecum is ultimately visualized in 95% of patients. Reach of sigmoidoscopy was based on the UKFSS Trial,[88] with 76-88% of procedures reaching the sigmoid-descending junction.

## Complications of Screening

The main source of reported harms (complications) from colorectal cancer screening comes from colonoscopy.[76] Such harms could be from a screening or surveillance colonoscopy, or from a diagnostic colonoscopy to evaluate a patient after a positive finding on another screening test.

### Colonoscopy

In accordance with the systematic evidence review,[76] we assumed the risk of colonoscopy complications is dependent on age. As noted by Lin et al.[76] serious adverse events from screening colonoscopy or colonoscopy in asymptomatic persons are relatively uncommon, with 95% confidence intervals of 2 to 5 perforations per 10,000 and 5 to 14 major bleeds per 10,000. Our estimates for the risk of complications from colonoscopy are from a study by van Hees et al.[89] that estimated risks among Medicare beneficiaries of serious gastrointestinal events, other

gastrointestinal events, and cardiovascular events by age and polypectomy status. van Hees et al. found that colonoscopies without polypectomy were not associated with an excess risk for complications, and that the risks increased exponentially with age (**Figure 9**). We assumed 2 per 100,000 colonoscopies result in a fatal complication, based on the risk of perforation at age 65 and the risk of dying of a perforation reported by Gatto et al.[90]

We assumed no differences in the risk of complications among colonoscopies with polypectomy for colonoscopies conducted for screening vs. those for diagnostic follow-up or surveillance. However, the model-predicted proportion of colonoscopies with polypectomy is highest among colonoscopies for diagnostic follow-up.

### Sigmoidoscopy

As with colonoscopy, we assume risks of complications from colonoscopy are conditional on polypectomy. Because we assume that polyps detected at sigmoidoscopy are not removed or biopsied during the procedure, we assumed that the risk of complications with sigmoidoscopy is 0.

### CT Colonography

The evidence review found no perforations in 11 prospective CT colonography studies limited to screening populations. We therefore assumed no complications from CT colonography. CT colonography often leads to the detection of suspicious findings outside of the colon.[19,66] Our models do not include the potential benefits or harms associated with the work-up and possible treatment of these extracolonic findings.

Because CT colonography is a radiologic procedure, it may increase the risk of radiation-induced cancers. Our models do not account for these risks, although their risks have been estimated to be small relative to the reduction in colorectal cancer risk from CT colonography screening.[91]

### Stool-Based Tests

Given the non-invasive nature of the tests, we assumed no direct harms from stool-based tests. We only assumed complications from diagnostic follow-up colonoscopy and surveillance.

# Outcomes

## Benefits

For this analysis, the primary benefits of screening are the life-years gained from the prevention or delay of colorectal cancer death. A small fraction of those who are screened may experience a loss of life-years as a result of fatal complications; these losses are accounted for in the life-years gained for a given screening strategy. We also report the numbers of colorectal cancer cases and deaths averted, and changes in the number of years lived with diagnosed colorectal cancer.

## Harms

We used the number of colonoscopies to represent the primary harms and burden of colorectal cancer screening. This metric includes colonoscopies for screening, diagnostic follow-up, and surveillance, as well as colonoscopies for the diagnosis of symptomatic cancers (i.e., cancers detected outside of screening or surveillance). Because the number of colonoscopies does not fully capture the burden of colorectal cancer screening, we also report the number of screening tests by type, diagnostic procedures, surveillance procedures, and complications.

All outcomes are presented for a cohort of persons born in 1975 who are unscreened and free of diagnosed colorectal cancer at age 40. Outcomes are tallied from age 40 to death and expressed per 1,000 persons at age 40.

# Outcomes Analyses

Ideally, all colorectal cancer screening strategies would be evaluated together on the basis of the primary measures of benefits and harms (i.e., life-years gained and colonoscopies required). However, doing so provides an incomplete picture of the tradeoffs involved due to large differences in the number of non-colonoscopy tests across screening modalities. Instead we first grouped together non-colonoscopy screening modalities with comparable burden to create classes of screening modalities. We then identified the subset of efficient screening strategies within each class. A strategy is efficient if no other strategy or combination of strategies within the class provides more life-years with the same (or fewer) number of colonoscopies. Finally, from the sets of efficient screening strategies we selected screening strategies (at most one per class of screening modalities) that were efficient, yielded comparable life-years gained, and provided a reasonable ratio of harms and benefits, as described in the sections that follow.

## Classes of Comparable Screening Modalities

Differences in the number of non-colonoscopy tests across screening modalities prohibited the analysis of all 204 unique screening strategies together to indentify which provide a reasonable tradeoff between benefits (life-years gained) and harms (colonoscopies). However, we grouped FIT, FIT-DNA, and gFOBT together as exclusively stool-based screening modalities with comparable burden, and SIG+FIT and SIG+gFOBT together as comparable modalities that combine flexible sigmoidoscopy with stool testing. The remaining modalities – flexible sigmoidoscopy alone, CT colonography, and colonoscopy – each remained a unique screening class due to differences in bowel preparation, invasiveness, and the need for sedation, among others. After this grouping, we were left with five classes of screening modalities: stool-based modalities, flexible sigmoidoscopy with stool-based modalities, flexible sigmoidoscopy alone, CT colonography, and colonoscopy.

## Efficient Strategies Within a Screening Class

We identified the set of efficient screening strategies within a screening class. We first identified

screening strategies that were projected to require more colonoscopies and provide fewer life-years gained than another strategy within the modality; these strategies are strongly dominated and were deemed inefficient. For each of the remaining strategies within a screening class we calculated the incremental number of colonoscopies per 1,000 (ΔCOL) and the incremental life-years gained per 1,000 (ΔLYG), relative to the next least effective strategy. We then calculated an "efficiency ratio," defined as the incremental number of colonoscopies required to achieve an additional year of life gained (ΔCOL/ΔLYG). In an approach that mirrors that of incremental cost-effectiveness analysis, strategies that were less effective than another and had a higher efficiency ratio were weakly dominated and deemed inefficient.

We then derived an "efficient frontier" for each screening modality, which is the line connecting all non-dominated and therefore recommendable strategies when the strategies are plotted in colonoscopies versus life-years gained space.[33] We also considered weakly dominated strategies that had life-years gained within 98% of the efficient frontier to be "near-efficient" and eligible for recommendation. This is the same as the approach used in our 2008 analysis for the USPSTF.

## Recommended Strategies Across Screening Classes

We identified sets of recommended colorectal cancer screening strategies from the sets of efficient strategies for the classes of screening modalities. We assumed that, for ease of clinical implementation, a set of recommended strategies would have the same ages to begin and end screening. We also assumed that recommended strategies would be efficient within their class of screening modality, provide comparable life-years gained, and provide a reasonable balance of harms and benefits. Finally, we assumed that the recommended colonoscopy strategy would have at least as many life-years gained as the colonoscopy strategy included in the 2008 USPSTF recommendations (i.e., 10-yearly colonoscopy from age 50 to age 75,or "COL 50-75, 10").

These criteria were implemented as follows. For each age to begin and end screening, we first selected a colonoscopy strategy that had predicted life-years gained at least as large as the predicted life-years gained (from the current analysis) for the colonoscopy strategy included in the 2008 recommendation. We used the colonoscopy strategy as a basis of comparison for all other classes of screening modalities because, unlike the others, no additional tests are required (i.e., all harms and burdens are accounted for). For each class of screening modality we then identified the efficient and near efficient options, if any, with the selected ages to begin and end screening. From these, we eliminated from consideration any strategies with life-years gained outside of the *a priori* chosen range of 90% to 110% of the colonoscopy strategy; this limited recommended strategies to those that have comparable effectiveness. Finally, from the remaining strategies we identified the strategy that yielded the most life-years gained with an efficiency ratio no larger than the ratio of the selected colonoscopy strategy. We placed this restriction on the efficiency ratio because non-colonoscopy strategies require use of additional tests, while colonoscopy does not. If all of these criteria were met, the strategy with the most life-years gained within a class of screening modalities was included in the recommended set (i.e., at most one strategy was selected per class). It was possible to have no recommended strategy within a class of screening modalities. This process was repeated for each age to begin and end screening and colonoscopy strategy.

# Sensitivity Analyses

We conducted additional analyses in which we used the best- and worst-case values for test sensitivity (**Table 4**). We also evaluated FIT with cut-off for positivity of 50 ng of hemoglobin per ml of buffer (i.e., 10 μg of hemoglobin per g of feces) (**Appendix Table 2**). Because the number of colonoscopies does not fully capture the burden of colorectal cancer screening, particularly in terms of bowel preparation, we also considered the number of cathartic bowel preparations as an alternative proxy measure of the harms and burden of screening.

# Chapter 3. Results

## Outcomes Among an Unscreened Population

In an unscreened population, the models simulated nearly identical life expectancy among 40-year-olds: 39.6 years with SimCRC and 40.0 years with MISCAN and CRC-SPIN. The cumulative probability of developing colorectal cancer from ages 40 to 100 was 6.7% with MISCAN, 7.0% with SimCRC, and 7.2% with CRC-SPIN (**Figure 10**). The cumulative probability of dying from colorectal cancer among this population was 2.7% with CRC-SPIN and 2.8% with MISCAN and SimCRC (**Figure 10**).

## Outcomes Among a Screened Population

Predictions from each model for the number of screening-related procedures (by type), complications, colorectal cancer diagnoses, and colorectal cancer deaths per 1,000 persons free of diagnosed cancer at age 40, and reductions in colorectal cancer incidence and mortality by screening test, are presented in **Appendix Tables 3-10** for all 217 screening strategies. Compared to no colorectal cancer screening, all screening strategies yielded sizable reductions in colorectal cancer incidence and mortality. Reductions were lowest with fecal immunochemical testing every 3 years from ages 55 to 75 (i.e., "FIT 55-75, 3"), with incidence reductions ranging from 24-43% and mortality reductions ranging from 50-58% across models. Reductions were highest with colonoscopy screening every 5 years from ages 45 to 85 (i.e., "COL 45-85, 5"), with reductions across models ranging from 71-96% for incidence and 87-97% for mortality. For a given screening strategy, incidence and mortality reductions were lowest for MISCAN – the model with the shortest dwell time – and generally highest for CRC-SPIN – the model with the longest dwell time. Incidence and mortality reductions with SimCRC were generally only slightly lower than those of CRC-SPIN.

## Ages to Begin and End Screening and Screening Interval

The life-years gained relative to the number of colonoscopies and the efficient frontiers for each screening modality are displayed in **Figures 11-18**. Note that an additional frontier is provided that excludes screening beginning at age 45 (see below). While the age to begin screening, age to end screening, screening modality, and screening interval together define a specific screening strategy, we describe our findings for each of these policy variables separately in the sections that follow. All ranges listed are across models, unless otherwise noted.

### Age to Begin Screening

All else equal, the number of life-years gained from colorectal cancer screening and the number of colonoscopies required increased as the age to begin screening was lowered from age 55 to age 50 to age 45. For example, lowering the age to begin screening from age 50 to age 45

yielded 15-28 additional life-years gained and required an additional 827-856 colonoscopies per 1,000 for colonoscopy every 10 years to age 75; for annual FIT to age 75, initiating screening at age 45 instead of age 50 yielded 16-27 additional life-years per 1,000 and 238-263 additional colonoscopies per 1,000. For colonoscopy screening however, two of the three models (SimCRC and CRC-SPIN) found that lowering the age to begin screening to age 45 and lengthening the screening interval to 15 years maintained the same or slightly more life-years gained as colonoscopy screening every 10 years from age 50 without increasing the lifetime number of colonoscopies (i.e., 279-288 life-years gained and 4,009-4,081 colonoscopies per 1,000 with "COL 45-75, 15" vs. 270-275 life-years gained and 4,007-4,049 colonoscopies per 1,000 with "COL 50-75, 10;" both strategies require three screening colonoscopies per lifetime). In MISCAN, starting colonoscopy screening earlier and extending the interval yielded slightly fewer life-years gained (244 life-years gained per 1,000 with "COL 45-75, 15" vs. 248 per 1,000 with "COL 50-75, 10"). For all other screening modalities, both MISCAN and CRC-SPIN predicted fewer life-years gained when the age to begin screening was lowered from 50 to 45 and the screening interval was extended to the next shortest interval, while SimCRC continued to find the same or more life-years gained.

While the models were discordant for lowering the age to begin screening and extending the screening interval, all three models found that strategies in which colorectal cancer screening begins at age 45 predominated on the efficient frontier, that is, they generally provided additional years of life at a lower number of additional colonoscopies than strategies in which screening begins at a later age. This is illustrated by the observation that the efficient frontiers including all three ages to begin screening reside above the efficient frontiers excluding strategies with screening beginning at age 45. The USPSTF members considered these findings, noting that the additional life-years gained from starting screening at age 45 are small relative to the additional number of additional colonoscopies and that there continues to be insufficient empiric data to support lowering the recommended age to begin colorectal cancer screening from 50 to 45, as well as insufficient evidence to support a 15-year colonoscopy screening interval. As a result, in consultation with the USPSTF members, we present subsequent analyses for strategies with age to begin screening of 50 or 55.

The number of tests by type (i.e., stool tests, sigmoidoscopies, CT colonographies, and total colonoscopies), life-years gained, colorectal cancer deaths averted, and within-class efficiency ratios for each efficient and near efficient screening strategy with an age to begin screening of 50 or 55 are presented in **Tables 5-9**. In general, while the models differed slightly in terms of the absolute number of life-years gained from screening and the number of colorectal cancer deaths averted, they yielded consistent relative predictions across screening modalities and similar rankings within classes of screening modalities. For each class of screening, all three models found that screening strategies beginning at age 50 predominated among those that are on or near the efficient frontier, with the efficiency ratio varying with the age to end screening and the screening interval.

## Age to End Screening

All three models found that for all screening modalities, the life-years gained from raising the age to end screening from age 75 to age 80 or age 85 were small relative to the increase in the

required number of colonoscopies and the number of non-colonoscopy tests (**Figures 11-18** and **Tables 5-9**). For example, consider annual screening with FIT, starting at age 50 (**Figure 13** and **Table 6**). Raising the age to end screening from age 75 to age 80 increased life-years gained by 5-7 per 1,000 (2-3%) while increasing the number of colonoscopies by 98-119 per 1,000 (6-7%) and the number of FITs by 1,618-1,709 per 1,000 (10-11%). Raising the age to end screening further, from age 80 to age 85, yielded even smaller gains in life-years (2-3 per 1,000, a 1% increase) relative to the change in the number of colonoscopies required (66-79 per 1,000, a 4% increase). The number of FITs increased by 1,162-1,244 per 1,000 (a 7% increase). For colonoscopy screening every 10 years starting at age 50 (**Figure 11** and **Table 5**), increasing the age to end screening from age 70/75 to age 80/85 such that one additional screening colonoscopy is performed at age 80 also increased life-years gained by only 2-3 years per 1,000 (1% increase); the number of colonoscopies increased by 384-414 (9-10% increase).

Given these relatively small increases in life-years gained from extending the age to end screening beyond age 75, we simulated additional annual FIT and colonoscopy scenarios with age to end screening as low as 60. As the age to end screening was increased from age 60 to age 85, in 5-year increments, the additional in life-years gained and colonoscopies required increased at a decreasing rate (**Figure 19**). The USPSTF considered these findings showing small gains in life-years relative to the increases in the number of colonoscopies required when raising the age to end screening beyond age 75 and the lack of evidence from randomized trials on continued screening of persons aged 75 and older, and concluded that the evidence best supported an age to end screening of 75.

## Screening Modality and Interval

### Colonoscopy Screening Strategies

Of the 14 unique colonoscopy screening strategies evaluated with screening beginning at age 50 or later, the strategy with two lifetime screening colonoscopies at ages 55 and 70 (i.e., "COL 55-75, 15") yielded the fewest life-years gained (214-236 per 1,000 persons age 40) and the fewest colorectal cancer deaths averted (20.1-22.4 per 1,000) at a burden of 2,968-3,079 total colonoscopies per 1,000 persons age 40 (**Table 5**). The strategy with eight lifetime screening colonoscopies ("COL 50-85, 5") yielded the most life-years gained (266-286) and the most colorectal cancer deaths averted (23.6-25.7) with the highest colonoscopy burden (6,502-6,586). The colonoscopy strategy included in the 2008 USPSTF recommendations – colonoscopy at ages 50, 60, and 70 ("COL 50-75, 10") – yielded 248-275 life-years gained and 21.9-24.4 colorectal cancer deaths averted at a burden of 4,007-4,101 colonoscopies and had an efficiency ratio of 39-65 additional colonoscopies per incremental life-year gained compared to the next less effective efficient colonoscopy strategy. Colonoscopy strategies with a 5-year screening interval and/or with an age to end screening of 80 or 85 were substantially less efficient in all three models (i.e., higher efficiency ratios, exceeding 100 colonoscopies per life year-gained) (**Table 5**).

### Stool-Based Screening Strategies (FIT, FIT-DNA, and gFOBT)

Due to the similar level of burden and harms associated with FIT, FIT-DNA, and gFOBT, we evaluated these three stool-based tests together. Of the 54 unique stool-based screening strategies

evaluated with screening beginning at age 50 or 55, the strategy of FIT every three years from age 55 to age 75 ("FIT 55-75, 3") yielded the fewest life-years gained (152-178 per 1,000 at age 40) and the fewest colorectal cancer deaths averted (13.9-16.1 per 1,000) at a burden of 807-895 colonoscopies per 1,000 and 5,250-5,306 stool tests per 1,000 (**Table 6**). Annual FIT-DNA from age 50 to age 85 ("FIT-DNA 50-85, 1") yielded the most life-years gained (252-275 per 1,000), averted the most colorectal cancer deaths (22.5-24.7 per 1,000), and required the greatest colonoscopy burden (2,870-2,994 per 1,000); the number of stool tests ranged from 12,542-12,888 per 1,000. Annual FIT from ages 50-75 ("FIT 50-75, 1") – a strategy included in the 2008 USPSTF recommendations – yielded 231-260 life-years gained and 20.0-22.7 colorectal cancer deaths averted at a burden of 1,739-1,899 colonoscopies and 15,444-15,843 stool tests per 1,000. This strategy was efficient (MISCAN) or nearly efficient (SimCRC and CRC-SPIN) at approximately 17-24 additional colonoscopies per life-year gained compared to the next less effective efficient stool-based strategy. Annual gFOBT from ages 50-75 ("gFOBT 50-75, 1") – also a strategy included in the 2008 USPSTF recommendations – yielded 232-261 life-years gained and 20.3-22.9 colorectal cancer deaths averted at a burden of 2,230-2,287 colonoscopies and 12,914-13,026 stool tests per 1,000 (**Appendix Table 4**), and was dominated by other stool-based strategies. FIT strategies comprised the vast majority of efficient and near-efficient stool-based strategies (**Figure 20**). FIT-DNA strategies annually from age 50 to age 75, 80 or 85 were efficient or near-efficient in all three models but with efficiency ratios exceeding 69 additional colonoscopies per additional life-year gained relative to the next less effective efficient strategy (**Table 6**). In only one model (CRC-SPIN) was a gFOBT strategy ("gFOBT 50-85, 1") found to be near-efficient.

### Sigmoidoscopy

Life-years gained with sigmoidoscopy screening ranged from 153-185 years per 1,000 persons age 40 with 10-yearly screening from ages 55 to 75 ("SIG 55-75, 10") to 184-229 years with 5-yearly screening between ages 50 to 85 ("SIG 50-85, 5") (**Table 7**). Colorectal cancer deaths averted ranged from 14.8-17.8 per 1,000 to 17.3-21.2 per 1,000 for these two strategies, respectively. Sigmoidoscopy every 5 years from age 50 to 75 (i.e., "SIG 50-75, 5") had an efficiency ratio of 18-22 additional colonoscopies per life-year gained relative to the next less expensive efficient sigmoidoscopy strategy.

### Combinations of Sigmoidoscopy and Stool-Based Strategies (SIG+FIT, SIG+gFOBT)

Due to the similar level of burden and harms associated with the strategies involving sigmoidoscopy with stool-based screening, SIG+FIT and SIG+gFOBT, we evaluated them together. The models yielded different predictions for which of the 48 unique strategies evaluated with screening beginning at age 50 or 55 yielded the fewest life-years gained and the fewest colorectal cancer deaths averted. The least effective strategy was sigmoidoscopy every 5 years with gFOBT every 3 years with SimCRC, sigmoidoscopy every 10 years and FIT every 2 years with MISCAN, and sigmoidoscopy every 5 years with FIT every 3 years with CRC-SPIN (age to begin and end screening were 55 and 75, respectively, for all three models). The least effective strategy yielded 209-229 life-years gained per 1,000 and 19.7-21.7 colorectal cancer deaths averted per 1,000 and required 1,700-1,963 colonoscopies (**Table 8 and Appendix Tables 8a, 9b, and 9c**). The strategy of sigmoidoscopy every five years and FIT every three

years from ages 50-75 ("SIG+FIT 50-75, 5_3") – a strategy included in the 2008 USPSTF recommendations – was dominated by other strategies in all three models. Sigmoidoscopy every 10 years and annual FIT from ages 50-85 was the most effective strategy in two models (SimCRC and MISCAN) with life-years gained across the three models for this strategy ranging from 252-275 per 1,000 at age 40 and colorectal cancer deaths ranging from 22.5-24.7 per 1,000 at a burden of 2,469-2,675 colonoscopies, 2,177-2,396 sigmoidoscopies, and 14,983-15,814 stool tests per 1,000 (**Table 8**). In CRC-SPIN, sigmoidoscopy every 10 years from ages 50 to 85 with annual gFOBT was slightly more effective than the same strategy with FIT instead of gFOBT. This strategy was not included among the efficient and near-efficient strategies with SimCRC or MISCAN. Nearly all efficient or near-efficient strategies combining sigmoidoscopy and stool-based screening had FIT (as opposed to gFOBT) as the stool-based test (**Figure 21**).

**CT Colonography**

Of the 10 unique CT colonography screening strategies with age to begin screening of 50 or later, CT colonography every 10 years from ages 55 to 75 ("CTC 55-75, 10") was the least effective (172-214 life-years gained and 16.4-20.7 colorectal cancer deaths averted per 1,000 at age 40) at a burden of 1,220-1,396 colonoscopies and 2,250-2,296 CT colonographies per 1,000 (**Table 9**). CT colonography every five years from ages 50 to 85 was the most effective (231-268 life-years gained and 21.1-24.3 colorectal cancer deaths averted per 1,000) with the greatest burden of both colonoscopy (1,795-2,079 per 1,000) and CT colonography (4,627-4,900 per 1,000).

# Recommended Strategies

In light of the findings described in the previous sections showing limited benefits from extending the age to end screening beyond age 75 and the predominance of earlier ages to begin screening on the efficient frontier, and lack of empiric evidence to support lowering the recommended age to begin screening, colorectal cancer screening from ages 50 to 75 resulted in a reasonable balance between harms and benefits. Accordingly, we identified a set of recommended strategies that are efficient or near efficient for age to begin 50 and age to end 75.

**Table 10** contains all efficient or near-efficient strategies with age to begin 50 and age to end 75, and their associated benefits, burden and efficiency ratio (ratios are those reported in **Tables 5-9**) for each model. The table contains multiple strategies for each class of screening modality, varying in interval and, in the case of stool tests and of sigmoidoscopy plus stool tests, the modality. For colonoscopy, three strategies are presented: colonoscopy every 15 years, every 10 years, and every 5 years. In the strategy with colonoscopies every 15 years ("COL 50-75, 15" with colonoscopy at ages 50 and 65), 8-19 colonoscopies are needed to save one life-year relative to the next best colonoscopy strategy available (i.e., "COL 55-75, 15"). With a 10-year interval ("COL 50-75, 10" with colonoscopy at ages 50, 60, and 70), the efficiency ratio is 39-65 additional colonoscopies per additional life-year gained relative to the next-best colonoscopy strategy. With a 5-year interval ("COL 50-75, 5" with colonoscopies at 50, 55, 60, 65, 70, and 75), 114-273 additional colonoscopies would need to be performed for each additional life-year gained.

The final set of selected strategies depends on the baseline strategy chosen for colonoscopy, that is, whether colonoscopy with a 15-year, 10-year, or 5-year interval is selected for colonoscopy screening. We decided *a priori* that we would not consider colonoscopy strategies that yielded life-years gained lower than those predicted for the colonoscopy strategy included in the 2008 USPSTF recommendations, that is, lower that the life-years with "COL 50-75, 10". Colonoscopy from age 50 to age 75 with a 15-year interval yielded fewer life-years gained than colonoscopy from age 50 to age 75 with a 10-year interval, so we therefore only identified sets of recommended strategies assuming either a 10-year or a 5-year colonoscopy interval was chosen. These sets of recommended strategies are described in the sections that follow.

## Baseline Colonoscopy Strategy: COL 50-75, 10

When colonoscopy at ages 50, 60 and 70 (i.e., "COL 50-75, 10") is chosen as the acceptable colonoscopy strategy, the benchmark number of life-years gained (per 1,000) and incremental efficiency ratio against which other strategies are compared are 275 and 55, respectively with SimCRC, 248 and 39, respectively, with MISCAN, and 270 and 65, respectively with CRC-SPIN (**Table 10**). Selecting the strategies from the other test classes that have life-years gained within 90%-110% of that of the selected colonoscopy strategy, while requiring fewer incremental colonoscopies per life-years gained, resulted in the following set of strategies: annual FIT; sigmoidoscopy every 10 years with annual FIT; and CT colonography every 5 years. Findings were consistent across the three models. Sigmoidoscopy alone was not selected because, for each model, the life-years gained for all sigmoidoscopy strategies were less than 90% of the selected colonoscopy strategy. Outcomes for these recommended strategies are presented in **Figure 22**.

## Baseline Colonoscopy Strategy: COL 50-75, 5

When colonoscopy from ages 50-75 with a 5-year interval ("COL 50-75, 5") is chosen as the acceptable colonoscopy strategy, the benchmark number of life-years gained (per 1,000) and incremental efficiency ratio are relatively high, at 285 and 188, respectively, with SimCRC, 264 and 114, respectively, with MISCAN, and 279 and 273, respectively, with CRC-SPIN (**Appendix Table 11**). With SimCRC and CRC-SPIN, the following strategies met the benchmarks for selection as recommended tests alongside colonoscopy every 5 years: FIT-DNA annually, sigmoidoscopy every 10 years with annual FIT, and CT colonography every 5 years. With MISCAN, only sigmoidoscopy every 10 years with annual FIT was included along with 5-yearly colonoscopy.

## Other Baseline Colonoscopy Strategies

The recommended tests selected to accompany "COL 50-80, 10", "COL 50-85, 10", "COL 50-80, 5", and "COL 50-85, 5" are included in **Appendix Tables 12-15**.

# Sensitivity Analyses

## Best- and Worst-Case for Test Sensitivity

Model predictions for the percent change in lifetime number of colonoscopies, lifetime number of non-colonoscopy tests, life-years gained and colorectal cancer deaths averted using the best- and worst-case assumptions for test sensitivity are presented in **Appendix Table 16**. Outcomes are presented for the set of model-recommended strategies with age to begin 50 and age to end 75, assuming the colonoscopy strategy with a 10-year interval is selected. The percent change in outcomes relative to the base-case analysis ranged from -2% to 3% for the colonoscopy strategy, -6% to 6% for the FIT strategy, -4% to 4% for the SIG+FIT strategy, and -5% to 7% for the CT colonography strategy.

## FIT With a Lower Cutoff for Positivity

Model predictions for the efficient and near efficient stool-based screening strategies with the inclusion of a quantitative FIT test with a lower positivity threshold of 50 ng of hemoglobin per ml of buffer (i.e., 10 μg of hemoglobin per g of feces) are presented in **Appendix Table 17**. In all models, FIT strategies with a lower positivity threshold (i.e., higher sensitivities and lower specificity compared with the higher positivity threshold) were included among those that are efficient or near efficient, with efficiency ratios exceeding 62 additional colonoscopies per additional life-year gained relative to the next less effective efficient strategy. As in the base-case analysis, FIT strategies with the higher positivity threshold of 100 ng of hemoglobin per ml of buffer (i.e., 20 μg of hemoglobin per g of feces) predominated among those that were efficient or near-efficient (**Appendix Figure 1**). With ages to begin and end screening of 50 and 75, respectively, and the selection of a 10-year screening interval for colonoscopy, the model-recommended stool-based screening strategy did not change with the inclusion of the FIT strategies with a lower positivity threshold; annual FIT (with a positivity threshold of 100 ng of hemoglobin per ml of buffer) continued to be the recommended strategy in all three models **Appendix Table 18**).

## Number of Cathartic Bowel Preparations as Measure of Burden of Screening

In our base-case analysis, CT colonography screening every 5 years was included in the set of recommended strategies with age to begin screening of 50 and age to end screening of 75, assuming selection of a 10-year interval for colonoscopy screening (**Table 10**). This CT colonography strategy provided 91-96% of the life-years gained with 10-yearly colonoscopy over the same age range, and required 2,080-2,395 fewer colonoscopies per 1000. However, when considering the burden of cathartic bowel preparations (associated with CT colonography procedures and colonoscopies) instead of colonoscopies alone as the measure of screening burden, the number of cathartic preparations for CT colonography and colonoscopy strategies is comparable (**Figure 23** and **Appendix Table 19**) and CT colonography is no longer included as a recommended test (**Table 11**).

# Chapter 4. Discussion

This report describes the findings of microsimulation modeling analyses performed in conjunction with the 2015 USPSTF recommendations for colorectal cancer screening. While the three CISNET colorectal cancer models differed slightly in terms of the absolute benefits and harms of screening, they yielded consistent relative predictions across screening modalities and similar rankings within classes of screening modalities. We found that with ages to begin and end colorectal cancer screening of 50 and 75, the following screening modalities and screening intervals were efficient and yielded comparable life-years gained: colonoscopy every 10 years, annual FIT, sigmoidoscopy every 10 years with annual FIT, and CT colonography every 5 years. However, CT colonography requires cathartic bowel preparation comparable to that required for colonoscopy. When the added burden of cathartic bowel preparations for CT colonography were accounted for in the burden of screening, CT colonography was not included as a recommended strategy because its efficiency ratio (i.e., ΔCatharticPreps / ΔLYG) exceeded that of colonoscopy.

In 2008, and in the current analysis, the USPSTF requested microsimulation modeling of an age to end as well as an age to begin screening. Our current model results for age to end screening at age 75 are consistent with our 2008 analysis. We found that for persons who were adequately screened up to age 75, there was limited benefit in terms of life-years gained for extending the age to end screening to age 80 or 85. Although the model recommended strategies are based on beginning screening at age 50, we also evaluated an age to begin of 45. The findings from all three models showed that starting colorectal cancer screening at age 45 rather than age 50 yields modest increases in both life-years gained (the primary measure of benefits) and the number of colonoscopies required (a proxy for harms, such as colonic perforations and bleeding) and, notably, provides a more favorable (i.e., efficient) balance between life-years gained and colonoscopies than starting at age 50. However, in consultation with the USPSTF members, we eliminated strategies with screening beginning at age 45 due to modest differences in life-years gained and the lack of empiric evidence to support lowering the recommended age to begin screening. When these strategies were eliminated from consideration, we found that strategies with screening beginning at age 50 yielded more life-years gained and were more efficient than those with age to begin of 55.

The SimCRC and CRC-SPIN models both found that if colonoscopy screening were to begin at age 45, the screening interval could be extended from 10 to 15 years. Doing so maintained the same (or slightly more) life-years gained as with colonoscopy every 10 years starting at age 50 without increasing the lifetime number of colonoscopies. MISCAN predicted only a small loss in life-years gained with this approach. Currently, empiric data to support these findings are lacking, although clinical studies evaluating sigmoidoscopy and colonoscopy suggest that the protective effect of these exams may indeed last more than 10 years.[7,92]

## Comparison With 2008 Decision Analysis

The current analysis includes three CISNET models, whereas our analysis for the USPSTF in

2008 included two models. The set of model-recommended strategies with age to begin at 50 and age to end at 75 is similar to those from our 2008 analysis. A few differences are important to note. First, a high-sensitivity guaiac test is no longer among the model-recommended strategies. In the current analysis, we have new empiric data to suggest that FIT has higher sensitivity and specificity for colorectal cancer than a high-sensitivity guaiac test,[76] making guaiac-based testing inefficient when compared to FIT. Previously, we had assumed similar sensitivity for FIT and gFOBT for colorectal cancer. Second, when only considering the burden of colonoscopies and not of other cathartic preparations, CT colonography is now part of the set of model-recommended strategies. We did not include CT colonography nor a DNA stool test in our 2008 analyses because these tests were deemed to have insufficient evidence.[93]

Finally, all three models now consistently show that beginning screening at age 45 is generally both more effective and more efficient at providing additional life-years gained than strategies beginning at age 50. In the 2008 analysis, the SimCRC model also found that beginning screening at age 40 was more efficient than beginning at age 50, whereas the MISCAN model favored beginning at age 50. The findings are now more consistent across models because another age to begin screening was considered (age 45 instead of age 40) and the MISCAN model has been updated based on the findings of the UKFSS Trial.

## Scope of the Decision Analysis

The aim of this analysis is to determine the optimal age to begin, age to end and screening interval for the general population at average risk for colorectal cancer and with average life expectancy.

This analysis is meant to inform population guidelines. Therefore we have assumed perfect adherence to screening regimens, including receipt of all screening, diagnostic follow-up (e.g., for positive stool tests), and surveillance tests. This assumption enables us to predict the maximum achievable benefit for each strategy, and specify optimal screening strategies.[94] In practice, such high adherence is not observed either for initial or repeat screening. Therefore this analysis does not provide information about achieved benefits and harms at a population level. In order to do so, longitudinal test-specific adherence data are needed.

Our analysis is not intended for individual-level decision-making, which would incorporate information about personal risk and patient preferences that would likely affect screening behavior. For example, many individuals in the population would not be classified as average risk nor as having average life-expectancy. There are several reasons why patients and clinicians should deviate from these model-recommended strategies. People at higher risk for colorectal cancer, e.g. because of predisposition because of a family history, were not included in the analysis. Previous model-analyses indicate that optimal screening for these individuals could be as intensive as colonoscopy every two years, depending on the degree of family history of an individual.[95] Even when at average risk for colorectal cancer, elderly people differ in their general health status and their exposure to prior screening. For example, our models have suggested a benefit of screening beyond age 75 in those without comorbidities (i.e. a better than average life-expectancy),[96] as well as those without prior screening.[71] In those with severe

comorbidities that have been regularly screened since age 50, screening beyond age 67-69 may result in an unfavorable balance between harms and benefits.[96]

## Strengths of the Modeling

Although randomized controlled trials are the gold standard for determining the effectiveness of screening, they have their limitations. They are expensive and time consuming and therefore limited in the number of strategies that can be evaluated. Decision models provide a useful tool to extrapolate evidence from randomized trials and address the question of which screening strategy is optimal with respect to age to begin, age to end and interval of screening. Our microsimulation models synthesize available evidence about the natural history of developing colorectal cancer and incorporate the evidence available from randomized trials to determine the impact of alternative screening strategies on incidence and mortality.

Having multiple independently-developed models that provide similar findings despite differences in assumptions provides a stronger case for model results. Also, our updated results are presented with a revised version of MISCAN that has been recalibrated using UKFSS Trial data.[51] The recalibrated model has a longer mean dwell time that the originally published model (though still shorter than the SimCRC or CRC-SPIN models). Longer dwell times correspond to longer periods of time during which screening can result in identification and removal of preclinical lesions (adenomas and preclinical colorectal cancer). The models have a range of average dwell times from adenoma to clinical cancer, which provides us with a range of outcomes that reflect a sensitivity analysis of the different underlying model assumptions.

## Limitations of the Modeling

Despite the strengths of modeling, some limitations are noteworthy. First, although our modeled results provide a lifetime framework for evaluating benefits and harms from a program of screening, much of our empiric data on sensitivity and specificity of screening tests are based on a single round of screening with relatively short periods of follow-up. Currently, there only is long-term evidence for the traditional guaiac FOBT (Hemoccult II) and sigmoidoscopy. Outcomes for repeat rounds of FIT and high-sensitivity guaiac FOBT have only been reported in smaller clinical studies, so evidence of test performance in repeat screening is scarce. One study suggests that the cumulative rate of false-positive exams after 10 years of screening is considerably lower than expected based on the false-positive rate in the first round of screening.[97] Additional larger studies with multiple rounds of screening would be informative for the model inputs for the longer term.

Second, we model the adenoma carcinoma sequence using the size of adenomas as an indicator for advanced adenomas. We do not explicitly model histology of tubular-villous, villous, or high-grade dysplasia in our definition of advanced adenoma, which is based on a size of 10 mm or larger. We also do not include the serrated polyp pathway,[42-43] in part due to insufficient evidence on the prevalence of serrated polyps by age and location, their malignant potential, and the ability of screening tests to detect them. All of this information is needed to fully incorporate

this pathway into our models.

In addition, we assume that colonoscopy sensitivity is the same for lesions in the distal and proximal colon. Whenever possible, test characteristics were based on the evidence review,[76] which found limited evidence for location-specific sensitivity of the tests. There is some evidence that shows a smaller mortality reduction for proximal than for distal colon cancer with colonoscopy,[98-103] implying that test sensitivity (and/or natural history) might differ by location. We based the reach of flexible sigmoidoscopy on what was achieved in the UKFSS Trial, because this is the largest population-based sigmoidoscopy screening study. Endoscopists in the UKFSS Trial aimed to visualize the sigmoid and most did not try to get beyond that point. A higher reach might occur in a US setting where endoscopists may aim to visualize as much of the colon as feasible and acceptable to the patient.

Finally, we did not perform a comprehensive analysis directly comparing all available test strategies. Cost-effectiveness analysis would be a way to perform such a comprehensive analysis, however cost analysis is not part of the USPSTF evaluation. Instead, we used the number of required colonoscopies as our proxy for harms and burden, and life-years gained as a measure of benefit. Not all components of screening burden and/or harm are captured with these measures. For example, many patients may also consider collecting feces for stool-based testing or undergoing a sigmoidoscopy to be burdensome. Furthermore, CT colonography, like colonoscopy. generally requires cathartic bowel preparation and is associated with radiation exposure. Future work should consider some means of providing a common denominator for resources that would make comparison of screening strategies across tests more informative.

## Summary

In summary, while the three CISNET colorectal cancer models differed slightly in terms of the absolute benefits and harms of screening, they yielded consistent rankings of screening strategies. All three models found that the following screening strategies from age 50 to age 75 provide comparable life-years gained and an efficient balance of benefits and harms: colonoscopy every 10 years, annual FIT, flexible sigmoidoscopy every 10 years with annual FIT, and CT colonography every 5 years, provided the burden of cathartic bowel preparation with CT colonography is not accounted for.

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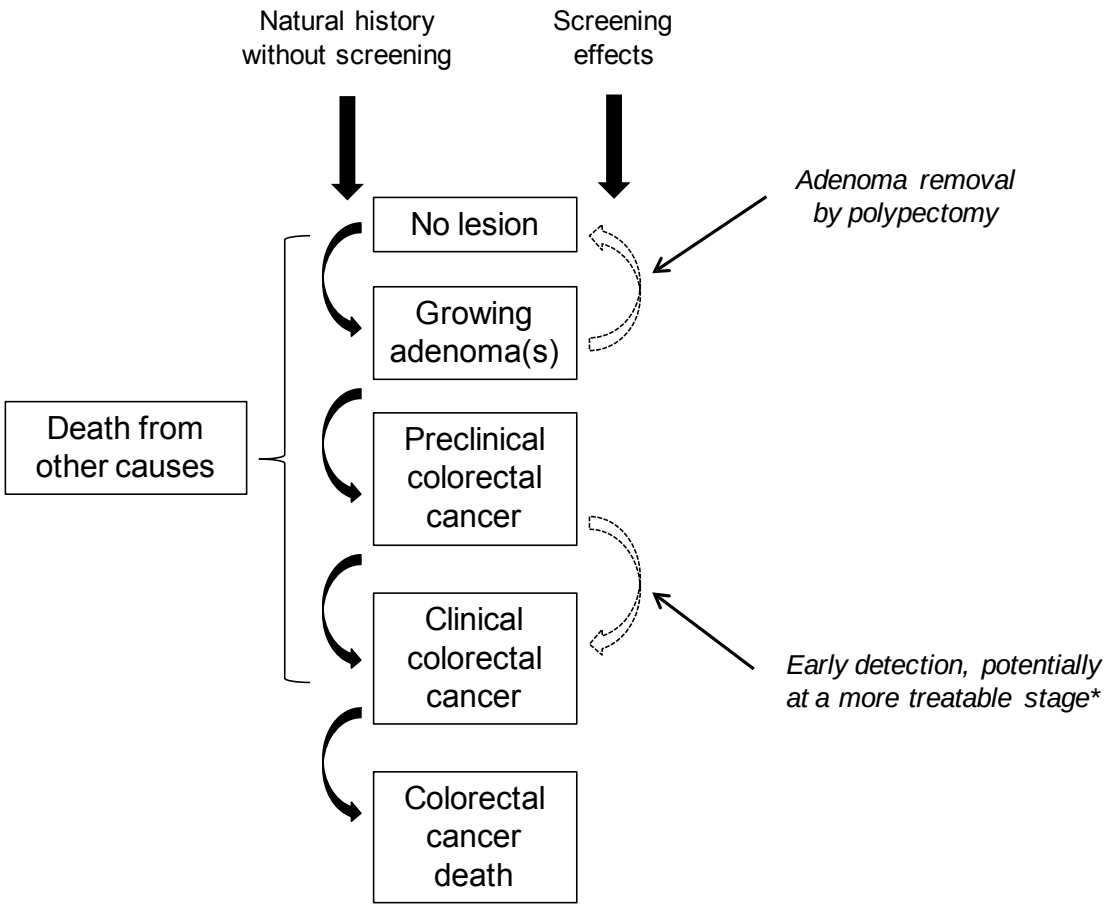
**Figure 1. Graphical representation of the natural history of colorectal cancer and the effects of screening as simulated by SimCRC, MISCAN, and CRC-SPIN**




* Early detection of colorectal cancer through screening (moving from preclinical to clinically-detected) may allow for detection of cancer at an earlier stage than symptom-detected cancer, and therefore create the conditions necessary for a better prognosis.

The opportunity to intervene in the natural history through screening (adenoma detection and removal, and early detection) is noted by the dotted lines. Screening can either remove a precancerous lesion (i.e., adenoma), thus moving a person to the "No lesion" state, or diagnose a preclinical cancer, which, if detected at an earlier stage, may be more amenable to treatment.

**Figure 2. Prevalence of adenomas by age from autopsy studies and as predicted by the models**

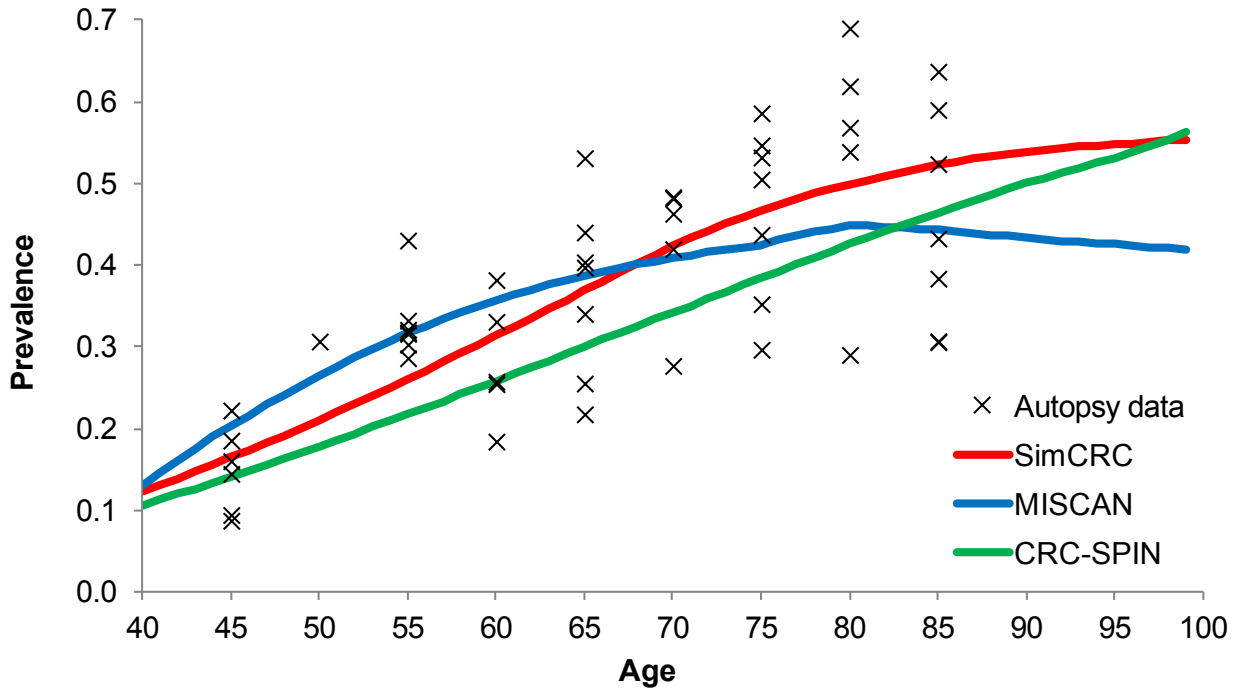


**Figure 3. Distribution of adenomas by location (including proportion in the distal colon or rectum) among persons aged 40 and older, by model**

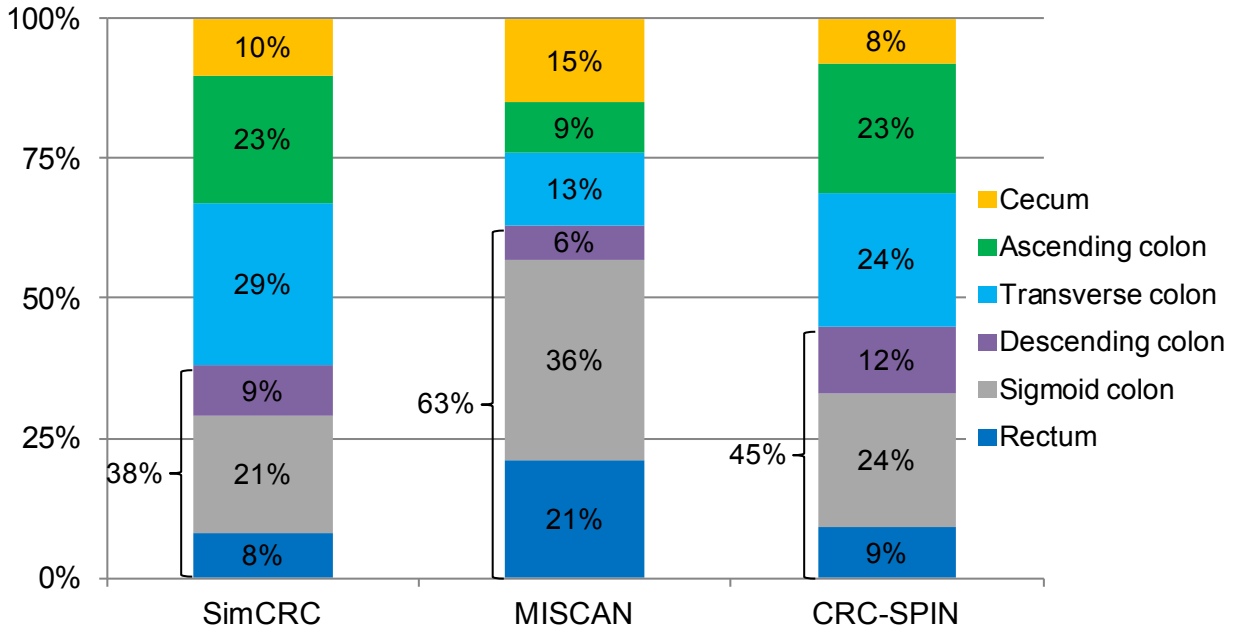
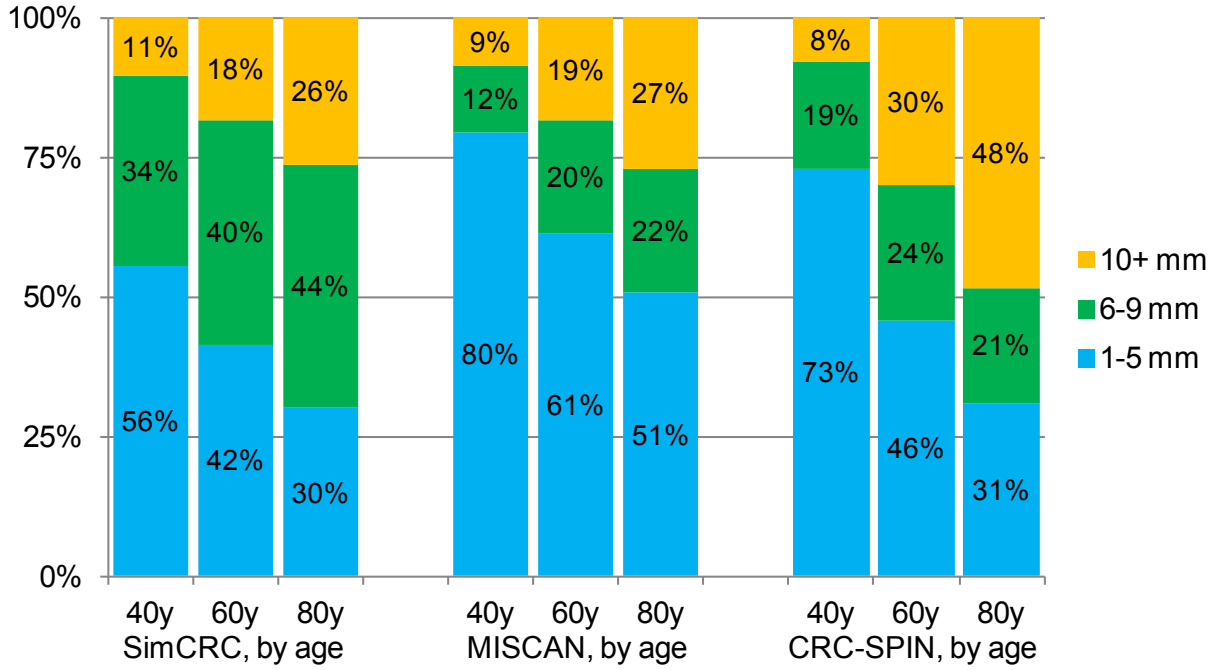
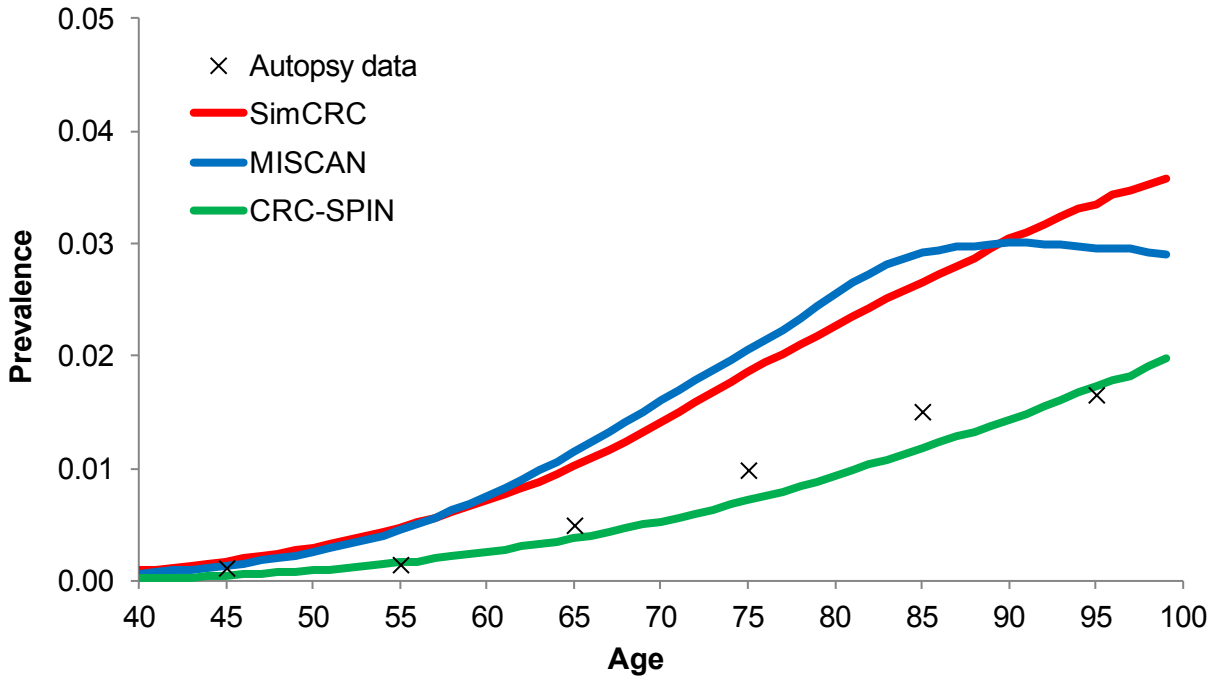


**Figure 4. Distribution* of adenomas by size of the most advanced adenoma among persons aged 40 and older, by age and model**



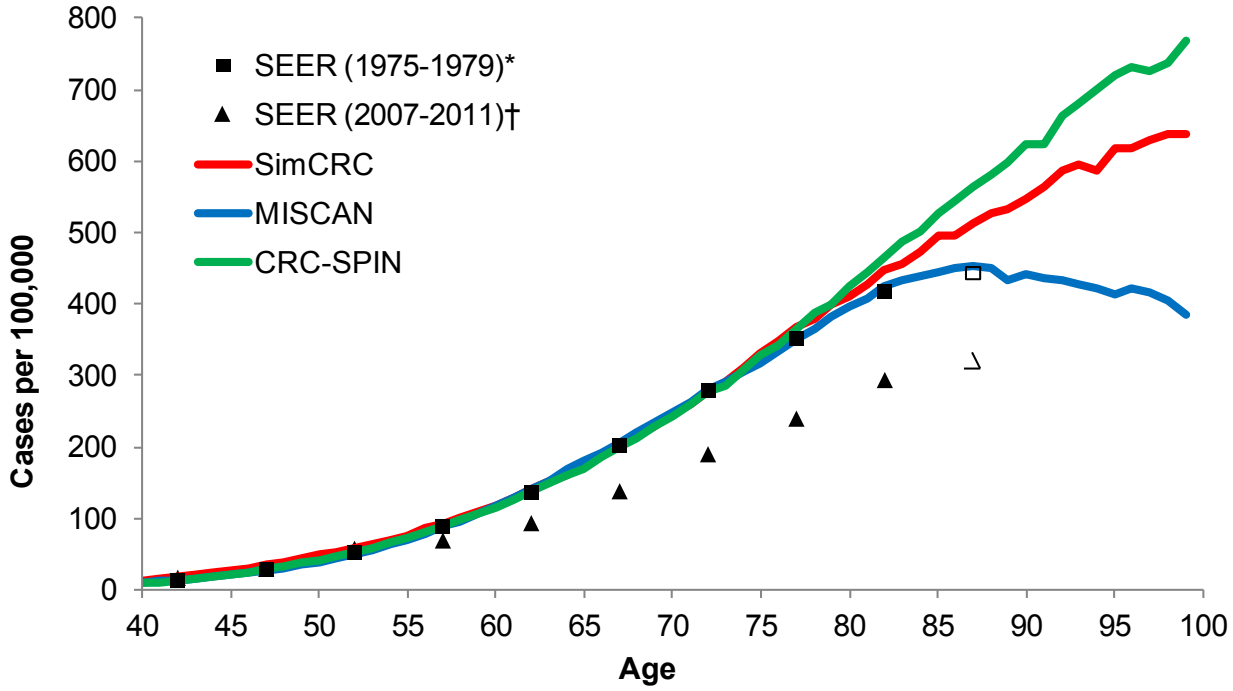

*Distributions may not sum to 100% due to rounding.

**Figure 5. Prevalence of preclinical colorectal cancer, by age and model**



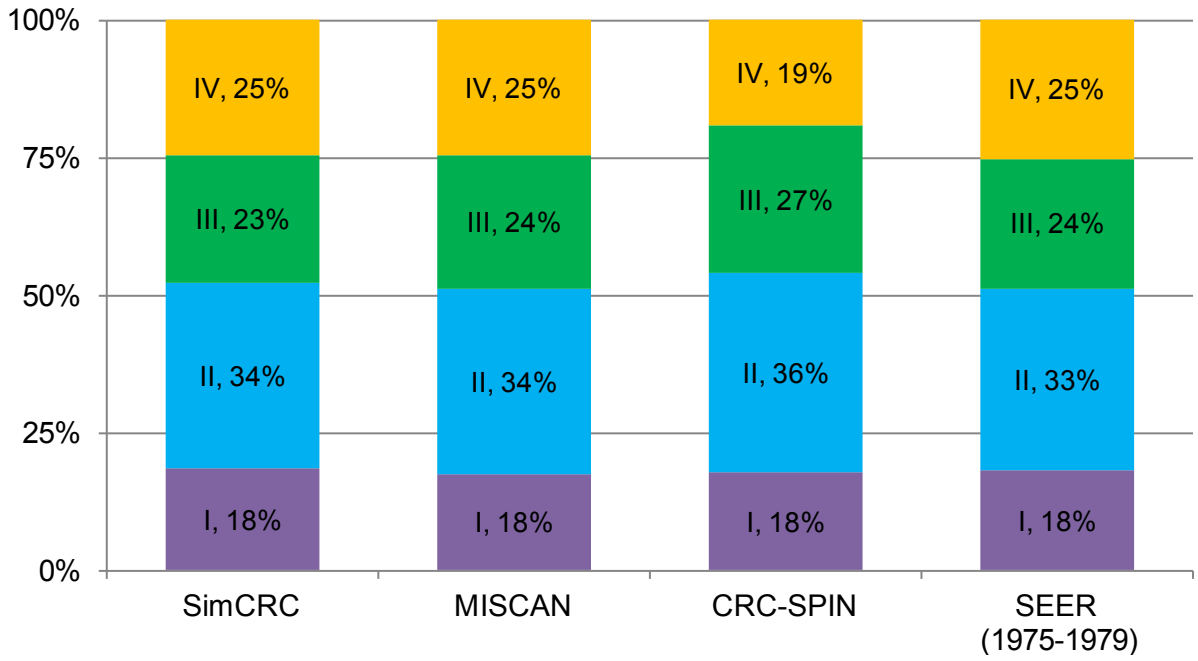

Note that the models were fit to data from multiple studies[44-45,48-53,60] on the prevalence of preclinical cancer. Autopsy data are plotted for the study by Berg et al.,[60] which is the only study that provided age-specific estimates.

**Figure 6. Colorectal cancer cases per 100,000 by age and model, compared with incidence rates from the SEER Program**



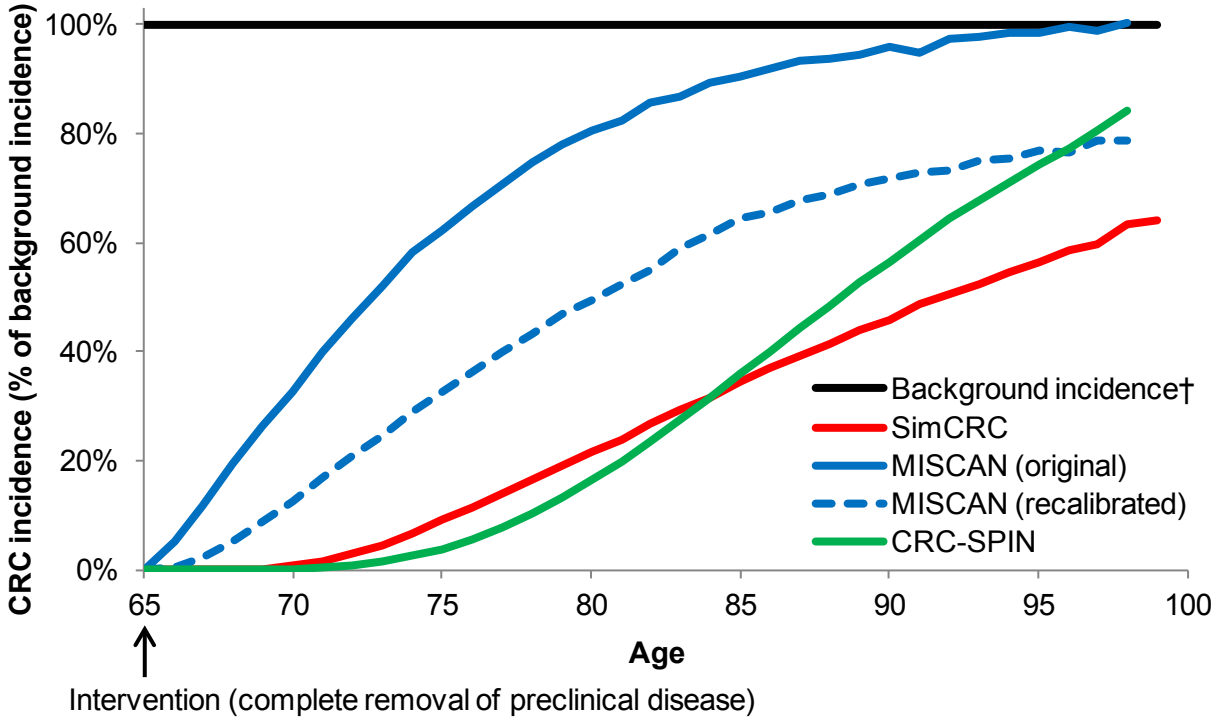

The models were calibrated to colorectal cancer incidence rates from 1975-1979 SEER data. This period was chosen since incidence rates at that time are likely to reflect those among a largely unscreened population. Incidence rates from 2007-2011 SEER data are also shown here for comparison. The 2007-2011 data reflect the incidence in a population in which more than half of those of screening age (50-74y) report being up-to-date with colorectal cancer screening.[14,104-105] Note that open symbols indicate incidence rates for the 85+ age group (plotted at age 87 for convenience).

**Figure 7. Distribution of the stage of colorectal cancer at diagnosis among persons aged 40 and older, by model***




*Distributions may not sum to 100% due to rounding.

**Figure 8. Maximum Clinical Incidence Reduction (MCLIR) following a perfect screening intervention* at age 65, by model**

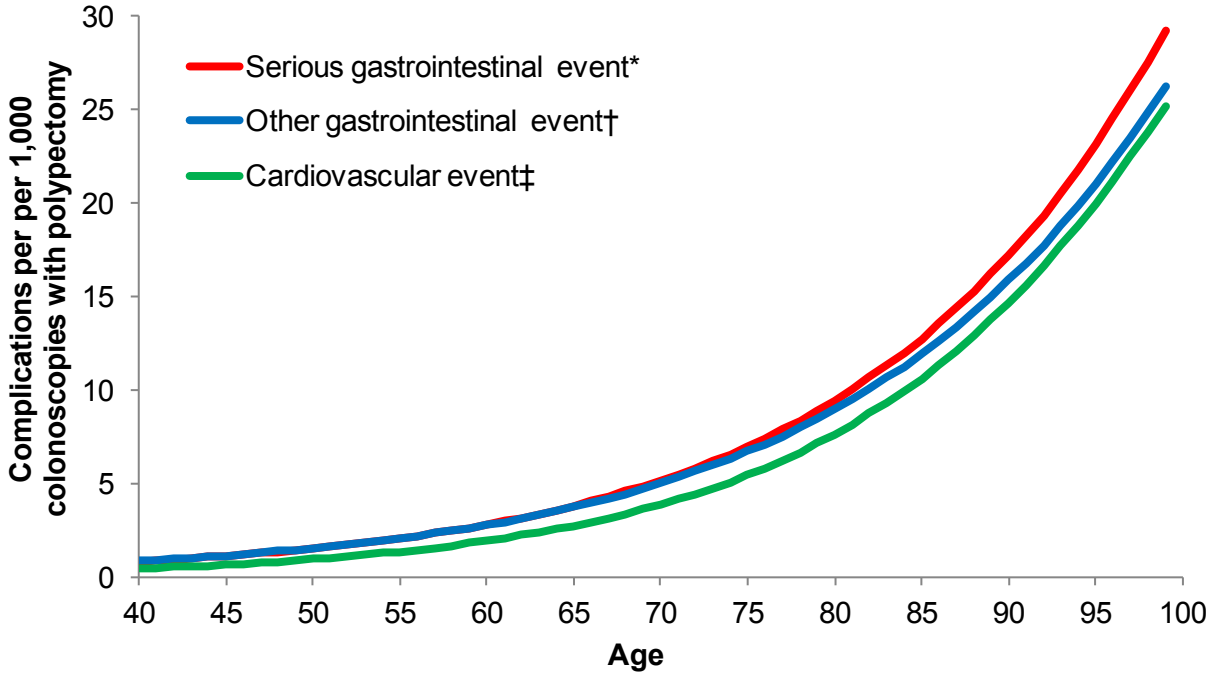



* Intervention is a hypothetical perfect screening test that detects and removes all adenomas and diagnoses all preclinical cancers.

† Incidence in the absence of the intervention.

Predictions are shown for both the original version of MISCAN with mean dwell time of 11 years and for the recalibrated version of MISCAN with a mean dwell time of 17 years. The latter version with the longer dwell time is used for the USPSTF analysis.

**Figure 9. Age-specific excess risks of complications from colonoscopy with polypectomy relative to colonoscopies without polypectomy as estimated by van Hees et al[89]**




* Perforations, gastrointestinal bleeding or transfusions. Excess risk per colonoscopy with polypectomy = 1/[exp(9.27953 − 0.06105 × Age) + 1] − 1/[exp(10.78719 − 0.06105 × Age) + 1].

† Paralytic ileus, nausea and vomiting, dehydration, abdominal pain. Excess risk per colonoscopy with polypectomy = 1/[exp(8.81404 − 0.05903 × Age) + 1] − 1/[exp(9.61197 − 0.05903 × Age) + 1].

‡ Myocardial infarction or angina, arrhythmias, congestive heart failure, cardiac or respiratory arrest, syncope, hypotension, or shock. Excess risk per colonoscopy with polypectomy = 1/[exp(9.09053 − 0.07056 × Age) + 1] − 1/[exp(9.38297 − 0.07056 × Age) + 1]

Complications include serious gastrointestinal events, other gastrointestinal events, and cardiovascular events.

**Figure 10. Cumulative probability of developing colorectal cancer and dying from colorectal cancer from age 40 to age 100 in the absence of screening, by model**

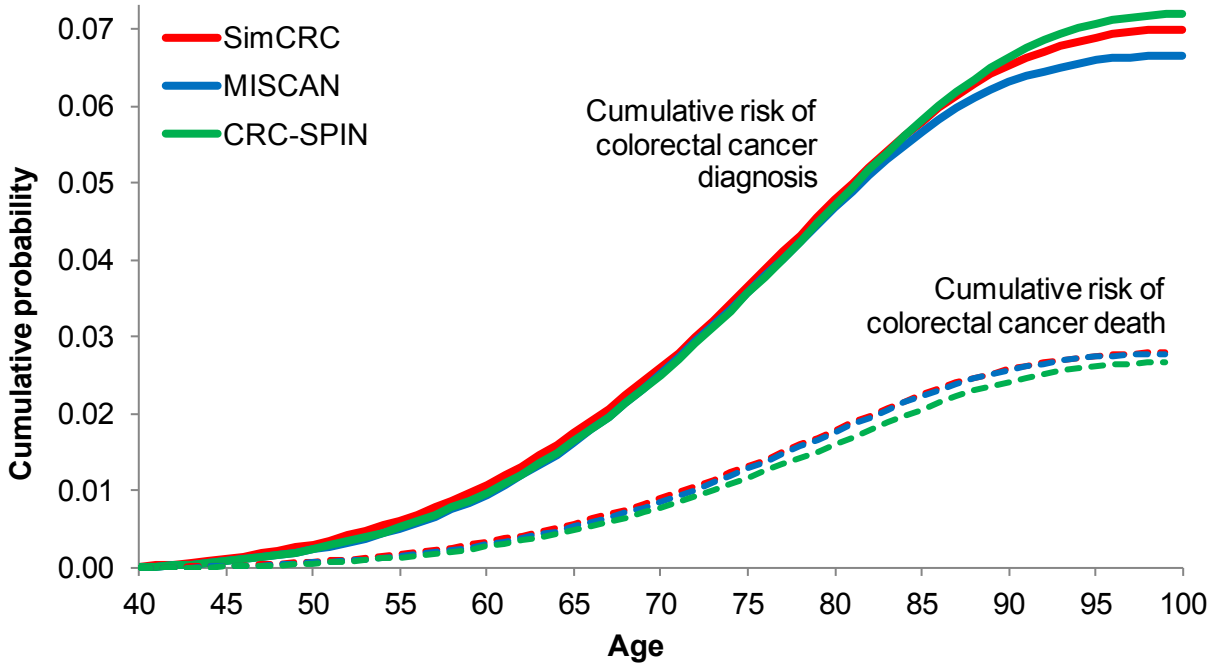


**Figure 11. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for colonoscopy screening strategies that vary by age to begin, age to end, and screening interval and efficient frontiers, by model**

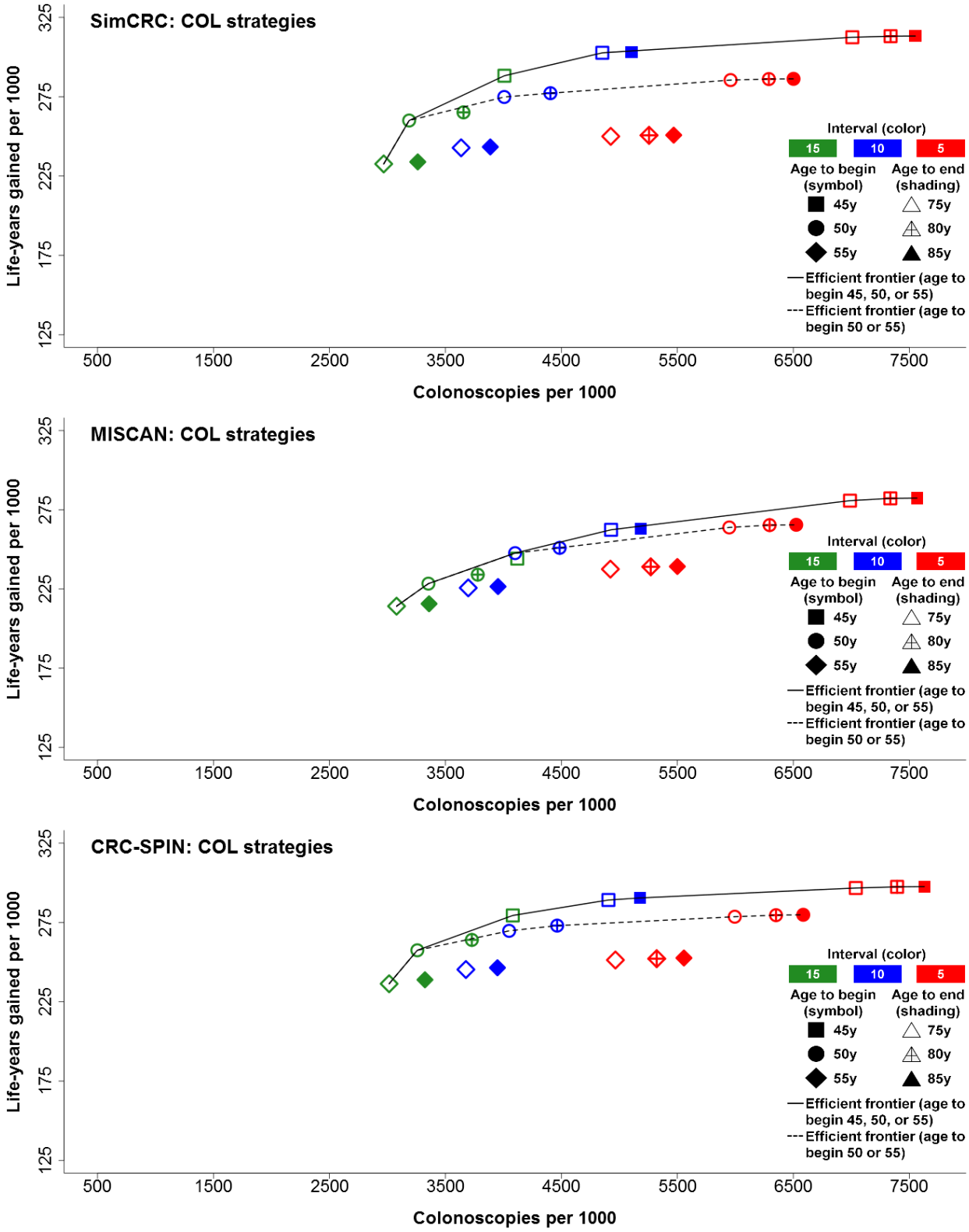


**Figure 12. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for gFOBT screening strategies that vary by age to begin, age to end, and screening interval, by model**

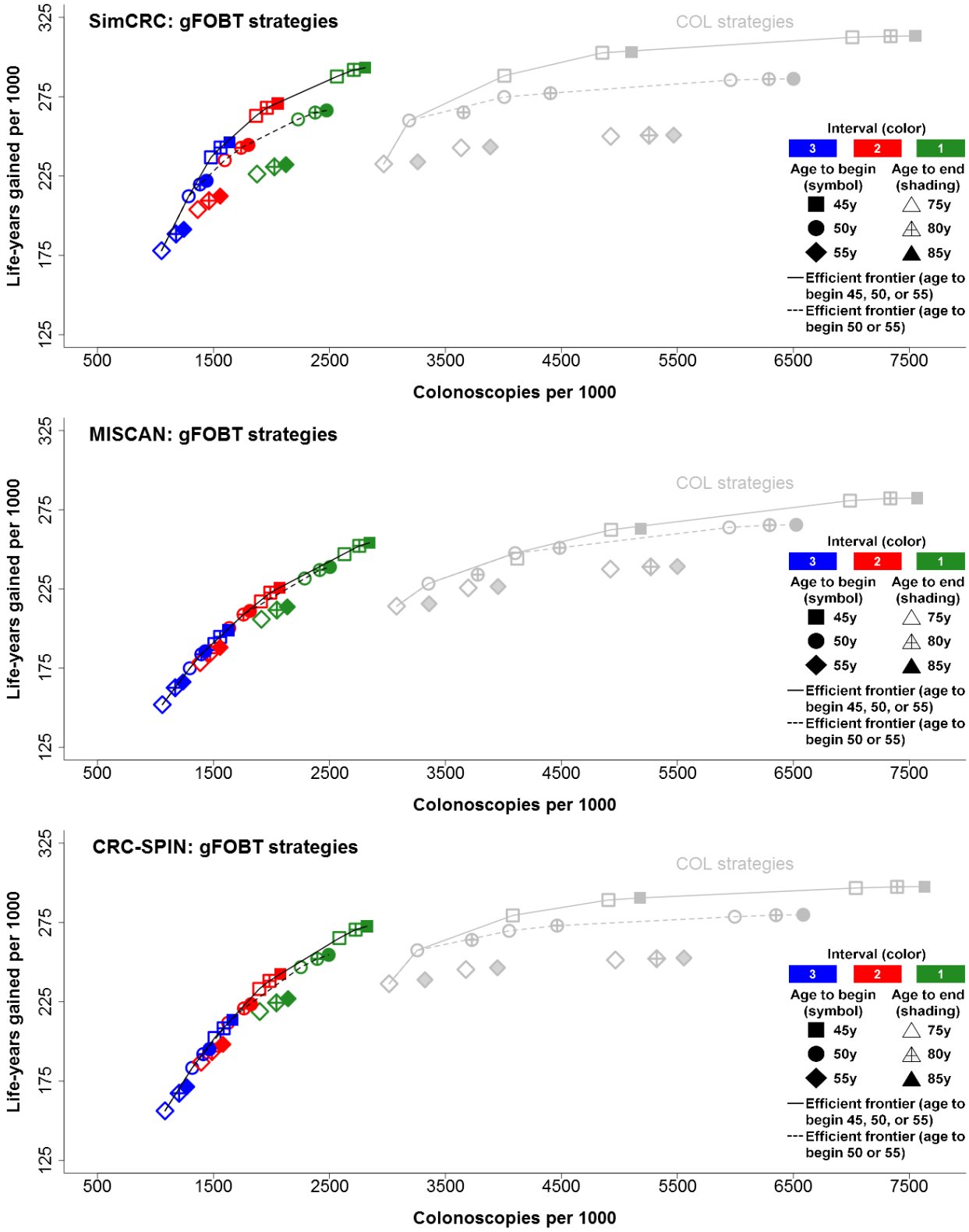


**Figure 13. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for FIT screening strategies that vary by age to begin, age to end, and screening interval, by model**

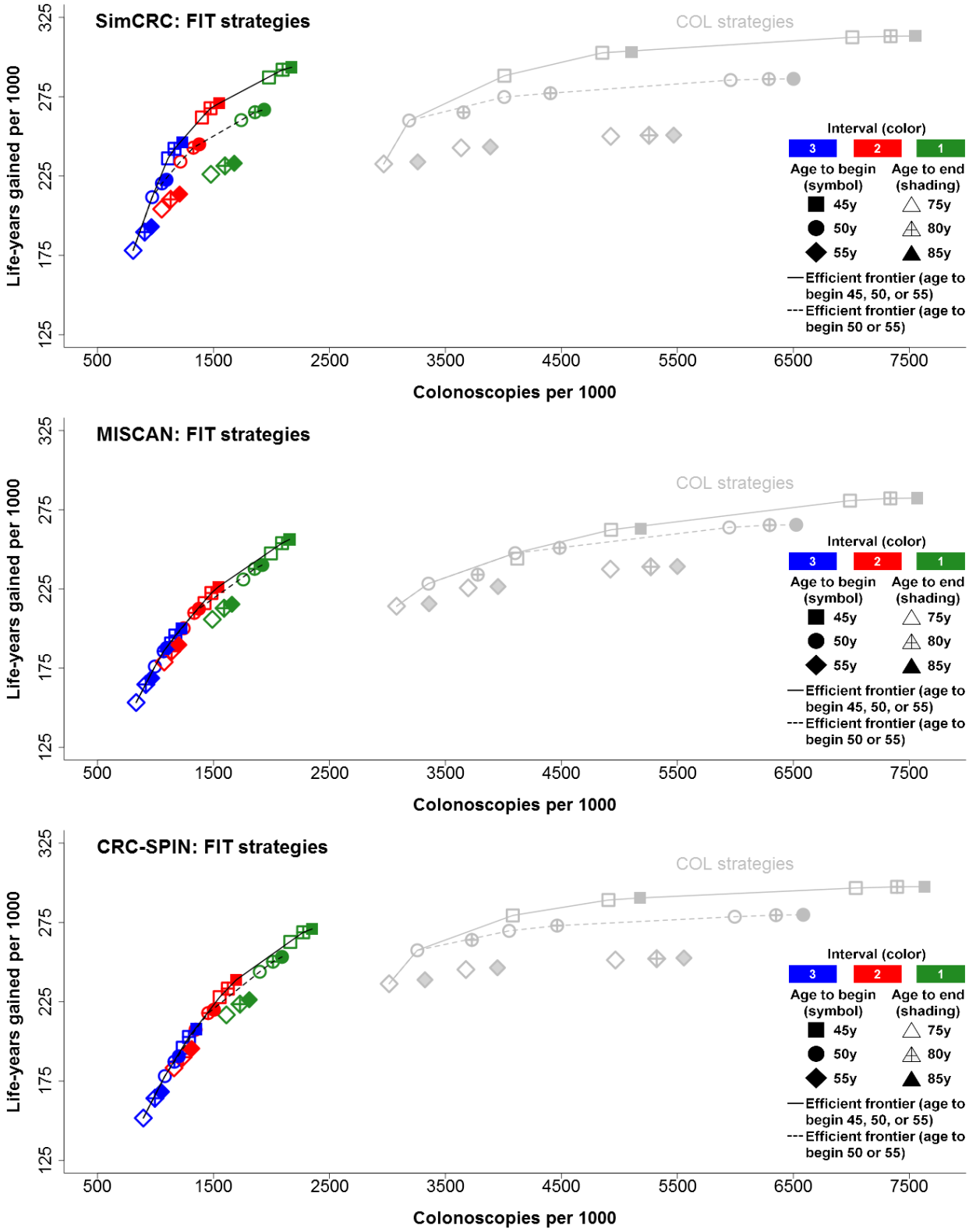


**Figure 14. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for FIT-DNA screening strategies that vary by age to begin, age to end, and screening interval, by model**

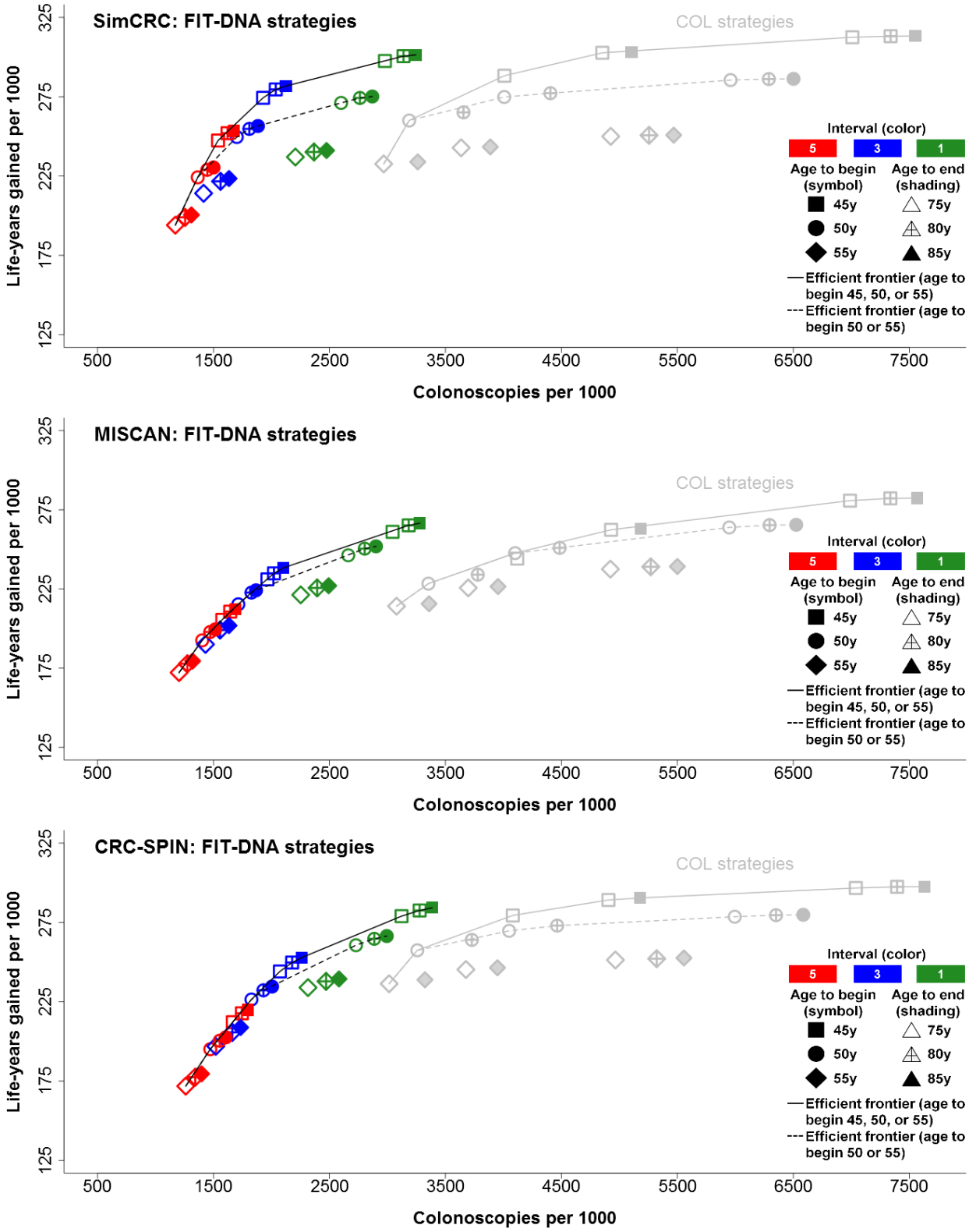


**Figure 15. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for SIG screening strategies that vary by age to begin, age to end, and screening interval, by model**

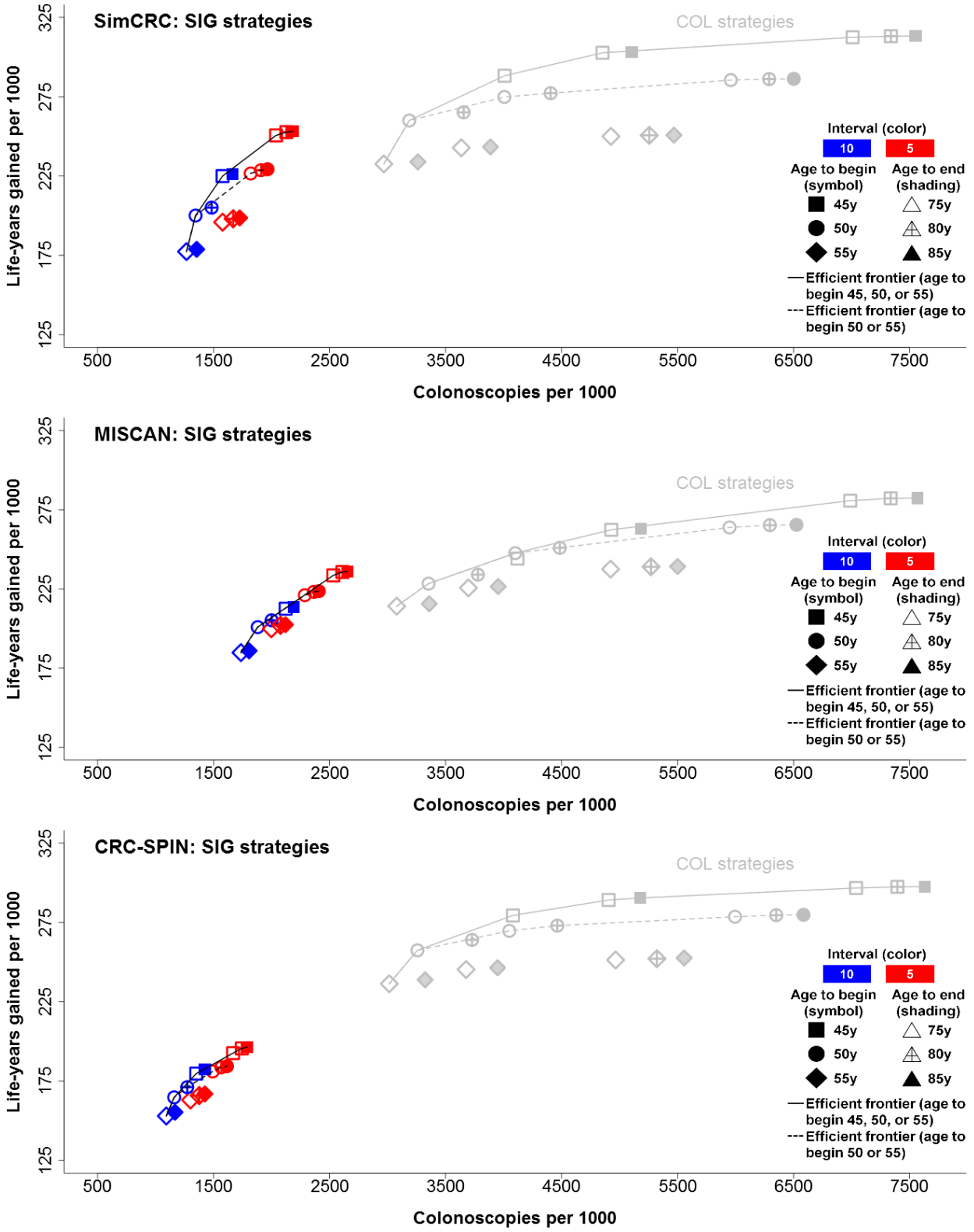


**Figure 16. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for SIG+gFOBT screening strategies that vary by age to begin, age to end, and screening interval, by model**

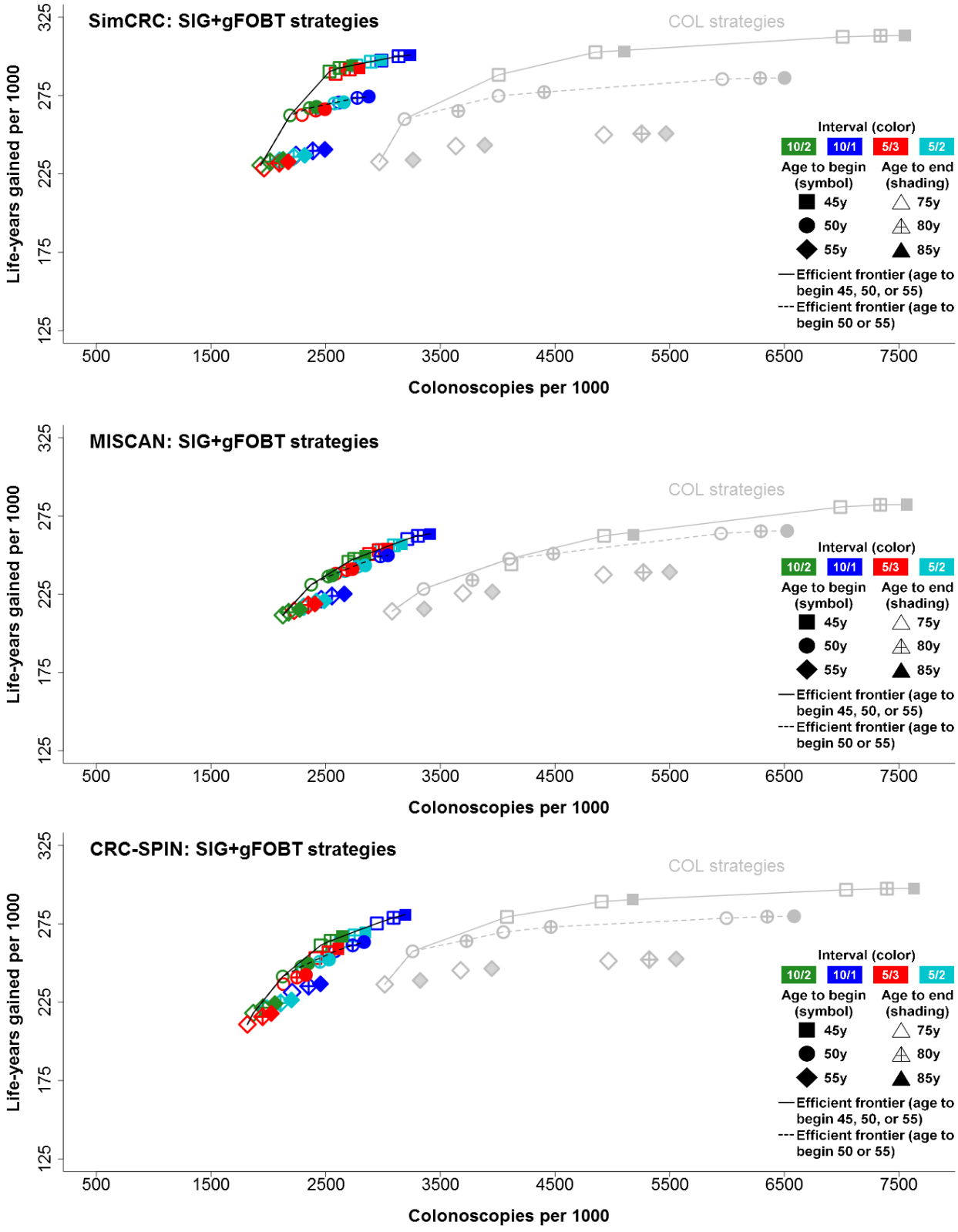


**Figure 17. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for SIG+FIT screening strategies that vary by age to begin, age to end, and screening interval, by model**

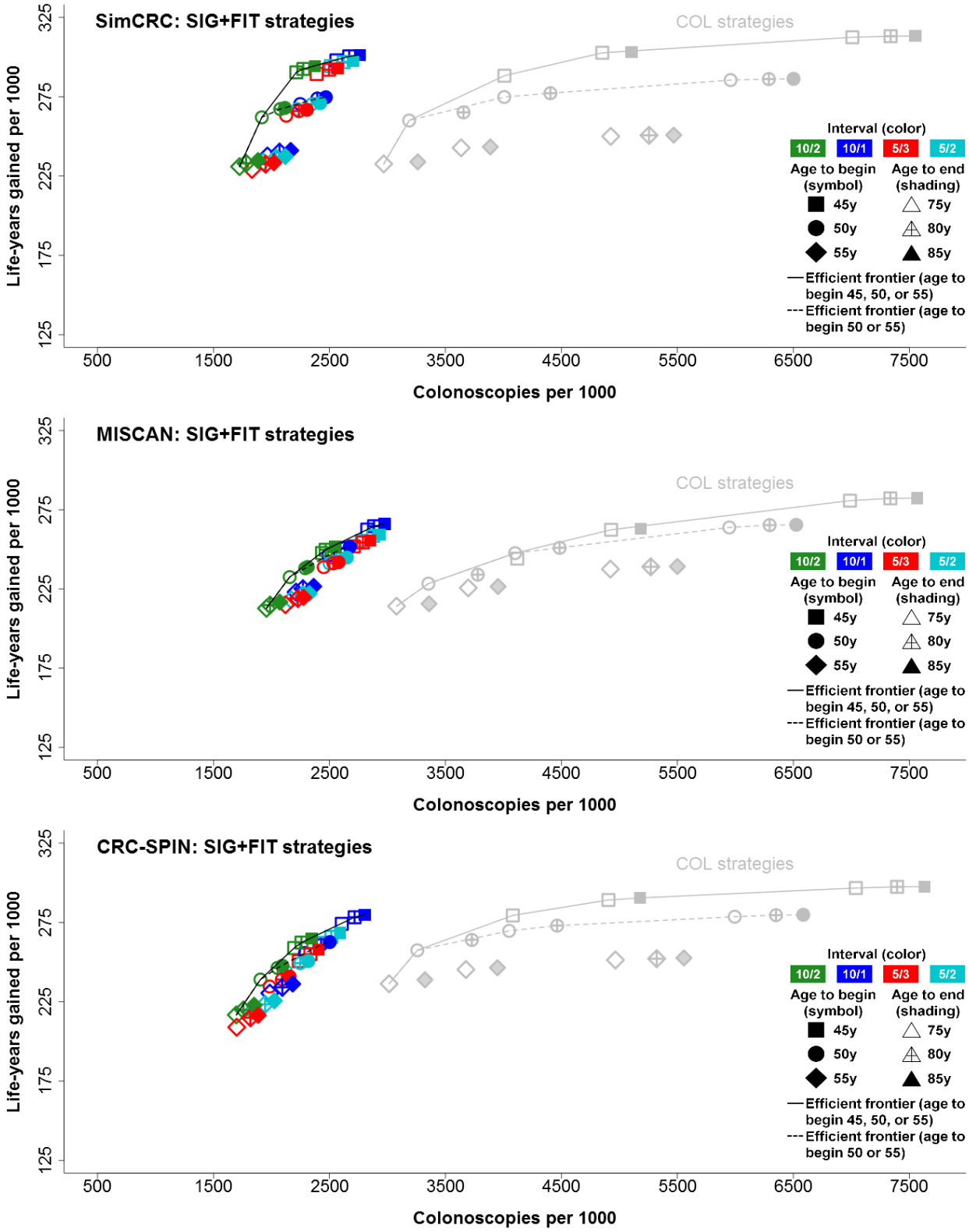


**Figure 18. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for CTC screening strategies that vary by age to begin, age to end, and screening interval, by model**

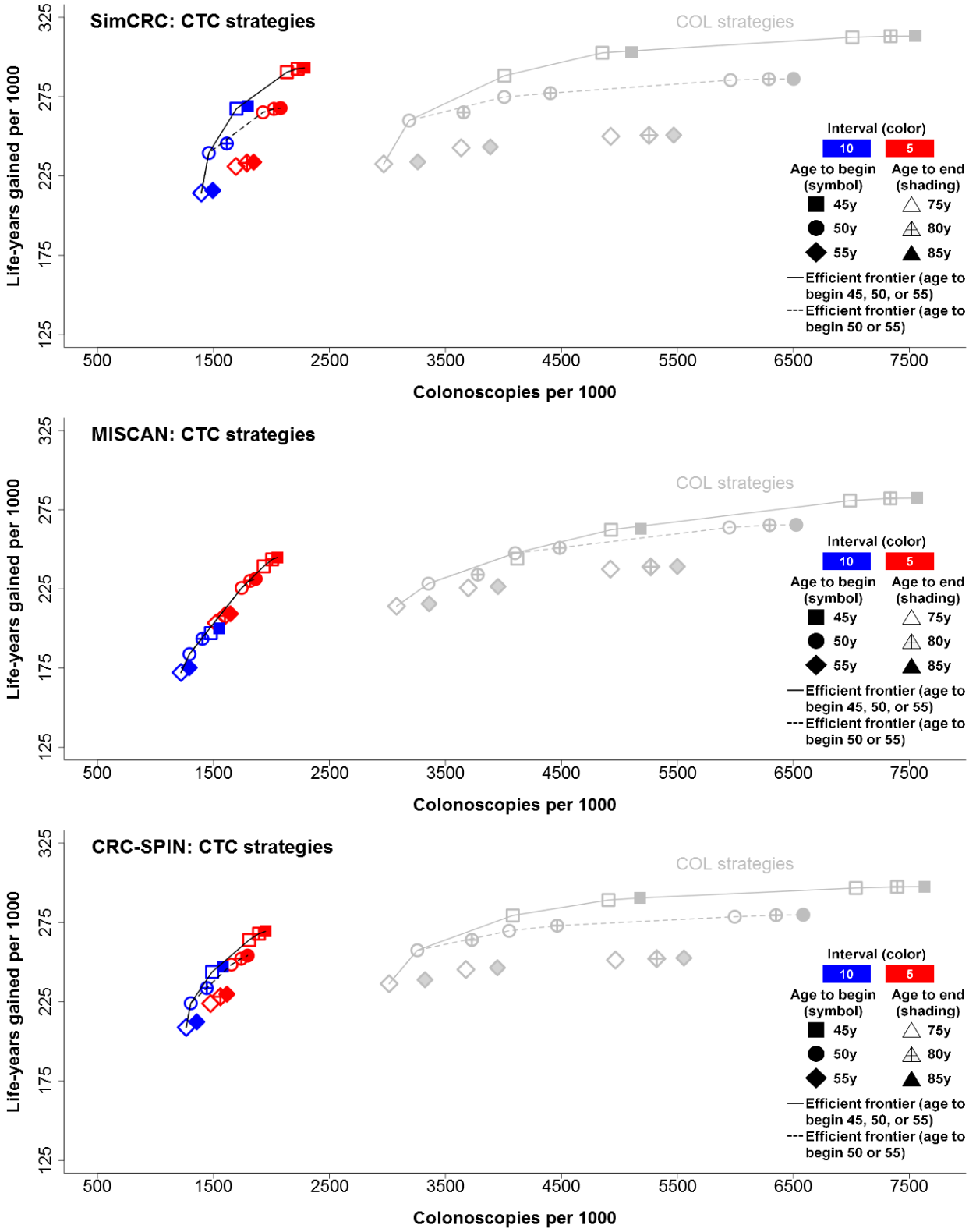
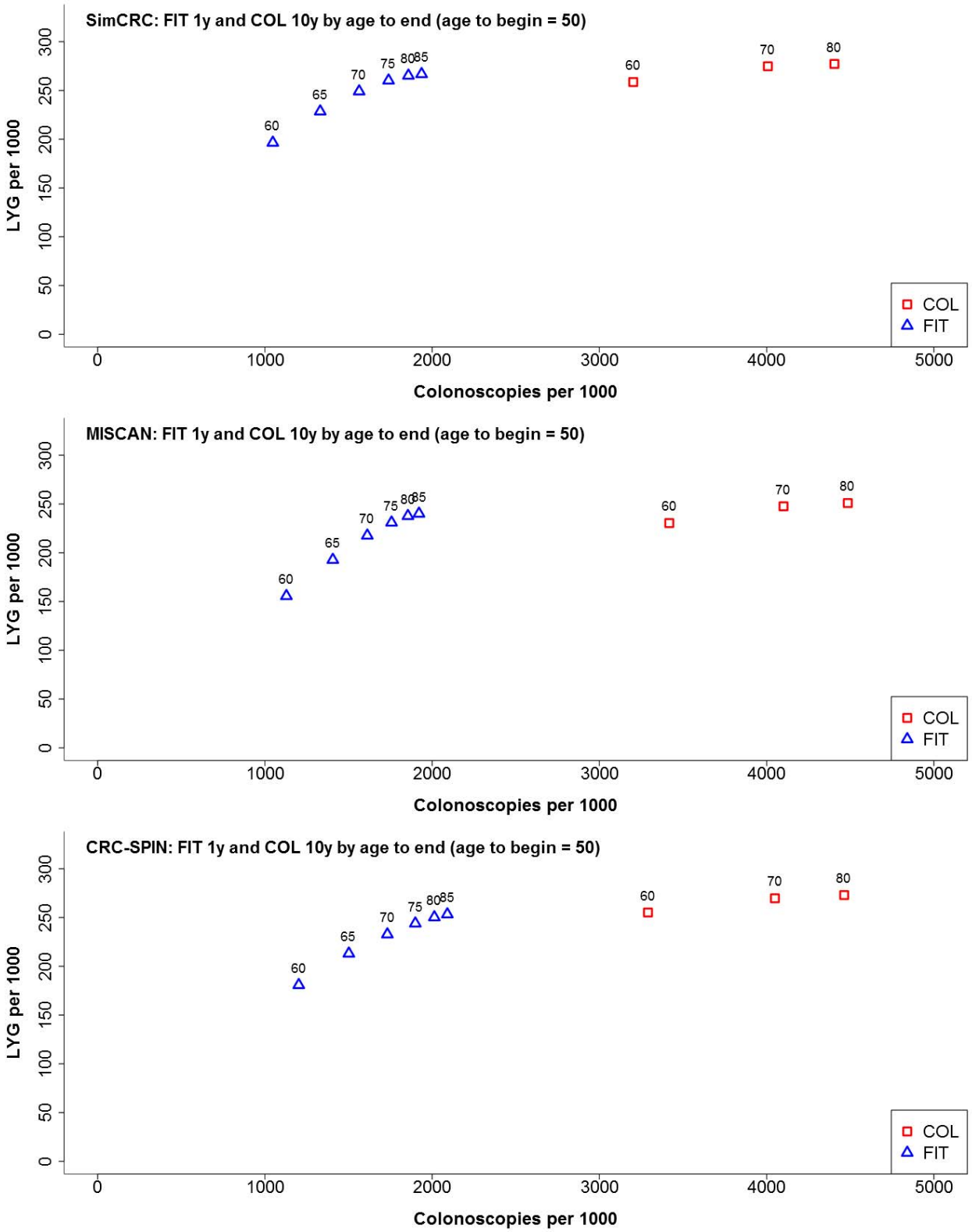


**Figure 19. Colonoscopies and life-years gained for a cohort of 40-year-olds for annual FIT and for 10-yearly colonoscopy screening strategies that vary by age to end screening,* by model**




*Screening begins at age 50 for all. Note change in scale of x-axis from prior graphs.

**Figure 20. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for stool-based screening strategies that vary by age to begin (50, 55), age to end (75, 80, 85), and screening interval (every 1, 2, or 3 years for FIT and gFOBT; every 1, 3, or 5 years for FIT-DNA), by model**

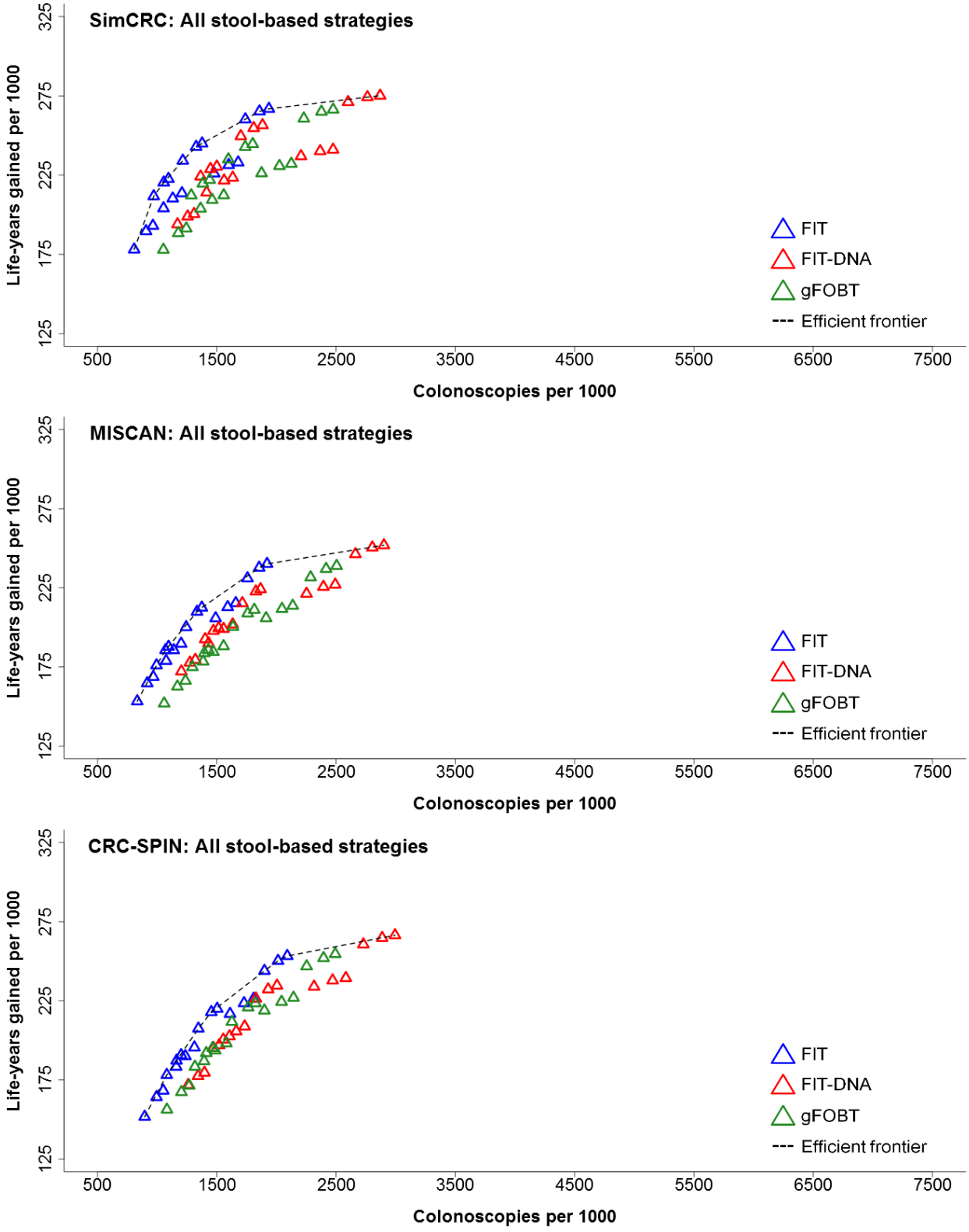


**Figure 21. Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for SIG+FOBT screening strategies that vary by age to begin (50, 55), age to end (75, 80, 85), and screening interval (every 5 or 10 years for SIG, every 1, 2, or 3 years for FIT and gFOBT), by model**

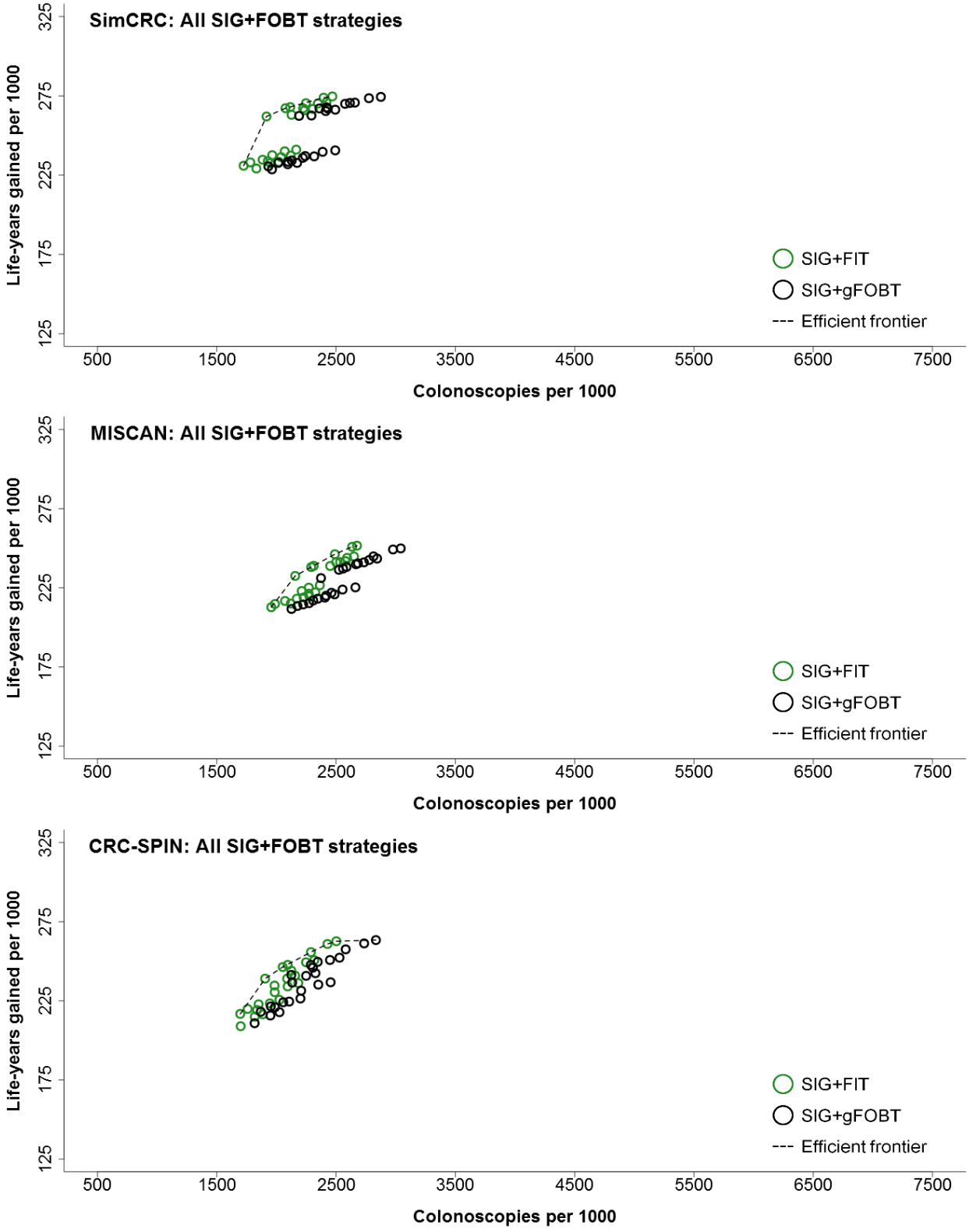
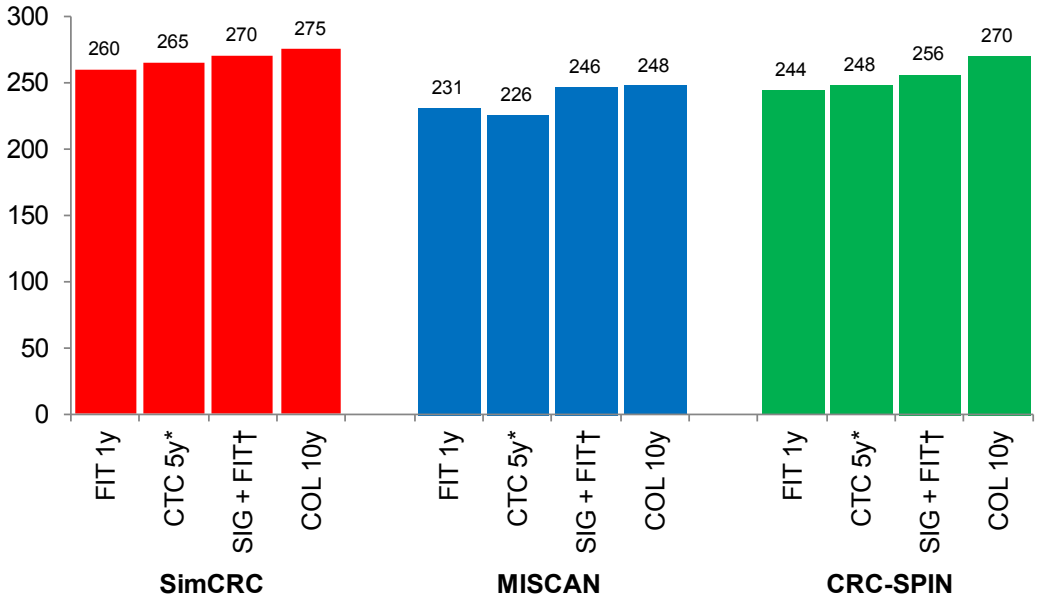


**Figure 22. Summary outcomes for the set of model-recommended strategies with age to begin screening of 50 and age to end screening of 75, assuming colonoscopy strategy with a 10-year interval is selected**

**Panel A: Life-years gained per 1,000 compared with no screening.**




**Panel B: Colorectal cancer deaths averted per 1,000 compared with no screening.**

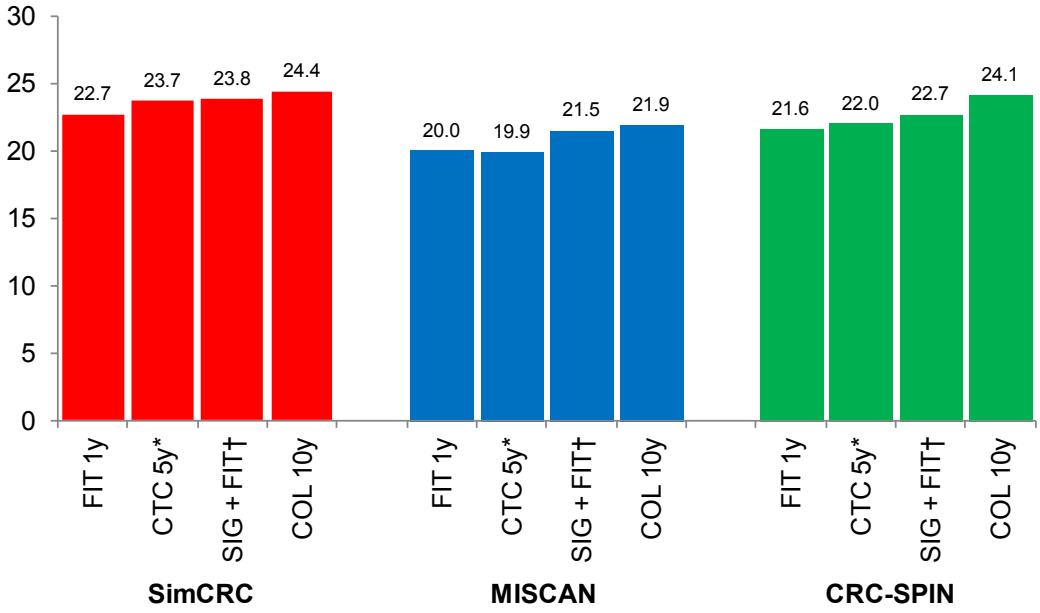
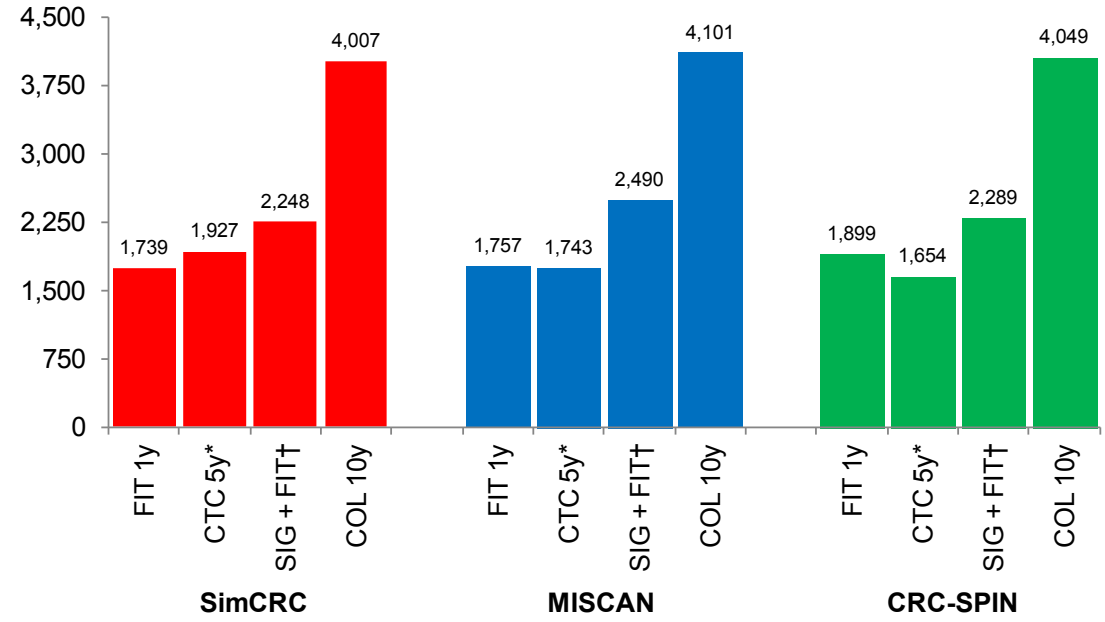
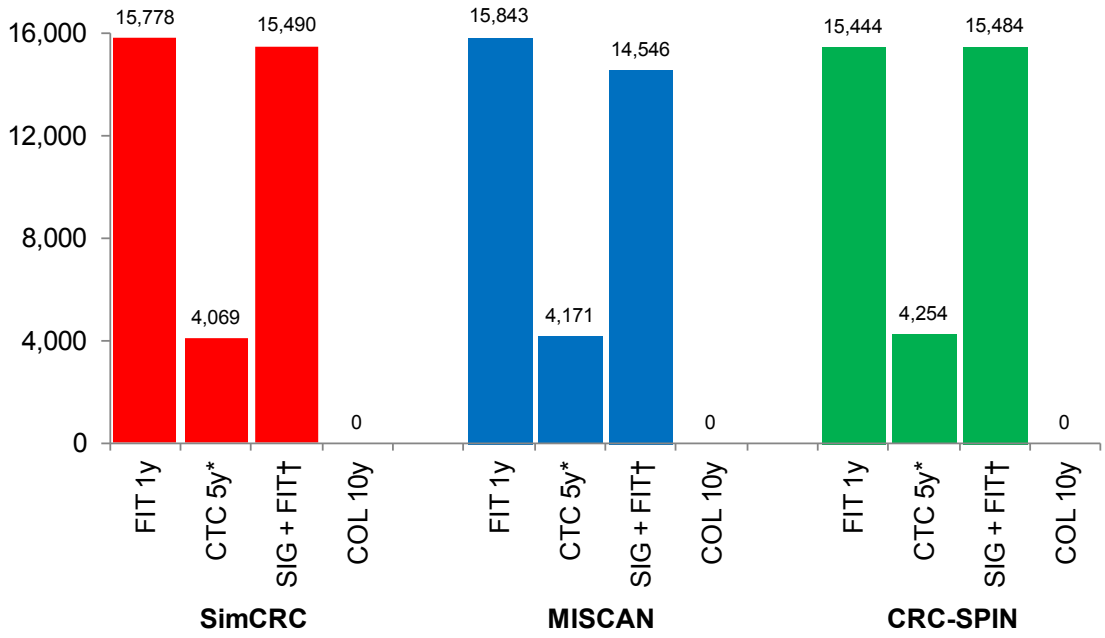


**Figure 22. Summary outcomes for the set of model-recommended strategies with age to begin screening of 50 and age to end screening of 75, assuming colonoscopy strategy with a 10-year interval is selected**

**Panel C: Number of colonoscopies required per 1,000.**




**Panel D: Non-colonoscopy tests‡ per 1,000.**




*The CTC strategy is only recommended if the burden of cathartic bowel preparation required with CTC is not included.
†SIG+FIT is sigmoidoscopy every 10 years with annual FIT.
‡For the SIG+FIT strategy, the number of SIGs and FITs per 1000 were 2,097 and 13,393, respectively for SimCRC; 1,903 and 12,642, respectively for MISCAN; and 2,079 and 13,404; respectively for CRC-SPIN.

**Figure 23. Cathartic bowel preparations and life-years gained (compared with no screening) for a cohort of 40-year-olds for CTC screening strategies that vary by age to begin, age to end, and screening interval, by model**

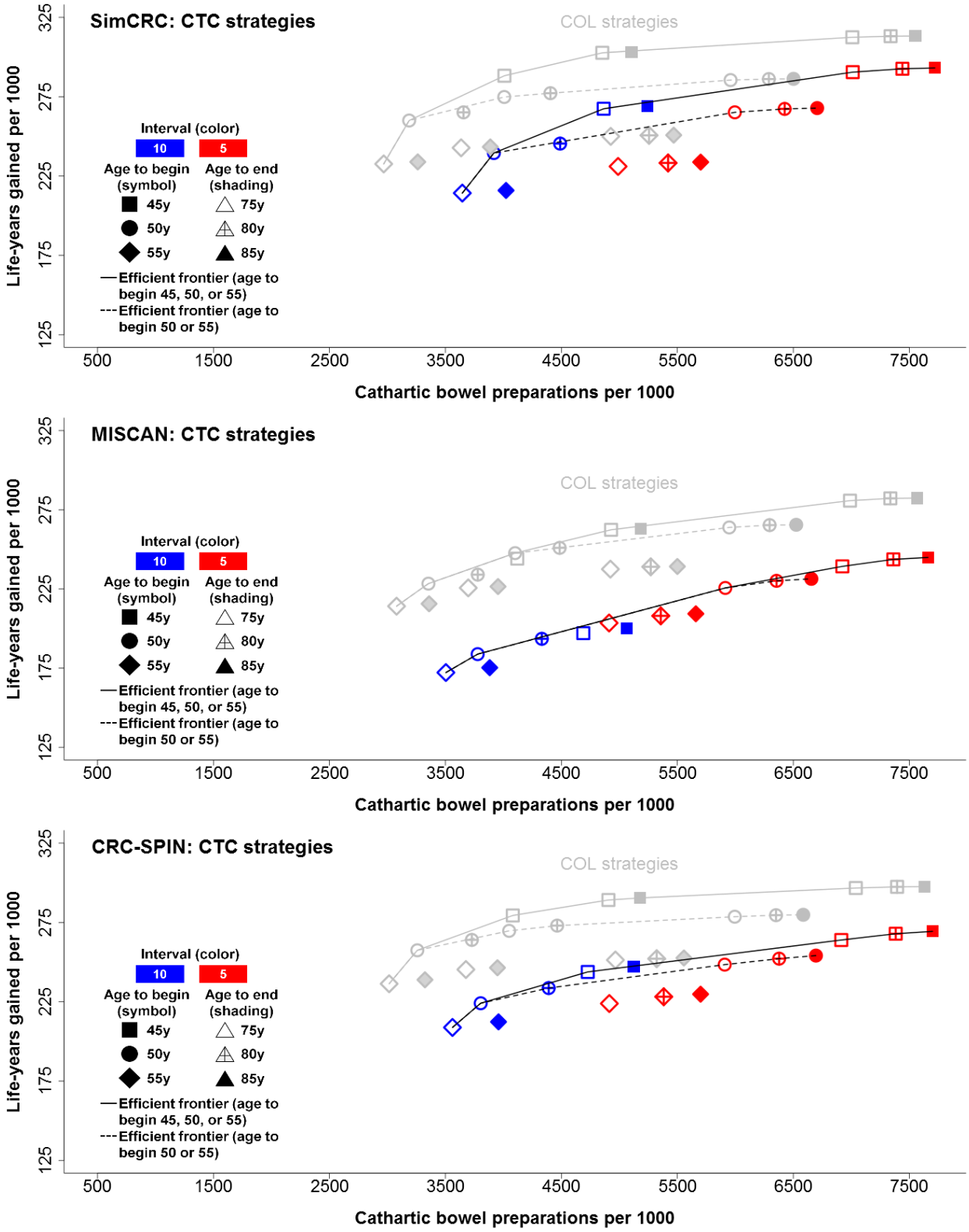


**Table 1. Comparison of natural history model structures**

| Property | SimCRC | MISCAN | CRC-SPIN |
|---|---|---|---|
| **Adenoma risk** | | | |
| Mechanism | Logistic function | Poisson process | Poisson process |
| Risk varies: | | | |
| Randomly across individuals | Yes | Yes | Yes |
| Systematically with age and sex | Yes | Yes | Yes |
| Systematically with race and birth-year cohort | Yes | Yes | No |
| **Adenoma growth** | | | |
| Mechanism | Time in each size category | Time in each size category | Growth Curve |
| Size modeled as continuous | No | No | Yes |
| Risk varies: | | | |
| Randomly across individuals | Yes | Yes | Yes |
| Systematically with location | Yes* | No | Yes* |
| Transition times correlated across size categories | No | Yes | Yes |
| **Transition to preclinical CRC** | | | |
| Mechanism | Logistic function | Overall transition probability | Adenoma size at transition |
| Risk varies: | | | |
| Randomly across adenomas by size within individuals | Yes | No† | Yes |
| Systematically with: | | | |
| Sex | Yes | No | Yes |
| Age | Yes | Yes‡ | No |
| Race and other risk factors | Yes | No | No |
| Adenoma size | No | Yes | Yes |
| Location | Yes* | No | Yes* |
| Transition times correlated across preclinical stages | No | Yes | Not applicable |
| **Transition to clinical CRC** | | | |
| Mechanism | Time to transition | Time to transition | Time to transition |
| Transition times: | | | |
| Vary randomly across CRCs within individuals | Yes | Yes | Yes |
| Vary systematically with: | | | |
| Sex and race | No | Yes | No |
| Location | Yes§ | Yes§ | Yes§ |
| Correlated with duration of preclinical CRC | No | Yes | No |

* Varies by proximal colon, distal colon and rectum for SimCRC and by colon and rectum for CRC-SPIN.

† The probability of transition is 0 for all non-progressive adenomas and for adenomas ≤5mm, 0.3 for progressive adenomas 6-9mm, and 1 for progressive adenomas ≥10mm.

‡ The probability that an adenoma is progressive depends on age.

§ Varies by proximal colon, distal colon and rectum for SimCRC and MISCAN and by colon and rectum for CRC-SPIN.

**Table 2. Screening strategies evaluated by the models**

| Screening modality | Screening interval* (y) | Age to begin screening | Age to end screening | # of (unique) strategies |
|---|---|---|---|---|
| No screening | -- | -- | -- | 1 (1) |
| Fecal immunochemical test (FIT) | 1, 2, 3 | 45, 50, 55 | 75, 80, 85 | 27 (27) |
| Sensitive guaiac-based fecal occult blood test (gFOBT) | 1, 2, 3 | 45, 50, 55 | 75, 80, 85 | 27 (27) |
| Multi-target stool-DNA test (FIT-DNA) | 1, 3, 5 | 45, 50, 55 | 75, 80, 85 | 27 (27) |
| Flexible sigmoidoscopy (SIG) | 5, 10 | 45, 50, 55 | 75, 80, 85 | 18 (15) |
| SIG+FIT† | 5_2, 5_3, 10_1, 10_2 | 45, 50, 55 | 75, 80, 85 | 36 (36) |
| SIG+gFOBT† | 5_2, 5_3, 10_1, 10_2 | 45, 50, 55 | 75, 80, 85 | 36 (36) |
| Computed tomographic colonography (CTC) | 5, 10 | 45, 50, 55 | 75, 80, 85 | 18 (15) |
| Colonoscopy (COL) | 5, 10, 15 | 45, 50, 55 | 75, 80, 85 | 27 (20) |
| **Total number of (unique) screening strategies evaluated with the models** | | | | **217 (204)** |

* For SIG+FIT and SIG+gFOBT, the first and second intervals are for SIG and the stool test, respectively.

† If the two tests are due in the same year, we assume the stool test is performed first. Those with a negative stool test then have the flexible sigmoidoscopy. Those with a positive stool test are referred for a diagnostic colonoscopy.

**Table 3. Comparison of the 2015 and 2008 CISNET colorectal cancer screening analyses for the U.S. Preventive Services Task Force**

| Characteristic | 2015 analysis | 2008 analysis |
|---|---|---|
| Simulation models | SimCRC, MISCAN, CRC-SPIN | SimCRC, MISCAN |
| Cohort of interest | US average-risk 40-year-olds* | US average-risk 40-year-olds* |
| Cohort year of birth | 1975 | 1968 |
| US life table (for all-cause survival) | 2009 | 2002 |
| CRC relative survival | SEER (1975-2003)† | SEER (1996-1999 data) |
| Age to begin screening | 45y, 50y, 55y | 40y, 50y, 60y |
| Age to end screening | 75y, 80y, 85y | 75y, 85y |
| Stool based screening modalities (intervals) | HII not included | HII (1y, 2y, 3y) |
| | gFOBT (1y, 2y, 3y) | gFOBT (1y, 2y, 3y) |
| | FIT (1y, 2y, 3y) | FIT (1y, 2y, 3y) |
| | FIT-DNA (1y, 3y, 5y) | FIT-DNA not included |
| Other screening modalities (intervals) | COL (5y, 10y, 15y) | COL (5y, 10y, 20y) |
| | SIG without biopsy‡ (5y, 10y) | SIG with biopsy‡ (5y, 10y, 20y) |
| | SIG without biopsy‡ + FIT (5y_2y, 5y_3y, 10y_1y, 10y_2y) | SIG + FIT not included |
| | SIG without biopsy‡ + gFOBT (5y_2y, 5y_3y, 10y_1y, 10y_2y) | SIG with biopsy‡ + gFOBT (5y_1y, 5y_2y, 5y_3y, 10y_1y, 10y_2y, 10y_3y, 20y_1y, 20y_2y, 20y_3y) |
| | CT colonography (5y, 10y) | CT colonography not included |
| Management of persons with a false-positive non-colonoscopy test‖ | Resume screening with original modality and schedule 10 years after the false-positive test | Resume screening with 10-yearly colonoscopy 10 years after the false-positive test |
| Age to end surveillance | 85, assuming the last surveillance colonoscopy detected no adenomas | Lifetime |
| Adherence with all procedures | 100% | 100% |

COL – colonoscopy; FIT – fecal immunochemical test; FIT-DNA – multi-target stool DNA test (fecal immunochemical test with a DNA stool test); gFOBT – sensitive guaiac-based fecal occult blood test; HII – Hemoccult II fecal occult blood test; SEER – Surveillance, Epidemiology and End Results Program; SIG – flexible sigmoidoscopy

* Previously unscreened for colorectal cancer and free of diagnosed colorectal cancer.

† CRC relative survival estimates from models fit to SEER data from 1975-2013 that predict stage-specific survival as a function of age at diagnosis, time since diagnosis, diagnosis year, sex, and (optionally) race.[56]

‡ With flexible sigmoidoscopy without biopsy, all persons with a polyp or suspected colorectal cancer are referred for a diagnostic colonoscopy. With flexible sigmoidoscopy with biopsy, only persons with an adenoma or colorectal cancer are referred for diagnostic colonoscopy.

‖ A positive non-colonoscopy test followed by a negative diagnostic colonoscopy (i.e., no adenomas or colorectal detected).

**Table 4. Screening test characteristics used in the analysis**

| Test characteristic | Base-Case Value | Source | Worst-Case Value | Best-Case Value | Source |
|---|---|---|---|---|---|
| **gFOBT (per person)** | | Zauber, 2008[106] | | | |
| Specificity | 0.925 | | Not varied | Not varied | Not applicable |
| Sensitivity for adenomas ≤5 mm | 0.075* | | 0.075 | 0.075 | Zauber, 2008[106] |
| Sensitivity for adenomas 6-9 mm | 0.124 | | 0.1 | 0.262 | Zauber, 2008[106] |
| Sensitivity for adenomas ≥10 mm | 0.239 | | 0.177 | 0.494 | Zauber, 2008[106] |
| Sensitivity for colorectal cancer | 0.7 | | 0.615 | 0.794 | Levi, 2011[84] Allison, 1996[83] |
| **FIT (per person)** | | Imperiale, 2014[16] | | | Imperiale, 2014[16] |
| Specificity | 0.964 | | Not varied | Not varied | |
| Sensitivity for adenomas ≤5 mm | 0.076† | | 0.067 | 0.086 | |
| Sensitivity for adenomas 6-9 mm | | | 0.067 | 0.086 | |
| Sensitivity for adenomas ≥10 mm | 0.238‡ | | 0.208 | 0.27 | |
| Sensitivity for colorectal cancer | 0.738 | | 0.623 | 0.833 | |
| **FIT-DNA (per person)** | | Imperiale, 2014[16] | | | Imperiale, 2014[16] |
| Specificity | 0.898 | | Not varied | Not varied | |
| Sensitivity for adenomas ≤5 mm | 0.172† | | 0.159 | 0.186 | |
| Sensitivity for adenomas 6-9 mm | | | 0.159 | 0.186 | |
| Sensitivity for adenomas ≥10 mm | 0.424‡ | | 0.387 | 0.462 | |
| Sensitivity for colorectal cancer | 0.923 | | 0.84 | 0.97 | |
| **Colonoscopy (within reach, per lesion)§** | | | | | |
| Specificity | 0.86‖ | Schroy, 2013[79] | Not varied | Not varied | Not applicable |
| Sensitivity for adenomas ≤5 mm | 0.75 | van Rijn, 2006[78] | 0.7 | 0.79 | Zauber, 2008[106] |
| Sensitivity for adenomas 6-9 mm | 0.85 | van Rijn, 2006[78] | 0.8 | 0.92 | Zauber, 2008[106] |
| Sensitivity for adenomas ≥10 mm | 0.95 | van Rijn, 2006[78] | 0.931 | 0.995 | Johnson, 2008[19] |
| Sensitivity for colorectal cancer | 0.95 | By assumption | 0.931 | 0.995 | By assumption |
| **Sigmoidoscopy (within reach, per lesion)** | | | | | By assumption |
| Specificity | 0.87‖ | Weissfeld, 2005[80] | Not varied | Not varied | |
| Sensitivity for adenomas ≤5 mm | 0.75 | By assumption | 0.7 | 0.79 | |
| Sensitivity for adenomas 6-9 mm | 0.85 | By assumption | 0.8 | 0.92 | |
| Sensitivity for adenomas ≥10 mm | 0.95 | By assumption | 0.931 | 0.995 | |
| Sensitivity for colorectal cancer | 0.95 | By assumption | 0.931 | 0.995 | |
| **CT colonography (per lesion)** | | Johnson, 2008[19] | | | Johnson, 2008[19] |
| Specificity | 0.88^ | | Not varied | Not varied | |
| Sensitivity for adenomas ≤5 mm¶ | -- | | -- | -- | |
| Sensitivity for adenomas 6-9 mm | 0.57 | | 0.489 | 0.716 | |
| Sensitivity for adenomas ≥10 mm | 0.84 | | 0.756 | 0.924 | |
| Sensitivity for colorectal cancer | 0.84 | | 0.756 | 0.924 | |

FIT – fecal immunochemical test; FIT-DNA – multi-target stool DNA test (fecal immunochemical test with a DNA stool test); gFOBT – sensitive guaiac-based fecal occult blood test; -- indicates sensitivity is not provided because adenoma size is smaller than the referral threshold for a colonoscopy of 6mm, that is, only persons with a ≥6mm lesion visualized at CT colonography are deemed to have a positive screening test.

* We assume that 1-5 mm adenomas do not bleed, and therefore cannot cause a positive stool test. We also assume that gFOBT can be positive due to bleeding from other causes, the probability of which is equal to positivity rate in persons without adenomas (i.e. 1 – 0.925).

† Sensitivity for persons with non-advanced adenomas. For persons with 1-5 mm adenomas, we assume that the sensitivity of the test is equal to the positivity rate in persons without adenomas (i.e., 1 – specificity). The sensitivity for persons with 6-9 mm adenomas is chosen such that the weighted average sensitivity for persons with 1-5 mm and with 6-9 mm adenoma(s) is equal to that of non-advanced adenomas.

‡ Sensitivity for persons with advanced adenomas (i.e., adenomas ≥ 10 mm and/or adenomas with advanced histology). Sensitivity was not reported for the subset of ≥ 10mm adenomas.

§ We assume the same test characteristics for screening colonoscopies as for colonoscopies for diagnostic follow-up or for surveillance. We assume no correlation in findings between CTC or sigmoidoscopy and subsequent diagnostic colonoscopy.

‖ The lack of specificity with endoscopy reflects the detection of non-adenomatous polyps, which, in the case of sigmoidoscopy, may lead to unnecessary diagnostic colonoscopy, and in the case of colonoscopy screening, leads to unnecessary polypectomy, which is associated with an increased risk of colonoscopy complications.

^ The lack of specificity with CTC reflects the detection of ≥ 6 mm non-adenomatous lesions, artifacts, stool, and adenomas smaller than the 6 mm threshold for referral to colonoscopy.

**Table 5. Efficient and near-efficient colonoscopy screening strategies with age to begin screening of 50 or 55, by model**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL/ΔLYG) |
| **SimCRC** | | | | | | | | | |
| COL 55-75, 15 | 0 | 0 | 0 | 2,968 | 233 | 22.2 | -- | -- | -- |
| COL 50-75, 15 | 0 | 0 | 0 | 3,187 | 260 | 22.8 | 220 | 27 | 8 |
| COL 50-80, 15 | 0 | 0 | 0 | 3,656 | 265 | 23.9 | | | Near-efficient* |
| COL 50-75, 10 | 0 | 0 | 0 | 4,007 | 275 | 24.4 | 820 | 15 | 55 |
| COL 50-80, 10 | 0 | 0 | 0 | 4,405 | 277 | 24.9 | 398 | 2 | 166 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,959 | 285 | 25.5 | 1,554 | 8 | 188 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,289 | 286 | 25.6 | 330 | 1 | 513 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,502 | 286 | 25.7 | 213 | <1 | 1,661 |
| **MISCAN** | | | | | | | | | |
| COL 55-75, 15 | 0 | 0 | 0 | 3,079 | 214 | 20.1 | -- | -- | -- |
| COL 50-75, 15 | 0 | 0 | 0 | 3,353 | 228 | 20.2 | 275 | 14 | 19 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,101 | 248 | 21.9 | 747 | 19 | 39 |
| COL 50-80, 10 | 0 | 0 | 0 | 4,485 | 251 | 22.6 | | | Near-efficient* |
| COL 50-75, 5 | 0 | 0 | 0 | 5,948 | 264 | 23.3 | 1,847 | 16 | 114 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,296 | 265 | 23.5 | 348 | 1 | 236 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,525 | 266 | 23.6 | 229 | <1 | 1,146 |
| **CRC-SPIN** | | | | | | | | | |
| COL 55-75, 15 | 0 | 0 | 0 | 3,015 | 236 | 22.4 | -- | -- | -- |
| COL 50-75, 15 | 0 | 0 | 0 | 3,258 | 257 | 22.7 | 243 | 21 | 12 |
| COL 50-80, 15 | 0 | 0 | 0 | 3,728 | 264 | 24.1 | | | Near-efficient* |
| COL 50-75, 10 | 0 | 0 | 0 | 4,049 | 270 | 24.1 | 792 | 12 | 65 |
| COL 50-80, 10 | 0 | 0 | 0 | 4,464 | 273 | 24.8 | 414 | 3 | 126 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,995 | 279 | 25.0 | 1,532 | 6 | 273 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,351 | 280 | 25.3 | 356 | 1 | 367 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,586 | 280 | 25.3 | 235 | <1 | 947 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; LYG – life-years gained compared with no screening; SIG – flexible sigmoidoscopy; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Strategy yields life-years gained within 98% of the efficient frontier.

**Table 6. Efficient and near-efficient stool-based screening strategies (FIT, FIT-DNA, or gFOBT) with age to begin of 50 or 55, by model**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL/ΔLYG) |
| **SimCRC** | | | | | | | | | |
| FIT 55-75, 3 | 5,306 | 0 | 0 | 807 | 178 | 16.1 | -- | -- | -- |
| FIT 50-75, 3 | 6,887 | 0 | 0 | 971 | 212 | 18.2 | 164 | 34 | 5 |
| FIT 50-80, 3 | 7,694 | 0 | 0 | 1,055 | 220 | 19.7 | 84 | 9 | 10 |
| FIT 50-85, 3 | 8,111 | 0 | 0 | 1,095 | 223 | 20.2 | | | Near-efficient* |
| FIT 50-75, 2 | 9,326 | 0 | 0 | 1,215 | 234 | 20.2 | 160 | 14 | 12 |
| FIT 50-80, 2 | 10,572 | 0 | 0 | 1,327 | 243 | 21.7 | 112 | 9 | 13 |
| FIT 50-85, 2 | 11,165 | 0 | 0 | 1,377 | 245 | 22.2 | | | Near-efficient* |
| FIT 50-75, 1 | 15,778 | 0 | 0 | 1,739 | 260 | 22.7 | | | Near-efficient* |
| FIT 50-80, 1 | 17,426 | 0 | 0 | 1,858 | 265 | 23.7 | 531 | 22 | 24 |
| FIT 50-85, 1 | 18,589 | 0 | 0 | 1,937 | 267 | 24.1 | 79 | 2 | 50 |
| FIT-DNA 50-75, 1 | 11,041 | 0 | 0 | 2,601 | 271 | 23.9 | | | Near-efficient* |
| FIT-DNA 50-80, 1 | 12,096 | 0 | 0 | 2,763 | 274 | 24.5 | 826 | 7 | 112 |
| FIT-DNA 50-85, 1 | 12,826 | 0 | 0 | 2,870 | 275 | 24.7 | 107 | 1 | 116 |
| **MISCAN** | | | | | | | | | |
| FIT 55-75, 3 | 5,250 | 0 | 0 | 833 | 153 | 13.9 | -- | -- | -- |
| FIT 55-80, 3 | 6,204 | 0 | 0 | 917 | 165 | 15.8 | | | Near-efficient* |
| FIT 55-85, 3 | 6,859 | 0 | 0 | 967 | 169 | 16.6 | | | Near-efficient* |
| FIT 50-75, 3 | 6,795 | 0 | 0 | 995 | 176 | 15.3 | 162 | 23 | 7 |
| FIT 50-80, 3 | 7,693 | 0 | 0 | 1,070 | 186 | 16.9 | 75 | 10 | 8 |
| FIT 50-85, 3 | 8,032 | 0 | 0 | 1,096 | 188 | 17.3 | | | Near-efficient* |
| FIT 50-75, 2 | 9,342 | 0 | 0 | 1,243 | 200 | 17.3 | | | Near-efficient* |
| FIT 50-80, 2 | 10,613 | 0 | 0 | 1,334 | 210 | 18.9 | 264 | 24 | 11 |
| FIT 50-85, 2 | 11,233 | 0 | 0 | 1,375 | 213 | 19.4 | 40 | 3 | 16 |
| FIT 50-75, 1 | 15,843 | 0 | 0 | 1,757 | 231 | 20.0 | | | Near-efficient* |
| FIT 50-80, 1 | 17,552 | 0 | 0 | 1,855 | 238 | 21.1 | 481 | 25 | 19 |
| FIT 50-85, 1 | 18,796 | 0 | 0 | 1,921 | 240 | 21.6 | 66 | 2 | 27 |
| FIT-DNA 50-75, 1 | 11,025 | 0 | 0 | 2,662 | 246 | 21.4 | | | Near-efficient* |
| FIT-DNA 50-80, 1 | 12,108 | 0 | 0 | 2,804 | 250 | 22.2 | | | Near-efficient* |
| FIT-DNA 50-85, 1 | 12,888 | 0 | 0 | 2,901 | 252 | 22.5 | 980 | 12 | 83 |
| **CRC-SPIN** | | | | | | | | | |
| FIT 55-75, 3 | 5,301 | 0 | 0 | 895 | 152 | 14.0 | -- | -- | -- |
| FIT 55-80, 3 | 6,254 | 0 | 0 | 995 | 164 | 15.9 | | | Near-efficient* |
| FIT 50-75, 3 | 6,857 | 0 | 0 | 1,081 | 178 | 15.8 | 186 | 26 | 7 |
| FIT 55-75, 2 | 7,575 | 0 | 0 | 1,160 | 183 | 17.1 | | | Near-efficient* |
| FIT 50-80, 3 | 7,660 | 0 | 0 | 1,163 | 187 | 17.2 | | | Near-efficient* |
| FIT 50-85, 3 | 8,084 | 0 | 0 | 1,201 | 191 | 17.9 | | | Near-efficient* |
| FIT 50-75, 2 | 9,241 | 0 | 0 | 1,346 | 207 | 18.3 | 265 | 29 | 9 |
| FIT 50-80, 2 | 10,476 | 0 | 0 | 1,454 | 218 | 19.9 | 108 | 10 | 10 |
| FIT 50-85, 2 | 11,071 | 0 | 0 | 1,504 | 220 | 20.4 | | | Near-efficient* |
| FIT 50-75, 1 | 15,444 | 0 | 0 | 1,899 | 244 | 21.6 | 445 | 26 | 17 |
| FIT 50-80, 1 | 17,062 | 0 | 0 | 2,013 | 250 | 22.6 | 114 | 6 | 18 |
| FIT 50-85, 1 | 18,224 | 0 | 0 | 2,091 | 253 | 23.2 | 78 | 3 | 26 |
| gFOBT 50-85, 1 | 15,321 | 0 | 0 | 2,493 | 255 | 23.3 | | | Near-efficient* |
| FIT-DNA 50-75, 1 | 10,745 | 0 | 0 | 2,729 | 261 | 23.2 | | | Near-efficient* |
| FIT-DNA 50-80, 1 | 11,795 | 0 | 0 | 2,886 | 265 | 23.9 | | | Near-efficient* |
| FIT-DNA 50-85, 1 | 12,542 | 0 | 0 | 2,994 | 266 | 24.3 | 903 | 13 | 69 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed-tomographic colonography; FIT – fecal immunochemical test; FIT-DNA – multi-target stool DNA test (fecal immunochemical test with a DNA stool test); gFOBT – sensitive guaiac-based fecal occult blood test; LYG – life-years gained compared with no screening; SIG – flexible sigmoidoscopy; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Strategy yields life-years gained within 98% of the efficient frontier.

**Table 7. Efficient and near-efficient flexible sigmoidoscopy screening strategies with age to begin screening of 50 or 55, by model**

| Model/strategy | | Outcomes per 1,000 40-year-olds | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL/ΔLYG) |
| **SimCRC** | | | | | | | | | |
| SIG 55-75, 10 | 0 | 2,277 | 0 | 1,267 | 177 | 17.3 | -- | -- | -- |
| SIG 50-75, 10 | 0 | 2,480 | 0 | 1,345 | 200 | 17.9 | 78 | 23 | 3 |
| SIG 50-80, 10 | 0 | 2,910 | 0 | 1,484 | 205 | 18.9 | | | Near-efficient* |
| SIG 50-75, 5 | 0 | 4,111 | 0 | 1,820 | 227 | 20.6 | 475 | 27 | 18 |
| SIG 50-80, 5 | 0 | 4,459 | 0 | 1,910 | 229 | 21.0 | 90 | 2 | 43 |
| SIG 50-85, 5 | 0 | 4,691 | 0 | 1,965 | 229 | 21.2 | 56 | 1 | 99 |
| **MISCAN** | | | | | | | | | |
| SIG 55-75, 10 | 0 | 2,155 | 0 | 1,736 | 185 | 17.8 | -- | -- | -- |
| SIG 50-75, 10 | 0 | 2,356 | 0 | 1,881 | 201 | 18.2 | 144 | 16 | 9 |
| SIG 50-80, 10 | 0 | 2,746 | 0 | 2,001 | 205 | 19.0 | | | Near-efficient* |
| SIG 50-75, 5 | 0 | 3,807 | 0 | 2,287 | 221 | 20.0 | 406 | 20 | 20 |
| SIG 50-80, 5 | 0 | 4,129 | 0 | 2,365 | 223 | 20.4 | 78 | 2 | 37 |
| SIG 50-85, 5 | 0 | 4,349 | 0 | 2,408 | 224 | 20.5 | 42 | <1 | 101 |
| **CRC-SPIN** | | | | | | | | | |
| SIG 55-75, 10 | 0 | 2,324 | 0 | 1,093 | 153 | 14.8 | -- | -- | -- |
| SIG 50-75, 10 | 0 | 2,515 | 0 | 1,161 | 165 | 14.7 | 68 | 12 | 6 |
| SIG 50-80, 10 | 0 | 2,983 | 0 | 1,273 | 171 | 16.0 | 113 | 6 | 18 |
| SIG 50-75, 5 | 0 | 4,298 | 0 | 1,493 | 181 | 16.5 | 220 | 10 | 22 |
| SIG 50-80, 5 | 0 | 4,705 | 0 | 1,567 | 184 | 17.0 | 74 | 3 | 28 |
| SIG 50-85, 5 | 0 | 4,987 | 0 | 1,616 | 184 | 17.3 | 49 | 1 | 71 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; LYG – life-years gained compared with no screening; SIG – flexible sigmoidoscopy; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Strategy yields life-years gained within 98% of the efficient frontier.

**Table 8. Efficient and near-efficient strategies combining flexible sigmoidoscopy and stool-based screening strategies with age to begin screening of 50 or 55, by model**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, SIG interval_FOBT interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL/ΔLYG) |
| **SimCRC** | | | | | | | | | |
| SIG+FIT 55-75, 10_2 | 6,468 | 1,956 | 0 | 1,725 | 231 | 21.9 | -- | -- | -- |
| SIG+FIT 50-75, 10_2 | 7,942 | 2,196 | 0 | 1,917 | 262 | 22.9 | 192 | 31 | 6 |
| SIG+FIT 50-80, 10_2 | 8,960 | 2,494 | 0 | 2,076 | 267 | 24.0 | 159 | 5 | 31 |
| SIG+FIT 50-85, 10_2 | 9,412 | 2,534 | 0 | 2,116 | 268 | 24.1 | | | Near-efficient* |
| SIG+FIT 50-75, 10_1 | 13,393 | 2,097 | 0 | 2,248 | 270 | 23.8 | | | Near-efficient* |
| SIG+FIT 50-80, 10_1 | 14,761 | 2,320 | 0 | 2,395 | 274 | 24.5 | 320 | 7 | 48 |
| SIG+FIT 50-85, 10_1 | 15,698 | 2,396 | 0 | 2,469 | 275 | 24.7 | 73 | 1 | 92 |
| **MISCAN** | | | | | | | | | |
| SIG+FIT 55-75, 10_2 | 5,908 | 1,728 | 0 | 1,957 | 213 | 19.8 | -- | -- | -- |
| SIG+FIT 55-80, 10_2 | 6,524 | 1,728 | 0 | 1,988 | 215 | 20.2 | | | Near-efficient* |
| SIG+FIT 50-75, 10_2 | 7,306 | 1,886 | 0 | 2,157 | 232 | 20.4 | 201 | 20 | 10 |
| SIG+FIT 50-80, 10_2 | 8,260 | 2,164 | 0 | 2,291 | 238 | 21.4 | 134 | 6 | 24 |
| SIG+FIT 50-85, 10_2 | 8,706 | 2,164 | 0 | 2,313 | 239 | 21.6 | | | Near-efficient* |
| SIG+FIT 50-75, 10_1 | 12,642 | 1,903 | 0 | 2,490 | 246 | 21.5 | 199 | 8 | 24 |
| SIG+FIT 50-80, 10_1 | 14,039 | 2,177 | 0 | 2,635 | 251 | 22.4 | 144 | 5 | 31 |
| SIG+FIT 50-85, 10_1 | 14,983 | 2,177 | 0 | 2,675 | 252 | 22.5 | 41 | 1 | 59 |
| **CRC-SPIN** | | | | | | | | | |
| SIG+FIT 55-75, 10_2 | 6,569 | 1,961 | 0 | 1,697 | 217 | 20.5 | -- | -- | -- |
| SIG+FIT 55-80, 10_2 | 7,255 | 2,005 | 0 | 1,759 | 220 | 21.0 | | | Near-efficient* |
| SIG+FIT 50-75, 10_2 | 8,033 | 2,192 | 0 | 1,905 | 239 | 21.1 | 208 | 22 | 9 |
| SIG+FIT 50-80, 10_2 | 9,098 | 2,500 | 0 | 2,053 | 246 | 22.4 | 148 | 7 | 20 |
| SIG+FIT 50-85, 10_2 | 9,591 | 2,544 | 0 | 2,094 | 248 | 22.7 | | | Near-efficient* |
| SIG+FIT 50-80, 5_2 | 8,405 | 3,922 | 0 | 2,248 | 249 | 22.7 | | | Near-efficient* |
| SIG+FIT 50-75, 10_1 | 13,404 | 2,079 | 0 | 2,289 | 256 | 22.7 | 237 | 9 | 25 |
| SIG+FIT 50-80, 10_1 | 14,812 | 2,307 | 0 | 2,428 | 261 | 23.6 | 139 | 5 | 27 |
| SIG+FIT 50-85, 10_1 | 15,814 | 2,389 | 0 | 2,502 | 263 | 23.9 | 74 | 2 | 43 |
| SIG+gFOBT 50-85, 10_1 | 13,372 | 2,220 | 0 | 2,834 | 263 | 24.0 | 332 | 1 | 449 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; FIT – fecal immunochemical test; gFOBT – sensitive guaiac-based fecal occult blood test; LYG – life-years gained compared with no screening; SIG – flexible sigmoidoscopy; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Strategy yields life-years gained within 98% of the efficient frontier.

**Table 9. Efficient and near-efficient computed tomographic colonography screening strategies with age to begin screening of 50 or 55, by model**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL/ΔLYG) |
| **SimCRC** | | | | | | | | | |
| CTC 55-75, 10 | 0 | 0 | 2,250 | 1,396 | 214 | 20.7 | -- | -- | -- |
| CTC 50-75, 10 | 0 | 0 | 2,458 | 1,460 | 239 | 21.1 | 64 | 25 | 3 |
| CTC 50-80, 10 | 0 | 0 | 2,874 | 1,615 | 245 | 22.4 | | | Near-efficient* |
| CTC 50-75, 5 | 0 | 0 | 4,069 | 1,927 | 265 | 23.7 | 467 | 26 | 18 |
| CTC 50-80, 5 | 0 | 0 | 4,405 | 2,021 | 267 | 24.1 | 94 | 2 | 44 |
| CTC 50-85, 5 | 0 | 0 | 4,627 | 2,079 | 268 | 24.3 | 58 | 1 | 111 |
| **MISCAN** | | | | | | | | | |
| CTC 55-75, 10 | 0 | 0 | 2,284 | 1,220 | 172 | 16.4 | -- | -- | -- |
| CTC 50-75, 10 | 0 | 0 | 2,485 | 1,293 | 184 | 16.1 | 73 | 12 | 6 |
| CTC 50-80, 10 | 0 | 0 | 2,927 | 1,405 | 194 | 17.9 | | | Near-efficient* |
| CTC 55-75, 5 | 0 | 0 | 3,388 | 1,523 | 204 | 18.9 | | | Near-efficient* |
| CTC 55-80, 5 | 0 | 0 | 3,759 | 1,598 | 208 | 19.8 | | | Near-efficient* |
| CTC 50-75, 5 | 0 | 0 | 4,171 | 1,743 | 226 | 19.9 | 450 | 42 | 11 |
| CTC 50-80, 5 | 0 | 0 | 4,539 | 1,817 | 230 | 20.7 | 74 | 4 | 16 |
| CTC 50-85, 5 | 0 | 0 | 4,792 | 1,864 | 231 | 21.1 | 47 | 1 | 37 |
| **CRC-SPIN** | | | | | | | | | |
| CTC 55-75, 10 | 0 | 0 | 2,296 | 1,265 | 209 | 19.8 | -- | -- | -- |
| CTC 50-75, 10 | 0 | 0 | 2,500 | 1,304 | 224 | 19.6 | 39 | 15 | 3 |
| CTC 50-80, 10 | 0 | 0 | 2,948 | 1,442 | 234 | 21.4 | | | Near-efficient* |
| CTC 50-75, 5 | 0 | 0 | 4,254 | 1,654 | 248 | 22.0 | 350 | 24 | 14 |
| CTC 50-80, 5 | 0 | 0 | 4,638 | 1,739 | 252 | 22.8 | 85 | 4 | 23 |
| CTC 50-85, 5 | 0 | 0 | 4,900 | 1,795 | 254 | 23.2 | 56 | 2 | 29 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; LYG – life-years gained compared with no screening; SIG – flexible sigmoidoscopy; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Strategy yields life-years gained within 98% of the efficient frontier.

**Table 10. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 75, and the set of recommended strategies assuming the colonoscopy strategy with a 10-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,187 | 260 | 22.8 | 220 | 27 | 8 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,007 | 275 | 24.4 | 820 | 15 | 55 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,959 | 285 | 25.5 | 1,554 | 8 | 188 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,887 | 0 | 0 | 971 | 212 | 18.2 | 164 | 34 | 5 |
| FIT 50-75, 2 | 9,326 | 0 | 0 | 1,215 | 234 | 20.2 | 160 | 14 | 12 |
| gFOBT 50-75, 3 | 6,456 | 0 | 0 | 1,286 | 212 | 18.4 | | | Dominated |
| FIT-DNA 50-75, 5 | 4,391 | 0 | 0 | 1,364 | 224 | 19.7 | | | Dominated |
| gFOBT 50-75, 2 | 8,388 | 0 | 0 | 1,597 | 235 | 20.5 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,990 | 0 | 0 | 1,701 | 250 | 21.8 | | | Dominated |
| FIT 50-75, 1* | 15,778 | 0 | 0 | 1,739 | 260 | 22.7 | 413 | 17 | 24* |
| gFOBT 50-75, 1 | 12,914 | 0 | 0 | 2,230 | 261 | 22.9 | | | Dominated |
| FIT-DNA 50-75, 1* | 11,041 | 0 | 0 | 2,601 | 271 | 23.9 | 664 | 4 | 155* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-75, 10 | 0 | 2,480 | 0 | 1,345 | 200 | 17.9 | 78 | 23 | 3 |
| SIG 50-75, 5 | 0 | 4,111 | 0 | 1,820 | 227 | 20.6 | 475 | 27 | 18 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-75, 10_2 | 7,942 | 2,196 | 0 | 1,917 | 262 | 22.9 | 192 | 31 | 6 |
| SIG+FIT 50-75, 5_3 | 5,367 | 3,700 | 0 | 2,127 | 263 | 23.3 | | | Dominated |
| SIG+gFOBT 50-75, 10_2 | 7,212 | 2,042 | 0 | 2,190 | 262 | 23.1 | | | Dominated |
| SIG+FIT 50-75, 5_2* | 7,296 | 3,559 | 0 | 2,224 | 267 | 23.7 | | | Dominated |
| SIG+FIT 50-75, 10_1* | 13,393 | 2,097 | 0 | 2,248 | 270 | 23.8 | 172 | 3 | 54* |
| SIG+gFOBT 50-75, 5_3 | 5,099 | 3,425 | 0 | 2,294 | 263 | 23.3 | | | Dominated |
| SIG+gFOBT 50-75, 5_2 | 6,689 | 3,211 | 0 | 2,431 | 267 | 23.7 | | | Dominated |
| SIG+gFOBT 50-75, 10_1 | 11,100 | 1,926 | 0 | 2,616 | 271 | 23.9 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-75, 10 | 0 | 0 | 2,458 | 1,460 | 239 | 21.1 | 64 | 25 | 3 |
| CTC 50-75, 5 | 0 | 0 | 4,069 | 1,927 | 265 | 23.7 | 467 | 26 | 18 |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,353 | 228 | 20.2 | 275 | 14 | 19 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,101 | 248 | 21.9 | 747 | 19 | 39 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,948 | 264 | 23.3 | 1,847 | 16 | 114 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,795 | 0 | 0 | 995 | 176 | 15.3 | 162 | 23 | 7 |
| FIT 50-75, 2* | 9,342 | 0 | 0 | 1,243 | 200 | 17.3 | 173 | 15 | 12* |
| gFOBT 50-75, 3 | 6,302 | 0 | 0 | 1,296 | 175 | 15.4 | | | Dominated |
| FIT-DNA 50-75, 5 | 4,380 | 0 | 0 | 1,402 | 193 | 17.1 | | | Dominated |
| gFOBT 50-75, 2 | 8,408 | 0 | 0 | 1,636 | 200 | 17.5 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,779 | 0 | 0 | 1,714 | 215 | 18.7 | | | Dominated |
| FIT 50-75, 1* | 15,843 | 0 | 0 | 1,757 | 231 | 20.0 | 383 | 18 | 21* |
| gFOBT 50-75, 1 | 12,927 | 0 | 0 | 2,287 | 232 | 20.3 | | | Dominated |
| FIT-DNA 50-75, 1* | 11,025 | 0 | 0 | 2,662 | 246 | 21.4 | 741 | 6 | 120* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-75, 10 | 0 | 2,356 | 0 | 1,881 | 201 | 18.2 | 144 | 16 | 9 |
| SIG 50-75, 5 | 0 | 3,807 | 0 | 2,287 | 221 | 20.0 | 406 | 20 | 20 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-75, 10_2 | 7,306 | 1,886 | 0 | 2,157 | 232 | 20.4 | 201 | 20 | 10 |
| SIG+gFOBT 50-75, 10_2 | 6,594 | 1,677 | 0 | 2,374 | 231 | 20.4 | | | Dominated |
| SIG+FIT 50-75, 5_3 | 4,737 | 3,380 | 0 | 2,451 | 239 | 21.2 | | | Dominated |
| SIG+FIT 50-75, 10_1 | 12,642 | 1,903 | 0 | 2,490 | 246 | 21.5 | 199 | 8 | 24 |
| SIG+FIT 50-75, 5_2 | 6,523 | 3,221 | 0 | 2,501 | 241 | 21.3 | | | Dominated |
| SIG+gFOBT 50-75, 5_3 | 4,462 | 3,146 | 0 | 2,587 | 238 | 21.2 | | | Dominated |
| SIG+gFOBT 50-75, 5_2 | 5,947 | 2,882 | 0 | 2,667 | 240 | 21.3 | | | Dominated |

**Table 10. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 75, and the set of recommended strategies assuming the colonoscopy strategy with a 10-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| SIG+gFOBT 50-75, 10_1 | 10,562 | 1,633 | 0 | 2,814 | 245 | 21.5 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-75, 10 | 0 | 0 | 2,485 | 1,293 | 184 | 16.1 | 73 | 12 | 6 |
| CTC 50-75, 5 | 0 | 0 | 4,171 | 1,743 | 226 | 19.9 | 450 | 42 | 11 |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,258 | 257 | 22.7 | 243 | 21 | 12 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,049 | 270 | 24.1 | 792 | 12 | 65 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,995 | 279 | 25.0 | 1,532 | 6 | 273 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,857 | 0 | 0 | 1,081 | 178 | 15.8 | 186 | 26 | 7 |
| gFOBT 50-75, 3 | 6,498 | 0 | 0 | 1,317 | 183 | 16.4 | | | Dominated |
| FIT 50-75, 2 | 9,241 | 0 | 0 | 1,346 | 207 | 18.3 | 265 | 29 | 9 |
| FIT-DNA 50-75, 5 | 4,370 | 0 | 0 | 1,473 | 195 | 17.8 | | | Dominated |
| gFOBT 50-75, 2 | 8,448 | 0 | 0 | 1,626 | 212 | 18.8 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,927 | 0 | 0 | 1,827 | 226 | 20.2 | | | Dominated |
| FIT 50-75, 1 | 15,444 | 0 | 0 | 1,899 | 244 | 21.6 | 445 | 26 | 17 |
| gFOBT 50-75, 1 | 13,026 | 0 | 0 | 2,253 | 247 | 21.9 | | | Dominated |
| FIT-DNA 50-75, 1* | 10,745 | 0 | 0 | 2,729 | 261 | 23.2 | 638 | 7 | 87* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-75, 10 | 0 | 2,515 | 0 | 1,161 | 165 | 14.7 | 68 | 12 | 6 |
| SIG 50-75, 5 | 0 | 4,298 | 0 | 1,493 | 181 | 16.5 | 220 | 10 | 22 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-75, 10_2 | 8.033 | 2,192 | 0 | 1,905 | 239 | 21.1 | 208 | 22 | 9 |
| SIG+FIT 50-75, 5_3 | 5,559 | 3,780 | 0 | 1,984 | 235 | 21.0 | | | Dominated |
| SIG+FIT 50-75, 5_2 | 7,506 | 3,611 | 0 | 2,125 | 244 | 21.8 | | | Dominated |
| SIG+gFOBT 50-75, 10_2 | 7,386 | 2,062 | 0 | 2,125 | 241 | 21.4 | | | Dominated |
| SIG+gFOBT 50-75, 5_3 | 5,314 | 3,531 | 0 | 2,132 | 237 | 21.2 | | | Dominated |
| SIG+FIT 50-75, 10_1* | 13,404 | 2,079 | 0 | 2,289 | 256 | 22.7 | 237 | 9 | 25 |
| SIG+gFOBT 50-75, 5_2 | 6,949 | 3,297 | 0 | 2,305 | 246 | 21.9 | | | Dominated |
| SIG+gFOBT 50-75, 10_1 | 11,376 | 1,940 | 0 | 2,581 | 258 | 22.9 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-75, 10 | 0 | 0 | 2,500 | 1,304 | 224 | 19.6 | 39 | 15 | 3 |
| CTC 50-75, 5 | 0 | 0 | 4,254 | 1,654 | 248 | 22.0 | 350 | 24 | 14 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; FIT – fecal immunochemical test; FIT-DNA – multi-target stool DNA test (fecal immunochemical test with a DNA stool test); gFOBT – sensitive guaiac-based fecal occult blood test; SIG – flexible sigmoidoscopy; LYG – life-years gained compared with no screening; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

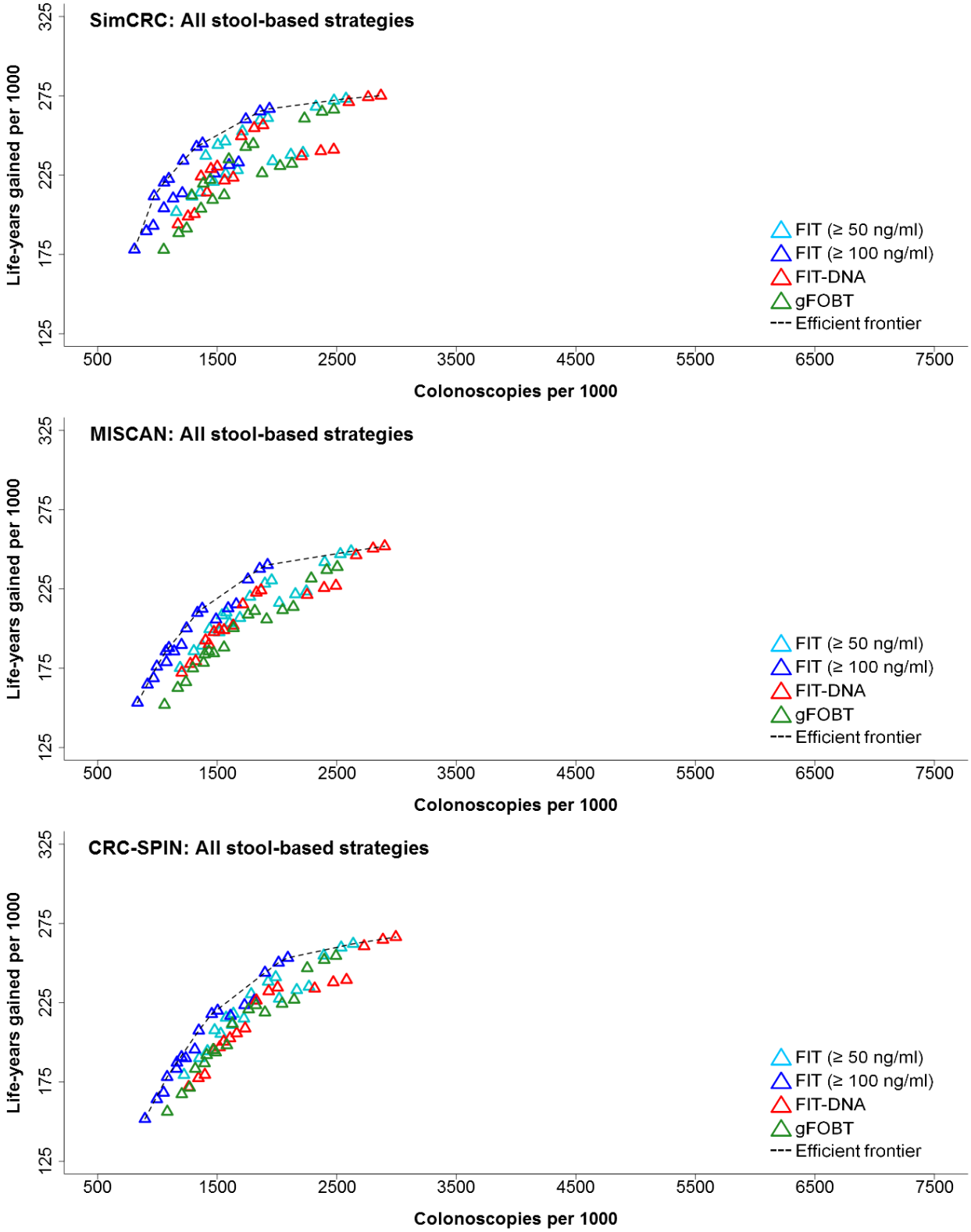
**Table 11. Outcomes for colonoscopy and CT colonography screening strategies with age to begin screening of 50 and age to end screening of 75, using the number of cathartic bowel preparations required as the proxy for the harms and burden of screening***

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | CTCs | COLs | cPREPs | LYG | CRC deaths averted | ΔcPREP | ΔLYG | Efficiency ratio (ΔcPREP / ΔLYG) |
| ***SimCRC*** | | | | | | | | |
| **Colonoscopy** | | | | | | | | |
| COL 50-75, 15 | 0 | 3,187 | 3,187 | 260 | 22.8 | 220 | 27 | 8 |
| COL 50-75, 10 | 0 | 4,007 | 4,007 | 275 | 24.4 | 820 | 15 | 55 |
| COL 50-75, 5 | 0 | 5,959 | 5,959 | 285 | 25.5 | 1,554 | 8 | 188 |
| **Computed tomographic colonography** | | | | | | | | |
| CTC 50-75, 10 | 2,458 | 1,460 | 3,918 | 239 | 21.1 | 272 | 25 | 11 |
| CTC 50-75, 5 | 4,069 | 1,927 | 5,996 | 265 | 23.7 | 2,077 | 26 | 81 |
| ***MISCAN*** | | | | | | | | |
| **Colonoscopy** | | | | | | | | |
| COL 50-75, 15 | 0 | 3,353 | 3,353 | 228 | 20.2 | 275 | 14 | 19 |
| COL 50-75, 10 | 0 | 4,101 | 4,101 | 248 | 21.9 | 747 | 19 | 39 |
| COL 50-75, 5 | 0 | 5,948 | 5,948 | 264 | 23.3 | 1,847 | 16 | 114 |
| **Computed tomographic colonography** | | | | | | | | |
| CTC 50-75, 10 | 2,485 | 1,293 | 3,778 | 184 | 16.1 | 274 | 12 | 24 |
| CTC 50-75, 5 | 4,171 | 1,743 | 5,914 | 226 | 19.9 | 2,135 | 42 | 51 |
| ***CRC-SPIN*** | | | | | | | | |
| **Colonoscopy** | | | | | | | | |
| COL 50-75, 15 | 0 | 3,258 | 3,258 | 257 | 22.7 | 243 | 21 | 12 |
| COL 50-75, 10 | 0 | 4,049 | 4,049 | 270 | 24.1 | 792 | 12 | 65 |
| COL 50-75, 5 | 0 | 5,995 | 5,995 | 279 | 25.0 | 1,532 | 6 | 273 |
| **Computed tomographic colonography** | | | | | | | | |
| CTC 50-75, 10 | 2,500 | 1,304 | 3,804 | 224 | 19.6 | 244 | 15 | 16 |
| CTC 50-75, 5 | 4,254 | 1,654 | 5,908 | 248 | 22.0 | 1,518 | 15 | 103 |

cPREPs – procedures with cathartic bowel preparation (i.e., CT colonographies and colonoscopies); COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; LYG – life-years gained compared with no screening; ΔcPREP – incremental number of procedures requiring cathartic bowel preparation compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* With this measure of harms and burden, the efficiency ratio for CT colonoscopy every 5 years exceeds that of the selected colonoscopy strategy (i.e., colonoscopy every 10 years). CT colonography every 10 years is not recommended because the life-years gained are less than 90% of the colonoscopy strategy.

**Appendix Figure 1. Sensitivity analysis: Colonoscopies and life-years gained (compared with no screening) for a cohort of 40-year-olds for stool-based screening strategies that vary by age to begin (50, 55), age to end (75, 80, 85), and screening interval (every 1, 2, or 3 years for FIT, FIT50, and gFOBT; every 1, 3, or 5 years for FIT-DNA), by model**



**Appendix Table 1. Calibrated per lesion test sensitivity for stool-based tests used in the SimCRC and MISCAN models**

| Model/stool test | Per-lesion sensitivity* | | | |
|---|---|---|---|---|
| | Adenoma 1-5 mm† | Adenoma 6-9 mm | Adenoma ≥10 mm | Preclinical colorectal cancer |
| *SimCRC* | | | | |
| gFOBT | 0 | 0.042 | 0.148 | 0.658 |
| FIT | 0 | 0.060 | 0.173 | 0.710 |
| FIT-DNA | 0 | 0.115 | 0.302 | 0.907 |
| *MISCAN* | | | | |
| gFOBT | 0 | 0.043 | 0.147 | 0.568‡ / 0.859‖ |
| FIT | 0 | 0.114 | 0.159 | 0.626‡ / 0.886‖ |
| FIT-DNA | 0 | 0.220 | 0.284 | 0.864‡ / 0.967‖ |

FIT – Fecal immunochemical test; gFOBT – sensitive guaiac-based fecal occult blood test; FIT-DNA – multi-target stool DNA test

* Estimates were derived by calibrating model outcomes to the per-person sensitivities given in **Table 4**.

† We assume 1-5mm adenomas do not bleed and therefore cannot cause a positive stool test.

‡ Sensitivity for a preclinical cancer while at an earlier stage than it would have been diagnosed in the absence of screening.

‖ Sensitivity for a preclinical cancer at the stage it would have been diagnosed in the absence of screening.

**Appendix Table 2. Fecal immunochemical test characteristics (per person) by cutoff for positivity**

| FIT cutoff for positivity | Value | Source |
|---|---|---|
| **≥100 ng of hemoglobin per ml of buffer (base-case analysis)** | | Imperiale, 2014[16] |
| Specificity | 0.964 | |
| Sensitivity for adenomas ≤5 mm | 0.076* | |
| Sensitivity for adenomas 6-9 mm | | |
| Sensitivity for adenomas ≥10 mm | 0.238† | |
| Sensitivity for colorectal cancer | 0.738 | |
| **≥50 ng of hemoglobin per ml of buffer (sensitivity analysis)** | | Imperiale, 2014[16] |
| Specificity | 0.92 | de Wijkerslooth, 2012[26] and by assumption |
| Sensitivity for adenomas ≤5 mm | 0.11* | de Wijkerslooth, 2012[26] and by assumption |
| Sensitivity for adenomas 6-9 mm | | |
| Sensitivity for adenomas ≥10 mm | 0.35† | de Wijkerslooth, 2012[26] |
| Sensitivity for colorectal cancer | 0.88 | de Wijkerslooth, 2012[26] |

FIT – fecal immunochemical test;

* Sensitivity for persons with non-advanced adenomas. For persons with 1-5 mm adenomas, we assume that the sensitivity of the test is equal to the positivity rate in persons without adenomas (i.e., 1 – specificity). The sensitivity for persons with 6-9 mm adenomas is chosen such that the weighted average sensitivity for persons with 1-5 mm and with 6-9 mm adenoma(s) is equal to that of non-advanced adenomas.

† Sensitivity for persons with advanced adenomas (i.e., adenomas ≥ 10 mm and/or adenomas with advanced histology). Sensitivity was not reported for the subset of ≥ 10mm adenomas.

**Appendix Table 3a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with colonoscopy screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| COL 45-75, 5 (7) | 0 | 0 | 0 | 4,995 | 0 | 2,012 | 2 | 7,009 | 19 | 6.6 | 1.5 | 124.0 | 312.5 | 90.5 | 94.7 |
| COL 45-75, 10 (4) | 0 | 0 | 0 | 3,053 | 0 | 1,797 | 3 | 4,853 | 16 | 9.3 | 2.2 | 160.0 | 302.7 | 86.7 | 92.2 |
| COL 45-75, 15 (3) | 0 | 0 | 0 | 2,383 | 0 | 1,621 | 5 | 4,009 | 15 | 12.7 | 3.2 | 196.6 | 288.2 | 81.8 | 88.4 |
| COL 45-80, 5 (8) | 0 | 0 | 0 | 5,302 | 0 | 2,035 | 2 | 7,339 | 21 | 6.2 | 1.3 | 122.9 | 313.1 | 91.2 | 95.3 |
| COL 45-80, 10 (4) | 0 | 0 | 0 | 3,053 | 0 | 1,797 | 3 | 4,853 | 16 | 9.3 | 2.2 | 160.0 | 302.7 | 86.7 | 92.2 |
| COL 45-80, 15 (3) | 0 | 0 | 0 | 2,383 | 0 | 1,621 | 5 | 4,009 | 15 | 12.7 | 3.2 | 196.6 | 288.2 | 81.8 | 88.4 |
| COL 45-85, 5 (9) | 0 | 0 | 0 | 5,505 | 0 | 2,045 | 1 | 7,552 | 22 | 6.0 | 1.3 | 122.8 | 313.3 | 91.4 | 95.4 |
| COL 45-85, 10 (5) | 0 | 0 | 0 | 3,281 | 0 | 1,821 | 3 | 5,104 | 19 | 9.0 | 2.0 | 160.3 | 303.2 | 87.1 | 92.8 |
| COL 45-85, 15 (3) | 0 | 0 | 0 | 2,383 | 0 | 1,621 | 5 | 4,009 | 15 | 12.7 | 3.2 | 196.6 | 288.2 | 81.8 | 88.4 |
| COL 50-75, 5 (6) | 0 | 0 | 0 | 4,116 | 0 | 1,838 | 4 | 5,959 | 18 | 9.6 | 2.5 | 184.6 | 285.5 | 86.2 | 91.0 |
| COL 50-75, 10 (3) | 0 | 0 | 0 | 2,388 | 0 | 1,612 | 6 | 4,007 | 14 | 13.1 | 3.6 | 215.7 | 274.8 | 81.3 | 87.2 |
| COL 50-75, 15 (2) | 0 | 0 | 0 | 1,761 | 0 | 1,416 | 11 | 3,187 | 12 | 17.4 | 5.2 | 246.1 | 260.0 | 75.1 | 81.5 |
| COL 50-80, 5 (7) | 0 | 0 | 0 | 4,424 | 0 | 1,861 | 3 | 6,289 | 20 | 9.2 | 2.3 | 183.5 | 286.1 | 86.9 | 91.6 |
| COL 50-80, 10 (4) | 0 | 0 | 0 | 2,738 | 0 | 1,663 | 4 | 4,405 | 17 | 11.8 | 3.0 | 214.1 | 277.2 | 83.1 | 89.1 |
| COL 50-80, 15 (3) | 0 | 0 | 0 | 2,152 | 0 | 1,498 | 6 | 3,656 | 16 | 15.2 | 4.1 | 245.0 | 265.1 | 78.3 | 85.5 |
| COL 50-85, 5 (8) | 0 | 0 | 0 | 4,627 | 0 | 1,872 | 3 | 6,502 | 22 | 9.1 | 2.3 | 183.4 | 286.3 | 87.0 | 91.8 |
| COL 50-85, 10 (4) | 0 | 0 | 0 | 2,738 | 0 | 1,663 | 4 | 4,405 | 17 | 11.8 | 3.0 | 214.1 | 277.2 | 83.1 | 89.1 |
| COL 50-85, 15 (3) | 0 | 0 | 0 | 2,152 | 0 | 1,498 | 6 | 3,656 | 16 | 15.2 | 4.1 | 245.0 | 265.1 | 78.3 | 85.5 |
| COL 55-75, 5 (5) | 0 | 0 | 0 | 3,297 | 0 | 1,622 | 7 | 4,926 | 18 | 14.2 | 4.1 | 261.0 | 250.0 | 79.7 | 85.5 |
| COL 55-75, 10 (3) | 0 | 0 | 0 | 2,161 | 0 | 1,466 | 8 | 3,635 | 16 | 16.4 | 4.7 | 284.7 | 242.8 | 76.5 | 83.3 |
| COL 55-75, 15 (2) | 0 | 0 | 0 | 1,632 | 0 | 1,325 | 11 | 2,968 | 13 | 19.6 | 5.8 | 306.6 | 232.6 | 72.0 | 79.3 |
| COL 55-80, 5 (6) | 0 | 0 | 0 | 3,605 | 0 | 1,644 | 6 | 5,256 | 20 | 13.8 | 3.9 | 259.9 | 250.6 | 80.3 | 86.0 |
| COL 55-80, 10 (3) | 0 | 0 | 0 | 2,161 | 0 | 1,466 | 8 | 3,635 | 16 | 16.4 | 4.7 | 284.7 | 242.8 | 76.5 | 83.3 |
| COL 55-80, 15 (2) | 0 | 0 | 0 | 1,632 | 0 | 1,325 | 11 | 2,968 | 13 | 19.6 | 5.8 | 306.6 | 232.6 | 72.0 | 79.3 |
| COL 55-85, 5 (7) | 0 | 0 | 0 | 3,807 | 0 | 1,655 | 6 | 5,468 | 21 | 13.6 | 3.9 | 259.8 | 250.8 | 80.5 | 86.2 |
| COL 55-85, 10 (4) | 0 | 0 | 0 | 2,389 | 0 | 1,491 | 7 | 3,887 | 18 | 16.1 | 4.5 | 285.0 | 243.3 | 76.9 | 83.9 |
| COL 55-85, 15 (3) | 0 | 0 | 0 | 1,888 | 0 | 1,365 | 9 | 3,262 | 17 | 19.1 | 5.4 | 308.3 | 233.9 | 72.7 | 80.6 |

COL = colonoscopy; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 3b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with colonoscopy screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| COL 45-75, 5 (7) | 0 | 0 | 0 | 4,826 | 0 | 2,156 | 7 | 6,989 | 18 | 19.9 | 3.9 | 297.7 | 280.7 | 70.2 | 85.9 |
| COL 45-75, 10 (4) | 0 | 0 | 0 | 2,967 | 0 | 1,953 | 9 | 4,928 | 16 | 23.2 | 5.1 | 336.8 | 262.4 | 65.2 | 81.8 |
| COL 45-75, 15 (3) | 0 | 0 | 0 | 2,328 | 0 | 1,780 | 12 | 4,119 | 15 | 26.3 | 6.3 | 367.5 | 244.1 | 60.4 | 77.4 |
| COL 45-80, 5 (8) | 0 | 0 | 0 | 5,158 | 0 | 2,172 | 6 | 7,337 | 20 | 19.3 | 3.6 | 297.1 | 282.2 | 71.0 | 87.0 |
| COL 45-80, 10 (4) | 0 | 0 | 0 | 2,967 | 0 | 1,953 | 9 | 4,928 | 16 | 23.2 | 5.1 | 336.8 | 262.4 | 65.2 | 81.8 |
| COL 45-80, 15 (3) | 0 | 0 | 0 | 2,328 | 0 | 1,780 | 12 | 4,119 | 15 | 26.3 | 6.3 | 367.5 | 244.1 | 60.4 | 77.4 |
| COL 45-85, 5 (9) | 0 | 0 | 0 | 5,384 | 0 | 2,176 | 6 | 7,566 | 21 | 19.2 | 3.6 | 297.2 | 282.4 | 71.1 | 87.2 |
| COL 45-85, 10 (5) | 0 | 0 | 0 | 3,211 | 0 | 1,965 | 8 | 5,185 | 18 | 23.0 | 4.8 | 338.3 | 263.2 | 65.4 | 82.6 |
| COL 45-85, 15 (3) | 0 | 0 | 0 | 2,328 | 0 | 1,780 | 12 | 4,119 | 15 | 26.3 | 6.3 | 367.5 | 244.1 | 60.4 | 77.4 |
| COL 50-75, 5 (6) | 0 | 0 | 0 | 3,982 | 0 | 1,958 | 8 | 5,948 | 18 | 21.4 | 4.5 | 326.5 | 263.8 | 67.8 | 83.7 |
| COL 50-75, 10 (3) | 0 | 0 | 0 | 2,316 | 0 | 1,774 | 11 | 4,101 | 15 | 25.1 | 5.9 | 359.6 | 247.6 | 62.4 | 78.8 |
| COL 50-75, 15 (2) | 0 | 0 | 0 | 1,723 | 0 | 1,615 | 16 | 3,353 | 13 | 28.6 | 7.6 | 381.2 | 228.4 | 57.0 | 72.7 |
| COL 50-80, 5 (7) | 0 | 0 | 0 | 4,315 | 0 | 1,974 | 7 | 6,296 | 20 | 20.9 | 4.2 | 325.8 | 265.3 | 68.7 | 84.7 |
| COL 50-80, 10 (4) | 0 | 0 | 0 | 2,671 | 0 | 1,805 | 9 | 4,485 | 17 | 24.0 | 5.2 | 360.2 | 250.9 | 63.9 | 81.2 |
| COL 50-80, 15 (3) | 0 | 0 | 0 | 2,104 | 0 | 1,663 | 12 | 3,779 | 16 | 27.1 | 6.5 | 384.2 | 234.0 | 59.3 | 76.7 |
| COL 50-85, 5 (8) | 0 | 0 | 0 | 4,541 | 0 | 1,978 | 7 | 6,525 | 21 | 20.8 | 4.2 | 326.0 | 265.5 | 68.8 | 84.9 |
| COL 50-85, 10 (4) | 0 | 0 | 0 | 2,671 | 0 | 1,805 | 9 | 4,485 | 17 | 24.0 | 5.2 | 360.2 | 250.9 | 63.9 | 81.2 |
| COL 50-85, 15 (3) | 0 | 0 | 0 | 2,104 | 0 | 1,663 | 12 | 3,779 | 16 | 27.1 | 6.5 | 384.2 | 234.0 | 59.3 | 76.7 |
| COL 55-75, 5 (5) | 0 | 0 | 0 | 3,211 | 0 | 1,702 | 10 | 4,923 | 17 | 24.1 | 5.6 | 365.7 | 237.5 | 63.8 | 79.7 |
| COL 55-75, 10 (3) | 0 | 0 | 0 | 2,108 | 0 | 1,577 | 12 | 3,697 | 15 | 26.6 | 6.5 | 390.2 | 225.7 | 60.0 | 76.5 |
| COL 55-75, 15 (2) | 0 | 0 | 0 | 1,596 | 0 | 1,467 | 15 | 3,079 | 14 | 29.3 | 7.6 | 406.9 | 214.1 | 56.0 | 72.5 |
| COL 55-80, 5 (6) | 0 | 0 | 0 | 3,544 | 0 | 1,718 | 9 | 5,271 | 19 | 23.5 | 5.3 | 365.1 | 239.0 | 64.7 | 80.8 |
| COL 55-80, 10 (3) | 0 | 0 | 0 | 2,108 | 0 | 1,577 | 12 | 3,697 | 15 | 26.6 | 6.5 | 390.2 | 225.7 | 60.0 | 76.5 |
| COL 55-80, 15 (2) | 0 | 0 | 0 | 1,596 | 0 | 1,467 | 15 | 3,079 | 14 | 29.3 | 7.6 | 406.9 | 214.1 | 56.0 | 72.5 |
| COL 55-85, 5 (7) | 0 | 0 | 0 | 3,770 | 0 | 1,722 | 9 | 5,500 | 20 | 23.4 | 5.3 | 365.2 | 239.2 | 64.8 | 80.9 |
| COL 55-85, 10 (4) | 0 | 0 | 0 | 2,353 | 0 | 1,590 | 11 | 3,954 | 17 | 26.5 | 6.3 | 391.8 | 226.5 | 60.2 | 77.3 |
| COL 55-85, 15 (3) | 0 | 0 | 0 | 1,858 | 0 | 1,488 | 13 | 3,359 | 16 | 29.1 | 7.3 | 410.2 | 215.6 | 56.2 | 73.9 |

COL = colonoscopy; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 3c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with colonoscopy screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| COL 45-75, 5 (7) | 0 | 0 | 0 | 4,974 | 0 | 2,062 | 3 | 7,039 | 19 | 3.9 | 1.1 | 52.8 | 296.7 | 94.6 | 95.9 |
| COL 45-75, 10 (4) | 0 | 0 | 0 | 3,038 | 0 | 1,863 | 4 | 4,906 | 17 | 5.6 | 1.6 | 72.4 | 289.1 | 92.3 | 94.1 |
| COL 45-75, 15 (3) | 0 | 0 | 0 | 2,372 | 0 | 1,704 | 6 | 4,081 | 16 | 7.7 | 2.3 | 96.2 | 279.4 | 89.3 | 91.5 |
| COL 45-80, 5 (8) | 0 | 0 | 0 | 5,308 | 0 | 2,085 | 2 | 7,395 | 21 | 3.2 | 0.9 | 51.0 | 297.4 | 95.5 | 96.8 |
| COL 45-80, 10 (4) | 0 | 0 | 0 | 3,038 | 0 | 1,863 | 4 | 4,906 | 17 | 5.6 | 1.6 | 72.4 | 289.1 | 92.3 | 94.1 |
| COL 45-80, 15 (3) | 0 | 0 | 0 | 2,372 | 0 | 1,704 | 6 | 4,081 | 16 | 7.7 | 2.3 | 96.2 | 279.4 | 89.3 | 91.5 |
| COL 45-85, 5 (9) | 0 | 0 | 0 | 5,532 | 0 | 2,096 | 2 | 7,630 | 23 | 3.0 | 0.8 | 50.4 | 297.6 | 95.9 | 97.1 |
| COL 45-85, 10 (5) | 0 | 0 | 0 | 3,286 | 0 | 1,889 | 3 | 5,178 | 19 | 4.7 | 1.3 | 70.5 | 290.4 | 93.4 | 95.2 |
| COL 45-85, 15 (3) | 0 | 0 | 0 | 2,372 | 0 | 1,704 | 6 | 4,081 | 16 | 7.7 | 2.3 | 96.2 | 279.4 | 89.3 | 91.5 |
| COL 50-75, 5 (6) | 0 | 0 | 0 | 4,120 | 0 | 1,870 | 4 | 5,995 | 19 | 5.9 | 1.7 | 94.8 | 278.6 | 91.8 | 93.6 |
| COL 50-75, 10 (3) | 0 | 0 | 0 | 2,376 | 0 | 1,666 | 7 | 4,049 | 15 | 8.8 | 2.7 | 116.8 | 269.7 | 87.8 | 89.9 |
| COL 50-75, 15 (2) | 0 | 0 | 0 | 1,751 | 0 | 1,496 | 11 | 3,258 | 13 | 12.7 | 4.1 | 143.1 | 257.5 | 82.3 | 84.8 |
| COL 50-80, 5 (7) | 0 | 0 | 0 | 4,455 | 0 | 1,892 | 4 | 6,351 | 21 | 5.2 | 1.5 | 93.2 | 279.6 | 92.8 | 94.4 |
| COL 50-80, 10 (4) | 0 | 0 | 0 | 2,746 | 0 | 1,713 | 5 | 4,464 | 18 | 6.8 | 2.0 | 110.8 | 273.0 | 90.5 | 92.6 |
| COL 50-80, 15 (3) | 0 | 0 | 0 | 2,154 | 0 | 1,568 | 7 | 3,728 | 17 | 9.1 | 2.7 | 132.4 | 264.0 | 87.4 | 89.9 |
| COL 50-85, 5 (8) | 0 | 0 | 0 | 4,678 | 0 | 1,905 | 3 | 6,586 | 22 | 4.9 | 1.4 | 92.5 | 279.8 | 93.1 | 94.7 |
| COL 50-85, 10 (4) | 0 | 0 | 0 | 2,746 | 0 | 1,713 | 5 | 4,464 | 18 | 6.8 | 2.0 | 110.8 | 273.0 | 90.5 | 92.6 |
| COL 50-85, 15 (3) | 0 | 0 | 0 | 2,154 | 0 | 1,568 | 7 | 3,728 | 17 | 9.1 | 2.7 | 132.4 | 264.0 | 87.4 | 89.9 |
| COL 55-75, 5 (5) | 0 | 0 | 0 | 3,322 | 0 | 1,637 | 7 | 4,966 | 18 | 9.2 | 2.8 | 155.4 | 251.3 | 87.2 | 89.4 |
| COL 55-75, 10 (3) | 0 | 0 | 0 | 2,168 | 0 | 1,501 | 8 | 3,677 | 16 | 10.7 | 3.3 | 169.8 | 245.3 | 85.1 | 87.6 |
| COL 55-75, 15 (2) | 0 | 0 | 0 | 1,630 | 0 | 1,374 | 11 | 3,015 | 14 | 13.6 | 4.4 | 188.3 | 236.4 | 81.1 | 83.7 |
| COL 55-80, 5 (6) | 0 | 0 | 0 | 3,656 | 0 | 1,660 | 6 | 5,322 | 20 | 8.5 | 2.6 | 153.2 | 252.2 | 88.2 | 90.2 |
| COL 55-80, 10 (3) | 0 | 0 | 0 | 2,168 | 0 | 1,501 | 8 | 3,677 | 16 | 10.7 | 3.3 | 169.8 | 245.3 | 85.1 | 87.6 |
| COL 55-80, 15 (2) | 0 | 0 | 0 | 1,630 | 0 | 1,374 | 11 | 3,015 | 14 | 13.6 | 4.4 | 188.3 | 236.4 | 81.1 | 83.7 |
| COL 55-85, 5 (7) | 0 | 0 | 0 | 3,879 | 0 | 1,672 | 6 | 5,557 | 22 | 8.2 | 2.5 | 152.5 | 252.6 | 88.6 | 90.6 |
| COL 55-85, 10 (4) | 0 | 0 | 0 | 2,416 | 0 | 1,525 | 7 | 3,949 | 19 | 9.9 | 3.0 | 168.3 | 246.4 | 86.3 | 88.8 |
| COL 55-85, 15 (3) | 0 | 0 | 0 | 1,902 | 0 | 1,413 | 9 | 3,324 | 17 | 11.9 | 3.7 | 184.6 | 238.9 | 83.4 | 86.1 |

COL = colonoscopy; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 4a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with gFOBT screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| gFOBT 45-75, 1 (31) | 15,590 | 0 | 0 | 0 | 1,337 | 1,220 | 7 | 2,564 | 11 | 18.3 | 3.9 | 292.1 | 287.7 | 73.8 | 86.0 |
| gFOBT 45-75, 2 (16) | 10,349 | 0 | 0 | 0 | 920 | 936 | 11 | 1,867 | 9 | 27.0 | 6.1 | 400.5 | 262.9 | 61.4 | 78.3 |
| gFOBT 45-75, 3 (11) | 7,749 | 0 | 0 | 0 | 706 | 757 | 16 | 1,479 | 8 | 33.7 | 8.3 | 464.2 | 236.8 | 51.8 | 70.2 |
| gFOBT 45-80, 1 (36) | 16,862 | 0 | 0 | 0 | 1,450 | 1,256 | 5 | 2,711 | 12 | 17.0 | 3.1 | 292.8 | 291.9 | 75.7 | 88.8 |
| gFOBT 45-80, 2 (18) | 11,061 | 0 | 0 | 0 | 989 | 963 | 8 | 1,960 | 10 | 25.9 | 5.2 | 404.7 | 268.0 | 62.9 | 81.6 |
| gFOBT 45-80, 3 (12) | 8,360 | 0 | 0 | 0 | 767 | 782 | 12 | 1,561 | 9 | 32.7 | 7.3 | 470.8 | 242.9 | 53.2 | 74.0 |
| gFOBT 45-85, 1 (41) | 17,756 | 0 | 0 | 0 | 1,530 | 1,275 | 4 | 2,808 | 14 | 16.7 | 2.8 | 294.6 | 293.2 | 76.2 | 90.0 |
| gFOBT 45-85, 2 (21) | 11,820 | 0 | 0 | 0 | 1,062 | 986 | 6 | 2,054 | 11 | 25.6 | 4.5 | 410.4 | 270.7 | 63.4 | 83.8 |
| gFOBT 45-85, 3 (14) | 8,932 | 0 | 0 | 0 | 826 | 803 | 9 | 1,639 | 10 | 32.5 | 6.5 | 479.1 | 246.4 | 53.5 | 76.7 |
| gFOBT 50-75, 1 (26) | 12,914 | 0 | 0 | 0 | 1,130 | 1,090 | 9 | 2,230 | 11 | 21.7 | 5.0 | 349.9 | 260.7 | 69.0 | 82.0 |
| gFOBT 50-75, 2 (13) | 8,388 | 0 | 0 | 0 | 764 | 819 | 14 | 1,597 | 9 | 30.7 | 7.5 | 447.5 | 235.0 | 56.1 | 73.2 |
| gFOBT 50-75, 3 (9) | 6,456 | 0 | 0 | 0 | 604 | 664 | 18 | 1,286 | 7 | 36.9 | 9.5 | 504.6 | 212.3 | 47.2 | 66.0 |
| gFOBT 50-80, 1 (31) | 14,193 | 0 | 0 | 0 | 1,244 | 1,127 | 7 | 2,377 | 12 | 20.4 | 4.2 | 350.7 | 265.0 | 70.9 | 84.9 |
| gFOBT 50-80, 2 (16) | 9,462 | 0 | 0 | 0 | 867 | 861 | 10 | 1,738 | 10 | 29.1 | 6.1 | 453.6 | 242.8 | 58.4 | 78.1 |
| gFOBT 50-80, 3 (11) | 7,125 | 0 | 0 | 0 | 673 | 697 | 14 | 1,383 | 9 | 35.7 | 8.2 | 513.5 | 219.7 | 48.9 | 70.6 |
| gFOBT 50-85, 1 (36) | 15,090 | 0 | 0 | 0 | 1,324 | 1,146 | 5 | 2,476 | 13 | 20.0 | 3.9 | 352.6 | 266.4 | 71.3 | 86.1 |
| gFOBT 50-85, 2 (18) | 9,970 | 0 | 0 | 0 | 917 | 877 | 8 | 1,801 | 11 | 28.9 | 5.7 | 457.7 | 244.6 | 58.7 | 79.6 |
| gFOBT 50-85, 3 (12) | 7,565 | 0 | 0 | 0 | 717 | 712 | 12 | 1,441 | 9 | 35.6 | 7.7 | 519.3 | 222.0 | 49.1 | 72.5 |
| gFOBT 55-75, 1 (21) | 10,357 | 0 | 0 | 0 | 932 | 931 | 13 | 1,876 | 10 | 26.7 | 6.6 | 419.6 | 226.2 | 61.8 | 76.3 |
| gFOBT 55-75, 2 (11) | 6,897 | 0 | 0 | 0 | 649 | 698 | 17 | 1,364 | 8 | 35.1 | 8.9 | 506.3 | 203.9 | 49.7 | 68.2 |
| gFOBT 55-75, 3 (7) | 5,014 | 0 | 0 | 0 | 484 | 545 | 23 | 1,052 | 7 | 41.8 | 11.6 | 547.6 | 178.0 | 40.2 | 58.5 |
| gFOBT 55-80, 1 (26) | 11,637 | 0 | 0 | 0 | 1,047 | 969 | 10 | 2,025 | 12 | 25.3 | 5.8 | 420.3 | 230.8 | 63.8 | 79.3 |
| gFOBT 55-80, 2 (13) | 7,622 | 0 | 0 | 0 | 720 | 728 | 13 | 1,461 | 9 | 34.0 | 7.9 | 510.8 | 209.4 | 51.4 | 71.8 |
| gFOBT 55-80, 3 (9) | 5,872 | 0 | 0 | 0 | 572 | 588 | 17 | 1,177 | 8 | 40.1 | 9.8 | 558.6 | 188.5 | 42.7 | 64.8 |
| gFOBT 55-85, 1 (31) | 12,539 | 0 | 0 | 0 | 1,127 | 989 | 8 | 2,125 | 13 | 24.9 | 5.5 | 422.3 | 232.2 | 64.3 | 80.5 |
| gFOBT 55-85, 2 (16) | 8,390 | 0 | 0 | 0 | 795 | 752 | 11 | 1,558 | 11 | 33.7 | 7.2 | 517.0 | 212.3 | 51.9 | 74.2 |
| gFOBT 55-85, 3 (11) | 6,352 | 0 | 0 | 0 | 623 | 607 | 14 | 1,244 | 9 | 40.0 | 9.2 | 566.1 | 191.4 | 42.8 | 67.2 |

gFOBT = highly-sensitive guaiac-based fecal occult blood test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 4b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with gFOBT screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| gFOBT 45-75, 1 (31) | 15,562 | 0 | 0 | 0 | 1,303 | 1,314 | 13 | 2,630 | 11 | 32.1 | 6.9 | 464.1 | 247.0 | 51.7 | 75.2 |
| gFOBT 45-75, 2 (16) | 10,351 | 0 | 0 | 0 | 897 | 995 | 18 | 1,909 | 9 | 39.9 | 9.3 | 547.9 | 217.1 | 40.1 | 66.6 |
| gFOBT 45-75, 3 (11) | 7,719 | 0 | 0 | 0 | 685 | 799 | 23 | 1,508 | 8 | 45.2 | 11.4 | 587.5 | 190.2 | 32.1 | 58.8 |
| gFOBT 45-80, 1 (36) | 16,849 | 0 | 0 | 0 | 1,410 | 1,337 | 10 | 2,757 | 12 | 31.2 | 6.0 | 468.1 | 252.2 | 53.1 | 78.4 |
| gFOBT 45-80, 2 (18) | 11,071 | 0 | 0 | 0 | 960 | 1,015 | 15 | 1,990 | 10 | 39.3 | 8.4 | 555.2 | 222.6 | 41.0 | 69.9 |
| gFOBT 45-80, 3 (12) | 8,129 | 0 | 0 | 0 | 724 | 813 | 21 | 1,557 | 9 | 44.8 | 10.7 | 595.3 | 194.7 | 32.6 | 61.5 |
| gFOBT 45-85, 1 (41) | 17,782 | 0 | 0 | 0 | 1,487 | 1,349 | 9 | 2,845 | 13 | 31.0 | 5.6 | 471.4 | 254.1 | 53.4 | 79.9 |
| gFOBT 45-85, 2 (21) | 11,855 | 0 | 0 | 0 | 1,029 | 1,030 | 13 | 2,072 | 11 | 39.3 | 7.7 | 563.5 | 225.9 | 41.0 | 72.4 |
| gFOBT 45-85, 3 (14) | 8,750 | 0 | 0 | 0 | 782 | 829 | 17 | 1,628 | 9 | 45.0 | 9.8 | 606.9 | 199.0 | 32.4 | 64.6 |
| gFOBT 50-75, 1 (26) | 12,927 | 0 | 0 | 0 | 1,103 | 1,169 | 14 | 2,287 | 11 | 33.8 | 7.5 | 487.5 | 231.6 | 49.2 | 72.9 |
| gFOBT 50-75, 2 (13) | 8,408 | 0 | 0 | 0 | 745 | 870 | 21 | 1,636 | 9 | 41.8 | 10.2 | 563.9 | 200.3 | 37.2 | 63.1 |
| gFOBT 50-75, 3 (9) | 6,302 | 0 | 0 | 0 | 574 | 697 | 25 | 1,296 | 8 | 46.9 | 12.4 | 597.7 | 174.9 | 29.6 | 55.4 |
| gFOBT 50-80, 1 (31) | 14,223 | 0 | 0 | 0 | 1,211 | 1,194 | 12 | 2,416 | 12 | 32.9 | 6.6 | 491.6 | 236.9 | 50.7 | 76.2 |
| gFOBT 50-80, 2 (16) | 9,497 | 0 | 0 | 0 | 842 | 901 | 16 | 1,759 | 10 | 40.8 | 8.8 | 575.2 | 208.9 | 38.6 | 68.2 |
| gFOBT 50-80, 3 (11) | 7,106 | 0 | 0 | 0 | 649 | 726 | 21 | 1,395 | 9 | 46.3 | 10.9 | 613.2 | 183.8 | 30.5 | 60.7 |
| gFOBT 50-85, 1 (36) | 15,161 | 0 | 0 | 0 | 1,289 | 1,206 | 10 | 2,505 | 13 | 32.6 | 6.2 | 494.9 | 238.9 | 51.0 | 77.7 |
| gFOBT 50-85, 2 (18) | 10,024 | 0 | 0 | 0 | 888 | 912 | 14 | 1,814 | 11 | 40.8 | 8.4 | 580.9 | 211.1 | 38.6 | 70.0 |
| gFOBT 50-85, 3 (12) | 7,408 | 0 | 0 | 0 | 677 | 733 | 19 | 1,430 | 9 | 46.4 | 10.5 | 619.0 | 185.7 | 30.3 | 62.2 |
| gFOBT 55-75, 1 (21) | 10,427 | 0 | 0 | 0 | 913 | 984 | 17 | 1,913 | 11 | 36.7 | 8.7 | 519.5 | 205.8 | 44.8 | 68.6 |
| gFOBT 55-75, 2 (11) | 6,940 | 0 | 0 | 0 | 634 | 729 | 22 | 1,386 | 9 | 44.3 | 11.1 | 588.2 | 178.4 | 33.5 | 59.9 |
| gFOBT 55-75, 3 (7) | 4,912 | 0 | 0 | 0 | 462 | 568 | 29 | 1,059 | 7 | 49.5 | 13.8 | 611.5 | 151.9 | 25.6 | 50.3 |
| gFOBT 55-80, 1 (26) | 11,733 | 0 | 0 | 0 | 1,022 | 1,011 | 14 | 2,047 | 12 | 35.7 | 7.7 | 523.7 | 211.7 | 46.4 | 72.2 |
| gFOBT 55-80, 2 (13) | 7,678 | 0 | 0 | 0 | 701 | 752 | 19 | 1,472 | 9 | 43.6 | 10.1 | 596.2 | 184.5 | 34.5 | 63.5 |
| gFOBT 55-80, 3 (9) | 5,773 | 0 | 0 | 0 | 544 | 603 | 23 | 1,170 | 8 | 48.6 | 12.1 | 628.2 | 162.6 | 27.0 | 56.4 |
| gFOBT 55-85, 1 (31) | 12,679 | 0 | 0 | 0 | 1,101 | 1,024 | 12 | 2,137 | 13 | 35.4 | 7.3 | 527.1 | 213.7 | 46.8 | 73.7 |
| gFOBT 55-85, 2 (16) | 8,478 | 0 | 0 | 0 | 772 | 769 | 16 | 1,557 | 11 | 43.6 | 9.4 | 605.0 | 188.1 | 34.6 | 66.3 |
| gFOBT 55-85, 3 (11) | 6,359 | 0 | 0 | 0 | 599 | 618 | 20 | 1,238 | 9 | 48.9 | 11.3 | 639.3 | 166.3 | 26.5 | 59.3 |

gFOBT = highly-sensitive guaiac-based fecal occult blood test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 4c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with gFOBT screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| gFOBT 45-75, 1 (31) | 15,706 | 0 | 0 | 0 | 1,322 | 1,253 | 11 | 2,586 | 11 | 15.6 | 4.1 | 189.9 | 265.1 | 78.2 | 84.5 |
| gFOBT 45-75, 2 (16) | 10,412 | 0 | 0 | 0 | 908 | 970 | 17 | 1,895 | 10 | 24.2 | 6.8 | 278.1 | 233.1 | 66.3 | 74.7 |
| gFOBT 45-75, 3 (11) | 7,792 | 0 | 0 | 0 | 695 | 791 | 24 | 1,510 | 8 | 31.3 | 9.3 | 338.4 | 202.2 | 56.4 | 65.1 |
| gFOBT 45-80, 1 (36) | 17,036 | 0 | 0 | 0 | 1,435 | 1,283 | 8 | 2,726 | 13 | 13.7 | 3.2 | 185.3 | 270.5 | 80.9 | 87.9 |
| gFOBT 45-80, 2 (18) | 11,148 | 0 | 0 | 0 | 974 | 994 | 15 | 1,983 | 11 | 22.5 | 5.9 | 275.2 | 238.2 | 68.7 | 78.0 |
| gFOBT 45-80, 3 (12) | 8,417 | 0 | 0 | 0 | 753 | 814 | 21 | 1,588 | 9 | 29.4 | 8.4 | 333.6 | 208.3 | 59.1 | 68.8 |
| gFOBT 45-85, 1 (41) | 17,991 | 0 | 0 | 0 | 1,517 | 1,300 | 6 | 2,823 | 14 | 12.8 | 2.7 | 183.9 | 272.6 | 82.2 | 89.8 |
| gFOBT 45-85, 2 (21) | 11,945 | 0 | 0 | 0 | 1,048 | 1,015 | 12 | 2,075 | 12 | 21.1 | 5.0 | 274.3 | 242.4 | 70.7 | 81.3 |
| gFOBT 45-85, 3 (14) | 9,012 | 0 | 0 | 0 | 811 | 834 | 18 | 1,663 | 10 | 28.0 | 7.4 | 333.8 | 213.7 | 61.1 | 72.4 |
| gFOBT 50-75, 1 (26) | 13,026 | 0 | 0 | 0 | 1,121 | 1,120 | 12 | 2,253 | 11 | 18.2 | 4.9 | 237.0 | 246.8 | 74.6 | 81.7 |
| gFOBT 50-75, 2 (13) | 8,448 | 0 | 0 | 0 | 755 | 851 | 21 | 1,626 | 9 | 27.7 | 8.0 | 322.3 | 211.7 | 61.5 | 70.3 |
| gFOBT 50-75, 3 (9) | 6,498 | 0 | 0 | 0 | 594 | 696 | 27 | 1,317 | 8 | 34.1 | 10.3 | 374.4 | 183.4 | 52.5 | 61.4 |
| gFOBT 50-80, 1 (31) | 14,364 | 0 | 0 | 0 | 1,234 | 1,152 | 10 | 2,395 | 12 | 16.2 | 4.0 | 231.3 | 252.0 | 77.4 | 85.2 |
| gFOBT 50-80, 2 (16) | 9,554 | 0 | 0 | 0 | 857 | 890 | 16 | 1,763 | 10 | 24.7 | 6.5 | 315.6 | 220.8 | 65.6 | 75.7 |
| gFOBT 50-80, 3 (11) | 7,184 | 0 | 0 | 0 | 661 | 728 | 23 | 1,412 | 9 | 31.7 | 9.0 | 370.7 | 192.0 | 55.9 | 66.3 |
| gFOBT 50-85, 1 (36) | 15,321 | 0 | 0 | 0 | 1,316 | 1,169 | 8 | 2,493 | 14 | 15.2 | 3.4 | 229.5 | 254.6 | 78.8 | 87.2 |
| gFOBT 50-85, 2 (18) | 10,089 | 0 | 0 | 0 | 906 | 904 | 14 | 1,824 | 11 | 23.9 | 5.9 | 315.8 | 223.5 | 66.7 | 77.8 |
| gFOBT 50-85, 3 (12) | 7,643 | 0 | 0 | 0 | 704 | 741 | 21 | 1,466 | 10 | 30.7 | 8.4 | 371.0 | 195.2 | 57.2 | 68.7 |
| gFOBT 55-75, 1 (21) | 10,467 | 0 | 0 | 0 | 927 | 957 | 16 | 1,899 | 11 | 22.3 | 6.2 | 297.6 | 218.9 | 68.9 | 76.9 |
| gFOBT 55-75, 2 (11) | 6,959 | 0 | 0 | 0 | 643 | 727 | 23 | 1,394 | 9 | 31.2 | 9.1 | 374.0 | 186.9 | 56.5 | 66.0 |
| gFOBT 55-75, 3 (7) | 5,053 | 0 | 0 | 0 | 477 | 574 | 31 | 1,082 | 7 | 38.8 | 12.1 | 422.7 | 156.3 | 45.9 | 54.7 |
| gFOBT 55-80, 1 (26) | 11,806 | 0 | 0 | 0 | 1,041 | 989 | 13 | 2,043 | 12 | 20.2 | 5.2 | 292.2 | 224.4 | 71.9 | 80.6 |
| gFOBT 55-80, 2 (13) | 7,706 | 0 | 0 | 0 | 712 | 755 | 20 | 1,487 | 10 | 29.2 | 8.0 | 369.9 | 193.7 | 59.3 | 70.0 |
| gFOBT 55-80, 3 (9) | 5,932 | 0 | 0 | 0 | 563 | 615 | 26 | 1,204 | 9 | 35.5 | 10.4 | 416.2 | 167.3 | 50.5 | 61.2 |
| gFOBT 55-85, 1 (31) | 12,765 | 0 | 0 | 0 | 1,124 | 1,008 | 11 | 2,143 | 13 | 19.2 | 4.7 | 290.6 | 226.9 | 73.3 | 82.6 |
| gFOBT 55-85, 2 (16) | 8,513 | 0 | 0 | 0 | 787 | 777 | 17 | 1,581 | 11 | 27.8 | 7.1 | 370.3 | 198.2 | 61.4 | 73.4 |
| gFOBT 55-85, 3 (11) | 6,429 | 0 | 0 | 0 | 613 | 633 | 23 | 1,269 | 10 | 34.2 | 9.5 | 415.5 | 171.4 | 52.3 | 64.3 |

gFOBT = highly-sensitive guaiac-based fecal occult blood test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 5a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with FIT screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| FIT 45-75, 1 (31) | 19,196 | 0 | 0 | 0 | 898 | 1,073 | 8 | 1,979 | 10 | 19.7 | 4.1 | 311.2 | 287.1 | 71.8 | 85.3 |
| FIT 45-75, 2 (16) | 11,580 | 0 | 0 | 0 | 591 | 797 | 12 | 1,401 | 8 | 29.1 | 6.4 | 428.8 | 261.9 | 58.3 | 77.2 |
| FIT 45-75, 3 (11) | 8,387 | 0 | 0 | 0 | 452 | 640 | 16 | 1,108 | 7 | 35.8 | 8.6 | 492.6 | 236.1 | 48.8 | 69.3 |
| FIT 45-80, 1 (36) | 20,838 | 0 | 0 | 0 | 982 | 1,109 | 5 | 2,096 | 11 | 18.3 | 3.2 | 312.4 | 292.0 | 73.9 | 88.6 |
| FIT 45-80, 2 (18) | 12,407 | 0 | 0 | 0 | 641 | 825 | 9 | 1,475 | 9 | 28.0 | 5.4 | 434.0 | 267.7 | 59.9 | 80.9 |
| FIT 45-80, 3 (12) | 8,963 | 0 | 0 | 0 | 490 | 661 | 13 | 1,164 | 7 | 34.9 | 7.5 | 500.0 | 242.1 | 50.1 | 73.0 |
| FIT 45-85, 1 (41) | 21,998 | 0 | 0 | 0 | 1,042 | 1,128 | 4 | 2,174 | 12 | 17.9 | 2.8 | 314.6 | 293.5 | 74.4 | 89.9 |
| FIT 45-85, 2 (21) | 13,293 | 0 | 0 | 0 | 696 | 848 | 6 | 1,550 | 10 | 27.7 | 4.6 | 440.9 | 270.9 | 60.4 | 83.5 |
| FIT 45-85, 3 (14) | 9,631 | 0 | 0 | 0 | 537 | 682 | 9 | 1,229 | 9 | 34.7 | 6.6 | 510.0 | 246.2 | 50.4 | 76.2 |
| FIT 50-75, 1 (26) | 15,778 | 0 | 0 | 0 | 770 | 959 | 10 | 1,739 | 10 | 23.1 | 5.2 | 366.9 | 260.2 | 67.0 | 81.3 |
| FIT 50-75, 2 (13) | 9,326 | 0 | 0 | 0 | 500 | 700 | 15 | 1,215 | 7 | 32.6 | 7.8 | 469.9 | 234.1 | 53.4 | 72.1 |
| FIT 50-75, 3 (9) | 6,887 | 0 | 0 | 0 | 391 | 562 | 19 | 971 | 6 | 38.8 | 9.8 | 526.7 | 211.7 | 44.5 | 64.9 |
| FIT 50-80, 1 (31) | 17,426 | 0 | 0 | 0 | 855 | 996 | 7 | 1,858 | 11 | 21.6 | 4.3 | 368.0 | 265.2 | 69.1 | 84.7 |
| FIT 50-80, 2 (16) | 10,572 | 0 | 0 | 0 | 576 | 741 | 10 | 1,327 | 9 | 30.8 | 6.3 | 477.5 | 242.9 | 55.9 | 77.6 |
| FIT 50-80, 3 (11) | 7,694 | 0 | 0 | 0 | 446 | 595 | 14 | 1,055 | 8 | 37.5 | 8.3 | 537.6 | 220.4 | 46.4 | 70.3 |
| FIT 50-85, 1 (36) | 18,589 | 0 | 0 | 0 | 915 | 1,016 | 5 | 1,937 | 12 | 21.2 | 3.9 | 370.3 | 266.8 | 69.7 | 86.1 |
| FIT 50-85, 2 (18) | 11,165 | 0 | 0 | 0 | 613 | 757 | 8 | 1,377 | 10 | 30.7 | 5.8 | 482.3 | 245.0 | 56.1 | 79.4 |
| FIT 50-85, 3 (12) | 8,111 | 0 | 0 | 0 | 475 | 608 | 11 | 1,095 | 8 | 37.4 | 7.8 | 543.6 | 222.6 | 46.5 | 72.2 |
| FIT 55-75, 1 (21) | 12,502 | 0 | 0 | 0 | 645 | 820 | 13 | 1,478 | 9 | 27.9 | 6.8 | 433.7 | 226.1 | 60.1 | 75.6 |
| FIT 55-75, 2 (11) | 7,616 | 0 | 0 | 0 | 436 | 601 | 17 | 1,053 | 7 | 36.7 | 9.1 | 524.4 | 204.1 | 47.5 | 67.6 |
| FIT 55-75, 3 (7) | 5,306 | 0 | 0 | 0 | 320 | 464 | 24 | 807 | 6 | 43.3 | 11.8 | 564.3 | 178.1 | 38.1 | 57.7 |
| FIT 55-80, 1 (26) | 14,163 | 0 | 0 | 0 | 731 | 858 | 10 | 1,599 | 11 | 26.4 | 5.8 | 434.9 | 231.4 | 62.3 | 79.2 |
| FIT 55-80, 2 (13) | 8,455 | 0 | 0 | 0 | 487 | 630 | 14 | 1,131 | 8 | 35.5 | 8.0 | 530.0 | 210.3 | 49.3 | 71.5 |
| FIT 55-80, 3 (9) | 6,258 | 0 | 0 | 0 | 385 | 504 | 17 | 907 | 7 | 41.5 | 9.9 | 577.3 | 189.7 | 40.6 | 64.6 |
| FIT 55-85, 1 (31) | 15,332 | 0 | 0 | 0 | 792 | 879 | 8 | 1,679 | 12 | 26.0 | 5.4 | 437.2 | 233.0 | 62.9 | 80.6 |
| FIT 55-85, 2 (16) | 9,350 | 0 | 0 | 0 | 544 | 654 | 11 | 1,208 | 10 | 35.2 | 7.2 | 537.3 | 213.6 | 49.7 | 74.3 |
| FIT 55-85, 3 (11) | 6,837 | 0 | 0 | 0 | 427 | 523 | 14 | 965 | 8 | 41.5 | 9.1 | 586.5 | 193.1 | 40.7 | 67.4 |

FIT = fecal immunochemical test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 5b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with FIT screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| FIT 45-75, 1 (31) | 19,256 | 0 | 0 | 0 | 869 | 1,112 | 14 | 1,995 | 10 | 33.9 | 7.1 | 485.5 | 247.4 | 49.0 | 74.3 |
| FIT 45-75, 2 (16) | 11,595 | 0 | 0 | 0 | 574 | 830 | 19 | 1,423 | 8 | 41.8 | 9.6 | 570.6 | 216.0 | 37.2 | 65.5 |
| FIT 45-75, 3 (11) | 8,377 | 0 | 0 | 0 | 440 | 671 | 24 | 1,134 | 7 | 46.7 | 11.6 | 607.6 | 190.6 | 29.9 | 58.2 |
| FIT 45-80, 1 (36) | 20,955 | 0 | 0 | 0 | 945 | 1,136 | 11 | 2,091 | 11 | 32.7 | 6.1 | 489.9 | 253.9 | 50.9 | 78.2 |
| FIT 45-80, 2 (18) | 12,438 | 0 | 0 | 0 | 617 | 849 | 16 | 1,482 | 9 | 41.1 | 8.5 | 579.1 | 222.4 | 38.3 | 69.3 |
| FIT 45-80, 3 (12) | 8,836 | 0 | 0 | 0 | 467 | 683 | 21 | 1,171 | 8 | 46.3 | 10.8 | 616.2 | 195.6 | 30.4 | 61.2 |
| FIT 45-85, 1 (41) | 22,193 | 0 | 0 | 0 | 999 | 1,148 | 9 | 2,156 | 12 | 32.4 | 5.6 | 493.6 | 256.3 | 51.3 | 80.0 |
| FIT 45-85, 2 (21) | 13,363 | 0 | 0 | 0 | 665 | 864 | 13 | 1,542 | 10 | 41.1 | 7.7 | 588.5 | 226.3 | 38.3 | 72.2 |
| FIT 45-85, 3 (14) | 9,534 | 0 | 0 | 0 | 508 | 699 | 17 | 1,224 | 8 | 46.5 | 9.8 | 629.0 | 200.3 | 30.1 | 64.6 |
| FIT 50-75, 1 (26) | 15,843 | 0 | 0 | 0 | 745 | 997 | 15 | 1,757 | 10 | 35.5 | 7.8 | 504.1 | 231.0 | 46.7 | 71.8 |
| FIT 50-75, 2 (13) | 9,342 | 0 | 0 | 0 | 486 | 735 | 21 | 1,243 | 8 | 43.5 | 10.5 | 581.7 | 200.2 | 34.6 | 62.2 |
| FIT 50-75, 3 (9) | 6,795 | 0 | 0 | 0 | 376 | 593 | 26 | 995 | 7 | 48.1 | 12.5 | 613.5 | 176.0 | 27.8 | 55.0 |
| FIT 50-80, 1 (31) | 17,552 | 0 | 0 | 0 | 822 | 1,021 | 12 | 1,855 | 11 | 34.2 | 6.7 | 508.6 | 237.7 | 48.6 | 75.9 |
| FIT 50-80, 2 (16) | 10,613 | 0 | 0 | 0 | 553 | 765 | 16 | 1,334 | 9 | 42.4 | 8.9 | 594.4 | 209.9 | 36.4 | 67.9 |
| FIT 50-80, 3 (11) | 7,693 | 0 | 0 | 0 | 429 | 620 | 21 | 1,070 | 8 | 47.4 | 10.9 | 630.2 | 185.6 | 28.8 | 60.8 |
| FIT 50-85, 1 (36) | 18,796 | 0 | 0 | 0 | 877 | 1,034 | 10 | 1,921 | 11 | 33.9 | 6.2 | 512.4 | 240.1 | 49.1 | 77.8 |
| FIT 50-85, 2 (18) | 11,233 | 0 | 0 | 0 | 585 | 775 | 14 | 1,375 | 9 | 42.3 | 8.4 | 600.7 | 212.5 | 36.4 | 69.9 |
| FIT 50-85, 3 (12) | 8,032 | 0 | 0 | 0 | 449 | 627 | 19 | 1,096 | 8 | 47.6 | 10.4 | 636.4 | 187.8 | 28.6 | 62.4 |
| FIT 55-75, 1 (21) | 12,586 | 0 | 0 | 0 | 626 | 847 | 18 | 1,490 | 9 | 38.1 | 9.0 | 531.0 | 205.8 | 42.8 | 67.7 |
| FIT 55-75, 2 (11) | 7,644 | 0 | 0 | 0 | 424 | 628 | 23 | 1,075 | 8 | 45.4 | 11.3 | 598.8 | 178.9 | 31.8 | 59.3 |
| FIT 55-75, 3 (7) | 5,250 | 0 | 0 | 0 | 311 | 493 | 29 | 833 | 6 | 50.3 | 13.9 | 621.1 | 153.3 | 24.4 | 50.1 |
| FIT 55-80, 1 (26) | 14,313 | 0 | 0 | 0 | 704 | 873 | 14 | 1,592 | 10 | 36.7 | 7.8 | 535.5 | 212.8 | 44.8 | 72.0 |
| FIT 55-80, 2 (13) | 8,501 | 0 | 0 | 0 | 470 | 650 | 19 | 1,139 | 8 | 44.6 | 10.2 | 607.6 | 185.6 | 33.0 | 63.3 |
| FIT 55-80, 3 (9) | 6,204 | 0 | 0 | 0 | 368 | 525 | 23 | 917 | 7 | 49.3 | 12.0 | 638.7 | 164.7 | 25.9 | 56.7 |
| FIT 55-85, 1 (31) | 15,566 | 0 | 0 | 0 | 760 | 887 | 12 | 1,659 | 11 | 36.4 | 7.2 | 539.4 | 215.3 | 45.4 | 73.9 |
| FIT 55-85, 2 (16) | 9,437 | 0 | 0 | 0 | 519 | 666 | 16 | 1,201 | 9 | 44.5 | 9.3 | 617.2 | 189.7 | 33.1 | 66.4 |
| FIT 55-85, 3 (11) | 6,859 | 0 | 0 | 0 | 408 | 540 | 20 | 967 | 8 | 49.6 | 11.2 | 650.8 | 168.7 | 25.5 | 59.8 |

FIT = fecal immunochemical test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 5c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with FIT screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality | Screening tests | | | | Follow-up | Surveillance | COLs for | Total | Compli- | CRC | CRC | LY with | LYG‡ | Reductions‡ (%) | |
| age to begin-age to end, screening interval (# of tests*) | Stool tests | SIGs | CTCs | COLs | COLs | COLs | symptoms | COLs | cations | cases | deaths† | CRC | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| FIT 45-75, 1 (31) | 18,733 | 0 | 0 | 0 | 927 | 1,225 | 11 | 2,163 | 11 | 17.2 | 4.4 | 213.2 | 262.7 | 76.0 | 83.5 |
| FIT 45-75, 2 (16) | 11,439 | 0 | 0 | 0 | 613 | 922 | 19 | 1,554 | 9 | 26.6 | 7.3 | 306.6 | 227.9 | 63.0 | 72.7 |
| FIT 45-75, 3 (11) | 8,327 | 0 | 0 | 0 | 467 | 743 | 26 | 1,235 | 8 | 33.6 | 9.9 | 364.2 | 196.0 | 53.2 | 62.9 |
| FIT 45-80, 1 (36) | 20,348 | 0 | 0 | 0 | 1,010 | 1,256 | 8 | 2,274 | 12 | 15.2 | 3.4 | 209.2 | 268.8 | 78.8 | 87.2 |
| FIT 45-80, 2 (18) | 12,260 | 0 | 0 | 0 | 661 | 947 | 16 | 1,624 | 10 | 24.8 | 6.4 | 303.3 | 233.3 | 65.5 | 76.2 |
| FIT 45-80, 3 (12) | 8,907 | 0 | 0 | 0 | 504 | 762 | 23 | 1,289 | 8 | 32.0 | 9.0 | 363.6 | 202.8 | 55.5 | 66.5 |
| FIT 45-85, 1 (41) | 21,506 | 0 | 0 | 0 | 1,071 | 1,273 | 7 | 2,351 | 13 | 14.3 | 2.9 | 208.2 | 270.9 | 80.1 | 89.2 |
| FIT 45-85, 2 (21) | 13,148 | 0 | 0 | 0 | 716 | 968 | 13 | 1,697 | 11 | 23.4 | 5.4 | 303.9 | 238.8 | 67.4 | 79.8 |
| FIT 45-85, 3 (14) | 9,577 | 0 | 0 | 0 | 549 | 783 | 19 | 1,351 | 9 | 30.5 | 8.0 | 363.5 | 207.8 | 57.5 | 70.2 |
| FIT 50-75, 1 (26) | 15,444 | 0 | 0 | 0 | 798 | 1,088 | 13 | 1,899 | 11 | 19.9 | 5.2 | 258.5 | 243.9 | 72.3 | 80.6 |
| FIT 50-75, 2 (13) | 9,241 | 0 | 0 | 0 | 519 | 805 | 22 | 1,346 | 9 | 29.9 | 8.5 | 348.0 | 207.5 | 58.3 | 68.4 |
| FIT 50-75, 3 (9) | 6,857 | 0 | 0 | 0 | 404 | 649 | 28 | 1,081 | 7 | 36.6 | 11.0 | 399.0 | 178.2 | 49.1 | 58.9 |
| FIT 50-80, 1 (31) | 17,062 | 0 | 0 | 0 | 883 | 1,120 | 10 | 2,013 | 12 | 17.8 | 4.1 | 254.3 | 250.3 | 75.3 | 84.5 |
| FIT 50-80, 2 (16) | 10,476 | 0 | 0 | 0 | 594 | 843 | 17 | 1,454 | 10 | 27.1 | 6.9 | 343.8 | 217.9 | 62.3 | 74.2 |
| FIT 50-80, 3 (11) | 7,660 | 0 | 0 | 0 | 458 | 681 | 24 | 1,163 | 8 | 34.0 | 9.5 | 396.1 | 187.2 | 52.7 | 64.5 |
| FIT 50-85, 1 (36) | 18,224 | 0 | 0 | 0 | 945 | 1,138 | 8 | 2,091 | 13 | 16.8 | 3.6 | 253.7 | 253.3 | 76.6 | 86.6 |
| FIT 50-85, 2 (18) | 11,071 | 0 | 0 | 0 | 631 | 858 | 15 | 1,504 | 11 | 26.2 | 6.3 | 343.5 | 220.0 | 63.6 | 76.4 |
| FIT 50-85, 3 (12) | 8,084 | 0 | 0 | 0 | 486 | 694 | 22 | 1,201 | 9 | 33.1 | 8.9 | 395.9 | 190.7 | 53.9 | 66.9 |
| FIT 55-75, 1 (21) | 12,290 | 0 | 0 | 0 | 672 | 923 | 16 | 1,611 | 10 | 24.0 | 6.5 | 317.7 | 216.7 | 66.6 | 75.8 |
| FIT 55-75, 2 (11) | 7,575 | 0 | 0 | 0 | 453 | 683 | 24 | 1,160 | 8 | 33.5 | 9.6 | 397.7 | 183.4 | 53.3 | 64.1 |
| FIT 55-75, 3 (7) | 5,301 | 0 | 0 | 0 | 330 | 532 | 33 | 895 | 7 | 41.1 | 12.7 | 443.5 | 151.7 | 42.8 | 52.5 |
| FIT 55-80, 1 (26) | 13,929 | 0 | 0 | 0 | 759 | 957 | 13 | 1,729 | 12 | 21.8 | 5.4 | 313.1 | 223.5 | 69.6 | 79.8 |
| FIT 55-80, 2 (13) | 8,410 | 0 | 0 | 0 | 504 | 712 | 21 | 1,237 | 9 | 31.4 | 8.5 | 393.0 | 190.1 | 56.3 | 68.3 |
| FIT 55-80, 3 (9) | 6,254 | 0 | 0 | 0 | 395 | 573 | 27 | 995 | 8 | 37.7 | 10.9 | 437.9 | 164.2 | 47.4 | 59.4 |
| FIT 55-85, 1 (31) | 15,093 | 0 | 0 | 0 | 821 | 977 | 11 | 1,809 | 13 | 20.7 | 4.8 | 311.4 | 226.3 | 71.2 | 82.1 |
| FIT 55-85, 2 (16) | 9,309 | 0 | 0 | 0 | 561 | 734 | 18 | 1,313 | 10 | 29.9 | 7.5 | 393.2 | 195.5 | 58.4 | 72.1 |
| FIT 55-85, 3 (11) | 6,836 | 0 | 0 | 0 | 436 | 591 | 24 | 1,051 | 9 | 36.4 | 9.9 | 437.0 | 168.2 | 49.3 | 62.9 |

FIT = fecal immunochemical test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 6a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with FIT-DNA screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| FIT-DNA 45-75, 1 (31) | 13,372 | 0 | 0 | 0 | 1,576 | 1,397 | 6 | 2,978 | 12 | 13.5 | 3.0 | 217.7 | 297.5 | 80.7 | 89.2 |
| FIT-DNA 45-75, 3 (11) | 7,158 | 0 | 0 | 0 | 906 | 1,012 | 10 | 1,928 | 9 | 23.0 | 5.2 | 345.7 | 274.3 | 67.1 | 81.5 |
| FIT-DNA 45-75, 5 (7) | 5,233 | 0 | 0 | 0 | 692 | 835 | 13 | 1,539 | 8 | 29.9 | 7.2 | 420.2 | 247.4 | 57.3 | 74.2 |
| FIT-DNA 45-80, 1 (36) | 14,415 | 0 | 0 | 0 | 1,703 | 1,432 | 4 | 3,139 | 13 | 12.3 | 2.4 | 216.1 | 300.5 | 82.4 | 91.3 |
| FIT-DNA 45-80, 3 (12) | 7,746 | 0 | 0 | 0 | 986 | 1,045 | 6 | 2,037 | 11 | 21.7 | 4.2 | 348.0 | 279.6 | 69.0 | 84.9 |
| FIT-DNA 45-80, 5 (8) | 5,621 | 0 | 0 | 0 | 751 | 860 | 9 | 1,621 | 10 | 29.0 | 6.3 | 426.4 | 252.0 | 58.5 | 77.5 |
| FIT-DNA 45-85, 1 (41) | 15,145 | 0 | 0 | 0 | 1,791 | 1,451 | 3 | 3,245 | 15 | 11.9 | 2.2 | 216.5 | 301.4 | 83.0 | 92.1 |
| FIT-DNA 45-85, 3 (14) | 8,217 | 0 | 0 | 0 | 1,052 | 1,067 | 4 | 2,124 | 12 | 21.3 | 3.7 | 351.7 | 281.7 | 69.6 | 86.7 |
| FIT-DNA 45-85, 5 (9) | 5,882 | 0 | 0 | 0 | 792 | 874 | 7 | 1,674 | 11 | 29.1 | 5.9 | 431.1 | 253.5 | 58.4 | 78.9 |
| FIT-DNA 50-75, 1 (26) | 11,041 | 0 | 0 | 0 | 1,332 | 1,261 | 8 | 2,601 | 12 | 16.7 | 4.1 | 276.5 | 271.1 | 76.2 | 85.5 |
| FIT-DNA 50-75, 3 (9) | 5,990 | 0 | 0 | 0 | 783 | 907 | 11 | 1,701 | 9 | 26.1 | 6.2 | 396.8 | 249.6 | 62.7 | 78.0 |
| FIT-DNA 50-75, 5 (6) | 4,391 | 0 | 0 | 0 | 601 | 748 | 15 | 1,364 | 8 | 32.8 | 8.2 | 461.0 | 224.2 | 53.1 | 70.5 |
| FIT-DNA 50-80, 1 (31) | 12,096 | 0 | 0 | 0 | 1,460 | 1,297 | 6 | 2,763 | 13 | 15.4 | 3.5 | 275.0 | 274.2 | 78.0 | 87.7 |
| FIT-DNA 50-80, 3 (11) | 6,543 | 0 | 0 | 0 | 861 | 941 | 8 | 1,809 | 10 | 24.8 | 5.2 | 399.5 | 254.7 | 64.5 | 81.3 |
| FIT-DNA 50-80, 5 (7) | 4,781 | 0 | 0 | 0 | 662 | 774 | 11 | 1,447 | 9 | 31.9 | 7.3 | 467.3 | 228.9 | 54.4 | 73.8 |
| FIT-DNA 50-85, 1 (36) | 12,826 | 0 | 0 | 0 | 1,549 | 1,316 | 5 | 2,870 | 14 | 15.0 | 3.2 | 275.4 | 275.1 | 78.5 | 88.5 |
| FIT-DNA 50-85, 3 (12) | 6,961 | 0 | 0 | 0 | 918 | 959 | 6 | 1,884 | 11 | 24.5 | 4.8 | 402.6 | 256.5 | 65.0 | 82.9 |
| FIT-DNA 50-85, 5 (8) | 5,043 | 0 | 0 | 0 | 703 | 788 | 9 | 1,500 | 10 | 32.0 | 6.9 | 472.1 | 230.4 | 54.3 | 75.3 |
| FIT-DNA 55-75, 1 (21) | 8,846 | 0 | 0 | 0 | 1,101 | 1,094 | 11 | 2,206 | 11 | 21.3 | 5.6 | 348.9 | 237.0 | 69.5 | 80.0 |
| FIT-DNA 55-75, 3 (7) | 4,668 | 0 | 0 | 0 | 636 | 764 | 15 | 1,415 | 9 | 31.2 | 8.1 | 456.0 | 214.1 | 55.4 | 71.0 |
| FIT-DNA 55-75, 5 (5) | 3,576 | 0 | 0 | 0 | 512 | 642 | 18 | 1,171 | 8 | 36.8 | 9.8 | 508.2 | 194.0 | 47.3 | 65.1 |
| FIT-DNA 55-80, 1 (26) | 9,880 | 0 | 0 | 0 | 1,228 | 1,131 | 9 | 2,367 | 13 | 20.1 | 5.0 | 347.3 | 240.2 | 71.3 | 82.2 |
| FIT-DNA 55-80, 3 (9) | 5,410 | 0 | 0 | 0 | 740 | 810 | 11 | 1,561 | 10 | 29.3 | 6.7 | 459.4 | 221.6 | 58.1 | 75.9 |
| FIT-DNA 55-80, 5 (6) | 3,970 | 0 | 0 | 0 | 573 | 669 | 14 | 1,255 | 9 | 35.9 | 8.8 | 514.9 | 198.9 | 48.6 | 68.6 |
| FIT-DNA 55-85, 1 (31) | 10,618 | 0 | 0 | 0 | 1,317 | 1,150 | 8 | 2,475 | 14 | 19.7 | 4.7 | 347.8 | 241.1 | 71.9 | 83.1 |
| FIT-DNA 55-85, 3 (11) | 5,801 | 0 | 0 | 0 | 795 | 829 | 9 | 1,634 | 11 | 29.0 | 6.3 | 462.7 | 223.4 | 58.6 | 77.4 |
| FIT-DNA 55-85, 5 (7) | 4,233 | 0 | 0 | 0 | 614 | 683 | 12 | 1,310 | 10 | 36.0 | 8.4 | 519.9 | 200.5 | 48.5 | 70.1 |

FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 6b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with FIT-DNA screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| FIT-DNA 45-75, 1 (31) | 13,328 | 0 | 0 | 0 | 1,531 | 1,501 | 11 | 3,044 | 12 | 27.0 | 5.8 | 389.7 | 261.1 | 59.4 | 79.2 |
| FIT-DNA 45-75, 3 (11) | 7,086 | 0 | 0 | 0 | 878 | 1,071 | 16 | 1,965 | 10 | 36.3 | 8.2 | 505.2 | 231.1 | 45.5 | 70.5 |
| FIT-DNA 45-75, 5 (7) | 5,219 | 0 | 0 | 0 | 674 | 881 | 21 | 1,576 | 9 | 41.8 | 10.1 | 556.9 | 205.5 | 37.2 | 63.7 |
| FIT-DNA 45-80, 1 (36) | 14,398 | 0 | 0 | 0 | 1,651 | 1,523 | 9 | 3,183 | 13 | 26.0 | 5.1 | 390.0 | 265.2 | 61.0 | 81.7 |
| FIT-DNA 45-80, 3 (12) | 7,445 | 0 | 0 | 0 | 922 | 1,085 | 14 | 2,022 | 10 | 35.7 | 7.5 | 508.9 | 234.9 | 46.4 | 72.9 |
| FIT-DNA 45-80, 5 (8) | 5,612 | 0 | 0 | 0 | 727 | 900 | 17 | 1,644 | 10 | 41.4 | 9.1 | 566.1 | 210.7 | 37.9 | 67.2 |
| FIT-DNA 45-85, 1 (41) | 15,178 | 0 | 0 | 0 | 1,738 | 1,534 | 8 | 3,280 | 14 | 25.6 | 4.8 | 391.2 | 266.6 | 61.5 | 82.8 |
| FIT-DNA 45-85, 3 (14) | 7,990 | 0 | 0 | 0 | 990 | 1,101 | 12 | 2,103 | 11 | 35.3 | 6.8 | 515.2 | 238.3 | 46.9 | 75.4 |
| FIT-DNA 45-85, 5 (9) | 5,883 | 0 | 0 | 0 | 763 | 909 | 16 | 1,688 | 10 | 41.6 | 8.7 | 571.7 | 212.3 | 37.5 | 68.6 |
| FIT-DNA 50-75, 1 (26) | 11,025 | 0 | 0 | 0 | 1,295 | 1,355 | 12 | 2,662 | 12 | 28.4 | 6.3 | 412.5 | 246.3 | 57.3 | 77.2 |
| FIT-DNA 50-75, 3 (9) | 5,779 | 0 | 0 | 0 | 740 | 956 | 18 | 1,714 | 9 | 37.9 | 9.0 | 518.9 | 215.3 | 43.1 | 67.5 |
| FIT-DNA 50-75, 5 (6) | 4,380 | 0 | 0 | 0 | 586 | 794 | 22 | 1,402 | 9 | 43.1 | 10.7 | 569.5 | 192.5 | 35.2 | 61.6 |
| FIT-DNA 50-80, 1 (31) | 12,108 | 0 | 0 | 0 | 1,417 | 1,377 | 10 | 2,804 | 13 | 27.3 | 5.6 | 413.1 | 250.5 | 58.9 | 79.8 |
| FIT-DNA 50-80, 3 (11) | 6,481 | 0 | 0 | 0 | 828 | 985 | 14 | 1,828 | 11 | 36.7 | 7.8 | 526.5 | 222.7 | 44.8 | 72.0 |
| FIT-DNA 50-80, 5 (7) | 4,776 | 0 | 0 | 0 | 640 | 813 | 19 | 1,472 | 9 | 42.7 | 9.7 | 578.8 | 197.8 | 35.9 | 65.2 |
| FIT-DNA 50-85, 1 (36) | 12,888 | 0 | 0 | 0 | 1,504 | 1,388 | 9 | 2,901 | 14 | 27.0 | 5.3 | 414.2 | 251.9 | 59.5 | 80.9 |
| FIT-DNA 50-85, 3 (12) | 6,745 | 0 | 0 | 0 | 861 | 993 | 13 | 1,867 | 11 | 36.6 | 7.5 | 529.6 | 224.1 | 45.0 | 73.1 |
| FIT-DNA 50-85, 5 (8) | 5,048 | 0 | 0 | 0 | 677 | 822 | 17 | 1,516 | 10 | 42.9 | 9.3 | 584.5 | 199.5 | 35.6 | 66.7 |
| FIT-DNA 55-75, 1 (21) | 8,874 | 0 | 0 | 0 | 1,076 | 1,162 | 14 | 2,252 | 12 | 31.0 | 7.4 | 446.6 | 221.3 | 53.4 | 73.3 |
| FIT-DNA 55-75, 3 (7) | 4,509 | 0 | 0 | 0 | 604 | 806 | 21 | 1,431 | 9 | 40.7 | 10.4 | 542.3 | 190.0 | 38.8 | 62.5 |
| FIT-DNA 55-75, 5 (5) | 3,574 | 0 | 0 | 0 | 500 | 679 | 24 | 1,203 | 8 | 45.1 | 11.7 | 584.8 | 172.2 | 32.2 | 58.0 |
| FIT-DNA 55-80, 1 (26) | 9,943 | 0 | 0 | 0 | 1,196 | 1,186 | 12 | 2,394 | 13 | 29.9 | 6.7 | 447.1 | 225.6 | 55.1 | 76.0 |
| FIT-DNA 55-80, 3 (9) | 5,260 | 0 | 0 | 0 | 699 | 841 | 17 | 1,557 | 10 | 39.2 | 9.0 | 549.8 | 199.1 | 41.1 | 67.8 |
| FIT-DNA 55-80, 5 (6) | 3,974 | 0 | 0 | 0 | 555 | 699 | 20 | 1,275 | 9 | 44.7 | 10.6 | 594.5 | 177.7 | 32.9 | 61.7 |
| FIT-DNA 55-85, 1 (31) | 10,733 | 0 | 0 | 0 | 1,285 | 1,197 | 11 | 2,493 | 14 | 29.5 | 6.4 | 448.3 | 227.0 | 55.6 | 77.1 |
| FIT-DNA 55-85, 3 (11) | 5,771 | 0 | 0 | 0 | 763 | 856 | 15 | 1,634 | 11 | 39.0 | 8.3 | 555.7 | 201.9 | 41.4 | 70.0 |
| FIT-DNA 55-85, 5 (7) | 4,248 | 0 | 0 | 0 | 593 | 709 | 19 | 1,320 | 10 | 44.9 | 10.2 | 600.3 | 179.5 | 32.6 | 63.3 |

FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 6c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with FIT-DNA screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| FIT-DNA 45-75, 1 (31) | 12,989 | 0 | 0 | 0 | 1,588 | 1,526 | 7 | 3,122 | 13 | 10.7 | 2.9 | 132.7 | 279.0 | 85.1 | 89.3 |
| FIT-DNA 45-75, 3 (11) | 7,061 | 0 | 0 | 0 | 922 | 1,136 | 15 | 2,073 | 10 | 20.3 | 5.7 | 235.4 | 244.1 | 71.8 | 78.6 |
| FIT-DNA 45-75, 5 (7) | 5,195 | 0 | 0 | 0 | 704 | 942 | 21 | 1,667 | 9 | 27.2 | 8.2 | 299.5 | 212.1 | 62.1 | 69.5 |
| FIT-DNA 45-80, 1 (36) | 14,025 | 0 | 0 | 0 | 1,716 | 1,556 | 5 | 3,278 | 14 | 9.1 | 2.2 | 127.6 | 282.5 | 87.3 | 91.8 |
| FIT-DNA 45-80, 3 (12) | 7,650 | 0 | 0 | 0 | 1,002 | 1,164 | 12 | 2,178 | 11 | 18.4 | 4.8 | 230.8 | 249.7 | 74.4 | 82.0 |
| FIT-DNA 45-80, 5 (8) | 5,586 | 0 | 0 | 0 | 762 | 965 | 18 | 1,745 | 10 | 25.4 | 7.2 | 296.5 | 217.7 | 64.7 | 73.2 |
| FIT-DNA 45-85, 1 (41) | 14,768 | 0 | 0 | 0 | 1,809 | 1,573 | 4 | 3,386 | 15 | 8.4 | 1.9 | 127.1 | 284.3 | 88.3 | 93.0 |
| FIT-DNA 45-85, 3 (14) | 8,124 | 0 | 0 | 0 | 1,069 | 1,184 | 10 | 2,263 | 13 | 17.2 | 4.2 | 229.3 | 252.9 | 76.1 | 84.5 |
| FIT-DNA 45-85, 5 (9) | 5,850 | 0 | 0 | 0 | 803 | 979 | 16 | 1,798 | 11 | 24.6 | 6.7 | 296.1 | 219.9 | 65.8 | 75.0 |
| FIT-DNA 50-75, 1 (26) | 10,745 | 0 | 0 | 0 | 1,348 | 1,371 | 9 | 2,729 | 13 | 13.0 | 3.6 | 177.6 | 260.7 | 81.8 | 86.6 |
| FIT-DNA 50-75, 3 (9) | 5,927 | 0 | 0 | 0 | 800 | 1,011 | 17 | 1,827 | 10 | 22.9 | 6.5 | 278.1 | 226.4 | 68.2 | 75.7 |
| FIT-DNA 50-75, 5 (6) | 4,370 | 0 | 0 | 0 | 612 | 837 | 23 | 1,473 | 9 | 29.8 | 9.0 | 337.4 | 195.1 | 58.5 | 66.4 |
| FIT-DNA 50-80, 1 (31) | 11,795 | 0 | 0 | 0 | 1,478 | 1,401 | 7 | 2,886 | 14 | 11.4 | 2.9 | 173.1 | 264.7 | 84.1 | 89.3 |
| FIT-DNA 50-80, 3 (11) | 6,476 | 0 | 0 | 0 | 876 | 1,040 | 14 | 1,931 | 11 | 20.8 | 5.5 | 272.6 | 232.2 | 71.0 | 79.4 |
| FIT-DNA 50-80, 5 (7) | 4,762 | 0 | 0 | 0 | 672 | 862 | 20 | 1,554 | 10 | 27.9 | 8.0 | 333.5 | 200.5 | 61.1 | 70.0 |
| FIT-DNA 50-85, 1 (36) | 12,542 | 0 | 0 | 0 | 1,571 | 1,418 | 6 | 2,994 | 15 | 10.7 | 2.5 | 172.5 | 266.4 | 85.1 | 90.6 |
| FIT-DNA 50-85, 3 (12) | 6,903 | 0 | 0 | 0 | 935 | 1,058 | 12 | 2,005 | 12 | 19.8 | 5.0 | 271.7 | 234.6 | 72.4 | 81.4 |
| FIT-DNA 50-85, 5 (8) | 5,028 | 0 | 0 | 0 | 713 | 875 | 18 | 1,606 | 11 | 27.1 | 7.5 | 333.0 | 202.6 | 62.3 | 72.0 |
| FIT-DNA 55-75, 1 (21) | 8,647 | 0 | 0 | 0 | 1,121 | 1,182 | 12 | 2,315 | 12 | 16.7 | 4.7 | 238.7 | 233.9 | 76.7 | 82.3 |
| FIT-DNA 55-75, 3 (7) | 4,640 | 0 | 0 | 0 | 652 | 847 | 21 | 1,520 | 10 | 27.6 | 8.2 | 334.5 | 196.9 | 61.5 | 69.3 |
| FIT-DNA 55-75, 5 (5) | 3,570 | 0 | 0 | 0 | 522 | 713 | 26 | 1,261 | 9 | 33.5 | 10.3 | 382.5 | 171.8 | 53.4 | 61.6 |
| FIT-DNA 55-80, 1 (26) | 9,673 | 0 | 0 | 0 | 1,250 | 1,212 | 10 | 2,471 | 14 | 15.1 | 4.0 | 235.2 | 237.9 | 78.9 | 84.9 |
| FIT-DNA 55-80, 3 (9) | 5,379 | 0 | 0 | 0 | 756 | 890 | 17 | 1,663 | 11 | 24.7 | 6.8 | 327.8 | 205.7 | 65.6 | 74.6 |
| FIT-DNA 55-80, 5 (6) | 3,967 | 0 | 0 | 0 | 582 | 738 | 23 | 1,343 | 10 | 31.5 | 9.3 | 380.0 | 177.5 | 56.1 | 65.4 |
| FIT-DNA 55-85, 1 (31) | 10,427 | 0 | 0 | 0 | 1,343 | 1,230 | 9 | 2,582 | 15 | 14.3 | 3.7 | 232.9 | 239.4 | 80.1 | 86.4 |
| FIT-DNA 55-85, 3 (11) | 5,774 | 0 | 0 | 0 | 812 | 907 | 15 | 1,734 | 12 | 23.6 | 6.2 | 326.6 | 208.8 | 67.1 | 76.9 |
| FIT-DNA 55-85, 5 (7) | 4,235 | 0 | 0 | 0 | 624 | 752 | 21 | 1,397 | 11 | 30.7 | 8.7 | 380.3 | 179.6 | 57.3 | 67.5 |

FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 7a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| SIG 45-75, 5 (7) | 0 | 4,912 | 0 | 0 | 873 | 1,153 | 13 | 2,039 | 11 | 19.8 | 6.3 | 250.2 | 250.6 | 71.7 | 77.4 |
| SIG 45-75, 10 (4) | 0 | 3,196 | 0 | 0 | 625 | 935 | 18 | 1,578 | 9 | 25.7 | 8.4 | 303.3 | 225.0 | 63.2 | 69.9 |
| SIG 45-80, 5 (8) | 0 | 5,258 | 0 | 0 | 939 | 1,178 | 11 | 2,128 | 12 | 18.9 | 5.9 | 249.8 | 252.7 | 72.9 | 79.0 |
| SIG 45-80, 10 (4) | 0 | 3,196 | 0 | 0 | 625 | 935 | 18 | 1,578 | 9 | 25.7 | 8.4 | 303.3 | 225.0 | 63.2 | 69.9 |
| SIG 45-85, 5 (9) | 0 | 5,489 | 0 | 0 | 982 | 1,190 | 11 | 2,183 | 13 | 18.8 | 5.7 | 250.5 | 253.2 | 73.2 | 79.6 |
| SIG 45-85, 10 (5) | 0 | 3,485 | 0 | 0 | 689 | 959 | 16 | 1,664 | 11 | 25.3 | 8.0 | 305.6 | 226.4 | 63.8 | 71.3 |
| SIG 50-75, 5 (6) | 0 | 4,111 | 0 | 0 | 761 | 1,044 | 15 | 1,820 | 10 | 22.7 | 7.4 | 299.1 | 226.6 | 67.5 | 73.6 |
| SIG 50-75, 10 (3) | 0 | 2,480 | 0 | 0 | 503 | 820 | 22 | 1,345 | 8 | 29.6 | 10.1 | 344.5 | 200.1 | 57.7 | 63.9 |
| SIG 50-80, 5 (7) | 0 | 4,459 | 0 | 0 | 827 | 1,069 | 14 | 1,910 | 11 | 21.8 | 6.9 | 298.6 | 228.7 | 68.8 | 75.2 |
| SIG 50-80, 10 (4) | 0 | 2,910 | 0 | 0 | 599 | 867 | 18 | 1,484 | 10 | 27.7 | 9.0 | 344.8 | 205.1 | 60.4 | 67.7 |
| SIG 50-85, 5 (8) | 0 | 4,691 | 0 | 0 | 871 | 1,082 | 13 | 1,965 | 12 | 21.7 | 6.8 | 299.4 | 229.3 | 69.0 | 75.8 |
| SIG 50-85, 10 (4) | 0 | 2,910 | 0 | 0 | 599 | 867 | 18 | 1,484 | 10 | 27.7 | 9.0 | 344.8 | 205.1 | 60.4 | 67.7 |
| SIG 55-75, 5 (5) | 0 | 3,342 | 0 | 0 | 651 | 909 | 18 | 1,578 | 10 | 27.0 | 8.9 | 359.3 | 195.9 | 61.5 | 68.2 |
| SIG 55-75, 10 (3) | 0 | 2,277 | 0 | 0 | 492 | 753 | 22 | 1,267 | 9 | 31.7 | 10.7 | 393.7 | 177.4 | 54.7 | 61.9 |
| SIG 55-80, 5 (6) | 0 | 3,692 | 0 | 0 | 718 | 935 | 17 | 1,669 | 11 | 26.0 | 8.4 | 358.9 | 198.0 | 62.8 | 69.8 |
| SIG 55-80, 10 (3) | 0 | 2,277 | 0 | 0 | 492 | 753 | 22 | 1,267 | 9 | 31.7 | 10.7 | 393.7 | 177.4 | 54.7 | 61.9 |
| SIG 55-85, 5 (7) | 0 | 3,926 | 0 | 0 | 762 | 948 | 16 | 1,725 | 12 | 25.8 | 8.3 | 359.7 | 198.6 | 63.0 | 70.4 |
| SIG 55-85, 10 (4) | 0 | 2,569 | 0 | 0 | 557 | 777 | 20 | 1,354 | 11 | 31.3 | 10.2 | 396.2 | 178.8 | 55.2 | 63.4 |

SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 7b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| SIG 45-75, 5 (7) | 0 | 4,572 | 0 | 0 | 929 | 1,588 | 15 | 2,533 | 12 | 27.9 | 7.3 | 366.7 | 233.6 | 58.1 | 73.6 |
| SIG 45-75, 10 (4) | 0 | 3,030 | 0 | 0 | 706 | 1,398 | 18 | 2,122 | 12 | 31.4 | 8.8 | 397.2 | 212.5 | 52.9 | 68.3 |
| SIG 45-80, 5 (8) | 0 | 4,893 | 0 | 0 | 991 | 1,606 | 14 | 2,611 | 13 | 27.3 | 6.9 | 367.3 | 235.7 | 59.0 | 75.1 |
| SIG 45-80, 10 (4) | 0 | 3,030 | 0 | 0 | 706 | 1,398 | 18 | 2,122 | 12 | 31.4 | 8.8 | 397.2 | 212.5 | 52.9 | 68.3 |
| SIG 45-85, 5 (9) | 0 | 5,112 | 0 | 0 | 1,027 | 1,612 | 13 | 2,653 | 14 | 27.2 | 6.8 | 368.1 | 236.1 | 59.1 | 75.5 |
| SIG 45-85, 10 (5) | 0 | 3,298 | 0 | 0 | 762 | 1,412 | 17 | 2,191 | 13 | 31.2 | 8.5 | 399.8 | 213.7 | 53.1 | 69.4 |
| SIG 50-75, 5 (6) | 0 | 3,807 | 0 | 0 | 820 | 1,450 | 16 | 2,287 | 12 | 29.1 | 7.8 | 386.1 | 221.1 | 56.3 | 71.9 |
| SIG 50-75, 10 (3) | 0 | 2,356 | 0 | 0 | 592 | 1,268 | 21 | 1,881 | 11 | 33.0 | 9.6 | 411.8 | 200.9 | 50.4 | 65.4 |
| SIG 50-80, 5 (7) | 0 | 4,129 | 0 | 0 | 882 | 1,468 | 15 | 2,365 | 13 | 28.5 | 7.4 | 386.9 | 223.2 | 57.3 | 73.4 |
| SIG 50-80, 10 (4) | 0 | 2,746 | 0 | 0 | 680 | 1,303 | 18 | 2,001 | 12 | 31.9 | 8.8 | 414.3 | 205.3 | 52.1 | 68.5 |
| SIG 50-85, 5 (8) | 0 | 4,349 | 0 | 0 | 919 | 1,474 | 14 | 2,408 | 14 | 28.4 | 7.3 | 387.7 | 223.6 | 57.3 | 73.8 |
| SIG 50-85, 10 (4) | 0 | 2,746 | 0 | 0 | 680 | 1,303 | 18 | 2,001 | 12 | 31.9 | 8.8 | 414.3 | 205.3 | 52.1 | 68.5 |
| SIG 55-75, 5 (5) | 0 | 3,092 | 0 | 0 | 715 | 1,265 | 18 | 1,998 | 12 | 31.2 | 8.8 | 414.8 | 199.8 | 53.1 | 68.4 |
| SIG 55-75, 10 (3) | 0 | 2,155 | 0 | 0 | 575 | 1,141 | 20 | 1,736 | 11 | 34.0 | 10.0 | 434.8 | 184.8 | 48.9 | 64.1 |
| SIG 55-80, 5 (6) | 0 | 3,416 | 0 | 0 | 777 | 1,284 | 16 | 2,077 | 13 | 30.6 | 8.4 | 415.6 | 202.0 | 54.0 | 69.9 |
| SIG 55-80, 10 (3) | 0 | 2,155 | 0 | 0 | 575 | 1,141 | 20 | 1,736 | 11 | 34.0 | 10.0 | 434.8 | 184.8 | 48.9 | 64.1 |
| SIG 55-85, 5 (7) | 0 | 3,637 | 0 | 0 | 814 | 1,290 | 16 | 2,120 | 13 | 30.5 | 8.2 | 416.3 | 202.4 | 54.1 | 70.3 |
| SIG 55-85, 10 (4) | 0 | 2,425 | 0 | 0 | 631 | 1,156 | 19 | 1,806 | 12 | 33.9 | 9.7 | 437.6 | 185.9 | 49.0 | 65.2 |

SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 7c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| SIG 45-75, 5 (7) | 0 | 5,128 | 5,128 | 0 | 759 | 883 | 27 | 1,669 | 9 | 28.4 | 9.9 | 265.1 | 192.6 | 60.4 | 63.2 |
| SIG 45-75, 10 (4) | 0 | 3,256 | 3,256 | 0 | 546 | 776 | 29 | 1,351 | 8 | 31.2 | 10.8 | 293.5 | 179.7 | 56.5 | 59.5 |
| SIG 45-80, 5 (8) | 0 | 5,535 | 5,535 | 0 | 816 | 902 | 25 | 1,743 | 10 | 26.9 | 9.3 | 260.6 | 195.6 | 62.5 | 65.3 |
| SIG 45-80, 10 (4) | 0 | 3,256 | 3,256 | 0 | 546 | 776 | 29 | 1,351 | 8 | 31.2 | 10.8 | 293.5 | 179.7 | 56.5 | 59.5 |
| SIG 45-85, 5 (9) | 0 | 5,817 | 5,817 | 0 | 855 | 913 | 24 | 1,792 | 11 | 26.3 | 9.0 | 260.2 | 196.5 | 63.4 | 66.3 |
| SIG 45-85, 10 (5) | 0 | 3,580 | 3,580 | 0 | 602 | 796 | 27 | 1,425 | 10 | 29.7 | 10.2 | 290.5 | 182.6 | 58.7 | 61.9 |
| SIG 50-75, 5 (6) | 0 | 4,298 | 4,298 | 0 | 656 | 810 | 28 | 1,493 | 9 | 29.7 | 10.3 | 290.8 | 181.1 | 58.6 | 61.5 |
| SIG 50-75, 10 (3) | 0 | 2,515 | 2,515 | 0 | 438 | 690 | 33 | 1,161 | 7 | 34.4 | 12.0 | 323.8 | 164.8 | 52.0 | 55.1 |
| SIG 50-80, 5 (7) | 0 | 4,705 | 4,705 | 0 | 712 | 829 | 26 | 1,567 | 10 | 28.3 | 9.7 | 287.1 | 183.7 | 60.6 | 63.6 |
| SIG 50-80, 10 (4) | 0 | 2,983 | 2,983 | 0 | 519 | 725 | 29 | 1,273 | 9 | 31.3 | 10.8 | 313.9 | 171.2 | 56.4 | 59.7 |
| SIG 50-85, 5 (8) | 0 | 4,987 | 4,987 | 0 | 752 | 839 | 25 | 1,616 | 10 | 27.6 | 9.5 | 285.7 | 184.4 | 61.6 | 64.6 |
| SIG 50-85, 10 (4) | 0 | 2,983 | 2,983 | 0 | 519 | 725 | 29 | 1,273 | 9 | 31.3 | 10.8 | 313.9 | 171.2 | 56.4 | 59.7 |
| SIG 55-75, 5 (5) | 0 | 3,494 | 3,494 | 0 | 556 | 716 | 30 | 1,301 | 9 | 31.9 | 11.1 | 328.7 | 163.1 | 55.5 | 58.6 |
| SIG 55-75, 10 (3) | 0 | 2,324 | 2,324 | 0 | 424 | 637 | 32 | 1,093 | 8 | 34.4 | 11.9 | 349.4 | 153.0 | 52.1 | 55.4 |
| SIG 55-80, 5 (6) | 0 | 3,902 | 3,902 | 0 | 614 | 735 | 28 | 1,377 | 9 | 30.5 | 10.5 | 324.0 | 165.9 | 57.5 | 60.7 |
| SIG 55-80, 10 (3) | 0 | 2,324 | 2,324 | 0 | 424 | 637 | 32 | 1,093 | 8 | 34.4 | 11.9 | 349.4 | 153.0 | 52.1 | 55.4 |
| SIG 55-85, 5 (7) | 0 | 4,184 | 4,184 | 0 | 653 | 745 | 27 | 1,425 | 10 | 29.8 | 10.2 | 323.0 | 166.9 | 58.5 | 61.8 |
| SIG 55-85, 10 (4) | 0 | 2,649 | 2,649 | 0 | 481 | 657 | 30 | 1,168 | 9 | 32.9 | 11.3 | 347.3 | 155.4 | 54.1 | 57.7 |

SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 8a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG+gFOBT screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| age to begin-age to end, screening interval (# of tests*) | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| SIG+gFOBT 45-75, 10_1 (4_31) | 13,505 | 2,288 | 0 | 0 | 1,549 | 1,431 | 6 | 2,986 | 12 | 13.1 | 3.0 | 208.5 | 297.3 | 81.3 | 89.3 |
| SIG+gFOBT 45-75, 10_2 (4_16) | 8,963 | 2,507 | 0 | 0 | 1,231 | 1,296 | 6 | 2,534 | 11 | 15.7 | 3.5 | 244.8 | 290.3 | 77.6 | 87.4 |
| SIG+gFOBT 45-75, 5_2 (7_16) | 8,223 | 3,834 | 0 | 0 | 1,368 | 1,395 | 6 | 2,768 | 12 | 13.7 | 3.2 | 217.7 | 294.1 | 80.4 | 88.7 |
| SIG+gFOBT 45-75, 5_3 (7_11) | 6,136 | 4,084 | 0 | 0 | 1,240 | 1,340 | 7 | 2,587 | 12 | 14.9 | 3.6 | 229.5 | 288.9 | 78.7 | 87.2 |
| SIG+gFOBT 45-80, 10_1 (4_36) | 14,574 | 2,427 | 0 | 0 | 1,669 | 1,463 | 4 | 3,136 | 14 | 12.0 | 2.4 | 207.4 | 300.1 | 82.8 | 91.3 |
| SIG+gFOBT 45-80, 10_2 (4_18) | 9,534 | 2,596 | 0 | 0 | 1,299 | 1,318 | 5 | 2,622 | 12 | 14.9 | 3.1 | 245.2 | 292.6 | 78.6 | 89.0 |
| SIG+gFOBT 45-80, 5_2 (8_18) | 8,787 | 4,094 | 0 | 0 | 1,465 | 1,424 | 4 | 2,893 | 13 | 12.8 | 2.7 | 217.3 | 296.6 | 81.7 | 90.4 |
| SIG+gFOBT 45-80, 5_3 (8_12) | 6,609 | 4,368 | 0 | 0 | 1,335 | 1,370 | 5 | 2,710 | 13 | 14.0 | 3.0 | 229.6 | 291.6 | 80.0 | 89.1 |
| SIG+gFOBT 45-85, 10_1 (5_41) | 15,322 | 2,537 | 0 | 0 | 1,755 | 1,482 | 3 | 3,239 | 15 | 11.6 | 2.2 | 207.9 | 300.9 | 83.3 | 92.1 |
| SIG+gFOBT 45-85, 10_2 (5_21) | 10,153 | 2,754 | 0 | 0 | 1,387 | 1,341 | 4 | 2,731 | 14 | 14.5 | 2.7 | 247.0 | 294.1 | 79.2 | 90.3 |
| SIG+gFOBT 45-85, 5_2 (9_21) | 9,291 | 4,277 | 0 | 0 | 1,543 | 1,442 | 3 | 2,988 | 14 | 12.5 | 2.4 | 218.4 | 297.5 | 82.1 | 91.3 |
| SIG+gFOBT 45-85, 5_3 (9_14) | 6,964 | 4,561 | 0 | 0 | 1,402 | 1,386 | 4 | 2,792 | 14 | 13.7 | 2.8 | 231.0 | 292.5 | 80.4 | 90.0 |
| SIG+gFOBT 50-75, 10_1 (3_26) | 11,100 | 1,926 | 0 | 0 | 1,312 | 1,297 | 8 | 2,616 | 12 | 16.2 | 4.1 | 264.8 | 270.5 | 76.8 | 85.4 |
| SIG+gFOBT 50-75, 10_2 (3_13) | 7,212 | 2,042 | 0 | 0 | 1,022 | 1,158 | 9 | 2,190 | 11 | 19.3 | 4.9 | 298.3 | 262.4 | 72.4 | 82.4 |
| SIG+gFOBT 50-75, 5_2 (6_13) | 6,689 | 3,211 | 0 | 0 | 1,162 | 1,262 | 8 | 2,431 | 12 | 17.0 | 4.3 | 274.3 | 267.0 | 75.7 | 84.6 |
| SIG+gFOBT 50-75, 5_3 (6_9) | 5,099 | 3,425 | 0 | 0 | 1,069 | 1,216 | 8 | 2,294 | 12 | 17.9 | 4.6 | 283.9 | 262.6 | 74.3 | 83.4 |
| SIG+gFOBT 50-80, 10_1 (4_31) | 12,172 | 2,091 | 0 | 0 | 1,438 | 1,332 | 6 | 2,776 | 13 | 15.0 | 3.5 | 263.7 | 273.5 | 78.5 | 87.6 |
| SIG+gFOBT 50-80, 10_2 (4_16) | 8,100 | 2,283 | 0 | 0 | 1,151 | 1,203 | 6 | 2,360 | 13 | 17.7 | 4.0 | 298.7 | 267.1 | 74.6 | 85.7 |
| SIG+gFOBT 50-80, 5_2 (7_16) | 7,423 | 3,473 | 0 | 0 | 1,275 | 1,295 | 6 | 2,576 | 13 | 15.9 | 3.7 | 274.1 | 270.0 | 77.3 | 86.7 |
| SIG+gFOBT 50-80, 5_3 (7_11) | 5,559 | 3,699 | 0 | 0 | 1,161 | 1,246 | 7 | 2,413 | 13 | 17.0 | 4.1 | 284.2 | 265.4 | 75.7 | 85.4 |
| SIG+gFOBT 50-85, 10_1 (4_36) | 12,922 | 2,188 | 0 | 0 | 1,521 | 1,350 | 5 | 2,875 | 15 | 14.7 | 3.3 | 264.1 | 274.4 | 79.0 | 88.3 |
| SIG+gFOBT 50-85, 10_2 (4_18) | 8,502 | 2,345 | 0 | 0 | 1,199 | 1,215 | 6 | 2,420 | 13 | 17.6 | 3.8 | 299.8 | 267.8 | 74.9 | 86.3 |
| SIG+gFOBT 50-85, 5_2 (8_18) | 7,818 | 3,651 | 0 | 0 | 1,342 | 1,311 | 5 | 2,658 | 14 | 15.7 | 3.5 | 274.9 | 270.7 | 77.6 | 87.4 |
| SIG+gFOBT 50-85, 5_3 (8_12) | 5,893 | 3,892 | 0 | 0 | 1,226 | 1,262 | 6 | 2,494 | 14 | 16.8 | 3.9 | 285.5 | 266.3 | 76.0 | 86.2 |
| SIG+gFOBT 55-75, 10_1 (3_21) | 8,817 | 1,625 | 0 | 0 | 1,096 | 1,135 | 10 | 2,241 | 12 | 20.6 | 5.5 | 334.1 | 237.1 | 70.6 | 80.3 |
| SIG+gFOBT 55-75, 10_2 (3_11) | 5,898 | 1,790 | 0 | 0 | 894 | 1,027 | 11 | 1,932 | 11 | 23.1 | 6.1 | 362.3 | 230.5 | 67.0 | 78.2 |
| SIG+gFOBT 55-75, 5_2 (5_11) | 5,432 | 2,622 | 0 | 0 | 983 | 1,104 | 11 | 2,097 | 12 | 21.4 | 5.8 | 342.5 | 233.5 | 69.4 | 79.3 |
| SIG+gFOBT 55-75, 5_3 (5_7) | 4,013 | 2,788 | 0 | 0 | 893 | 1,058 | 12 | 1,963 | 11 | 22.5 | 6.2 | 349.7 | 228.7 | 67.8 | 77.7 |
| SIG+gFOBT 55-80, 10_1 (3_26) | 9,891 | 1,749 | 0 | 0 | 1,212 | 1,167 | 9 | 2,387 | 13 | 19.6 | 5.0 | 333.3 | 239.7 | 72.0 | 82.1 |
| SIG+gFOBT 55-80, 10_2 (3_13) | 6,471 | 1,858 | 0 | 0 | 958 | 1,048 | 10 | 2,016 | 12 | 22.4 | 5.7 | 363.2 | 232.8 | 67.9 | 79.7 |
| SIG+gFOBT 55-80, 5_2 (6_13) | 5,985 | 2,877 | 0 | 0 | 1,079 | 1,134 | 9 | 2,221 | 13 | 20.5 | 5.3 | 342.3 | 235.9 | 70.7 | 81.1 |
| SIG+gFOBT 55-80, 5_3 (6_9) | 4,568 | 3,067 | 0 | 0 | 995 | 1,091 | 9 | 2,095 | 13 | 21.5 | 5.6 | 350.6 | 231.9 | 69.3 | 79.9 |
| SIG+gFOBT 55-85, 10_1 (4_31) | 10,643 | 1,861 | 0 | 0 | 1,299 | 1,186 | 8 | 2,493 | 14 | 19.2 | 4.8 | 334.0 | 240.6 | 72.5 | 82.9 |
| SIG+gFOBT 55-85, 10_2 (4_16) | 7,097 | 2,022 | 0 | 0 | 1,049 | 1,072 | 8 | 2,129 | 13 | 22.0 | 5.3 | 365.2 | 234.3 | 68.5 | 81.1 |
| SIG+gFOBT 55-85, 5_2 (7_16) | 6,501 | 3,056 | 0 | 0 | 1,157 | 1,152 | 8 | 2,317 | 14 | 20.2 | 5.1 | 343.4 | 236.9 | 71.2 | 81.9 |
| SIG+gFOBT 55-85, 5_3 (7_11) | 4,891 | 3,253 | 0 | 0 | 1,058 | 1,106 | 9 | 2,173 | 14 | 21.2 | 5.4 | 351.9 | 232.7 | 69.6 | 80.7 |

SIG = flexible sigmoidoscopy; gFOBT = highly-sensitive guaiac-based fecal occult blood test; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 8b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG+gFOBT screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality | Screening tests | | | | Follow-up | Surveillance | COLs for | Total | Compli- | CRC | CRC | LY with | LYG‡ | Reductions‡ (%) | |
| age to begin-age to end, screening interval (# of tests*) | Stool tests | SIGs | CTCs | COLs | COLs | COLs | symptoms | COLs | cations | cases | deaths† | CRC | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| SIG+gFOBT 45-75, 10_1 (4_31) | 13,058 | 2,016 | 0 | 0 | 1,525 | 1,676 | 10 | 3,212 | 13 | 26.3 | 5.6 | 385.0 | 260.3 | 60.4 | 80.0 |
| SIG+gFOBT 45-75, 10_2 (4_16) | 8,259 | 2,090 | 0 | 0 | 1,166 | 1,520 | 13 | 2,698 | 12 | 29.4 | 6.6 | 417.5 | 245.7 | 55.8 | 76.2 |
| SIG+gFOBT 45-75, 5_2 (7_16) | 7,406 | 3,400 | 0 | 0 | 1,312 | 1,663 | 12 | 2,987 | 13 | 26.9 | 6.1 | 383.2 | 253.3 | 59.5 | 78.2 |
| SIG+gFOBT 45-75, 5_3 (7_11) | 5,505 | 3,717 | 0 | 0 | 1,216 | 1,651 | 12 | 2,879 | 13 | 27.3 | 6.2 | 382.8 | 250.7 | 59.0 | 77.6 |
| SIG+gFOBT 45-80, 10_1 (4_36) | 14,103 | 2,016 | 0 | 0 | 1,609 | 1,686 | 9 | 3,304 | 14 | 26.0 | 5.2 | 387.3 | 262.3 | 60.9 | 81.2 |
| SIG+gFOBT 45-80, 10_2 (4_18) | 8,795 | 2,090 | 0 | 0 | 1,210 | 1,527 | 11 | 2,748 | 13 | 29.3 | 6.3 | 421.0 | 247.6 | 56.0 | 77.3 |
| SIG+gFOBT 45-80, 5_2 (8_18) | 7,880 | 3,649 | 0 | 0 | 1,401 | 1,684 | 10 | 3,095 | 14 | 26.3 | 5.5 | 385.4 | 256.3 | 60.6 | 80.2 |
| SIG+gFOBT 45-80, 5_3 (8_12) | 5,769 | 3,957 | 0 | 0 | 1,285 | 1,668 | 11 | 2,963 | 14 | 26.7 | 5.8 | 384.6 | 253.2 | 59.9 | 79.2 |
| SIG+gFOBT 45-85, 10_1 (5_41) | 14,915 | 2,161 | 0 | 0 | 1,704 | 1,698 | 8 | 3,410 | 15 | 25.8 | 4.9 | 389.4 | 263.7 | 61.2 | 82.3 |
| SIG+gFOBT 45-85, 10_2 (5_21) | 9,400 | 2,249 | 0 | 0 | 1,294 | 1,541 | 10 | 2,845 | 14 | 29.1 | 5.9 | 424.6 | 249.4 | 56.2 | 78.8 |
| SIG+gFOBT 45-85, 5_2 (9_21) | 8,399 | 3,782 | 0 | 0 | 1,466 | 1,690 | 9 | 3,165 | 14 | 26.2 | 5.3 | 387.2 | 257.1 | 60.6 | 80.8 |
| SIG+gFOBT 45-85, 5_3 (9_14) | 6,170 | 4,142 | 0 | 0 | 1,351 | 1,677 | 10 | 3,037 | 14 | 26.7 | 5.5 | 387.4 | 254.3 | 59.9 | 80.1 |
| SIG+gFOBT 50-75, 10_1 (3_26) | 10,562 | 1,633 | 0 | 0 | 1,276 | 1,525 | 12 | 2,814 | 13 | 28.1 | 6.3 | 403.4 | 244.9 | 57.8 | 77.2 |
| SIG+gFOBT 50-75, 10_2 (3_13) | 6,594 | 1,677 | 0 | 0 | 972 | 1,387 | 15 | 2,374 | 12 | 31.1 | 7.4 | 431.0 | 231.1 | 53.3 | 73.3 |
| SIG+gFOBT 50-75, 5_2 (6_13) | 5,947 | 2,882 | 0 | 0 | 1,129 | 1,525 | 12 | 2,667 | 13 | 28.0 | 6.5 | 400.8 | 239.9 | 57.9 | 76.6 |
| SIG+gFOBT 50-75, 5_3 (6_9) | 4,462 | 3,146 | 0 | 0 | 1,058 | 1,517 | 13 | 2,587 | 13 | 28.2 | 6.6 | 399.7 | 238.1 | 57.6 | 76.1 |
| SIG+gFOBT 50-80, 10_1 (4_31) | 11,686 | 1,844 | 0 | 0 | 1,414 | 1,554 | 10 | 2,977 | 14 | 27.0 | 5.6 | 405.1 | 249.2 | 59.5 | 80.0 |
| SIG+gFOBT 50-80, 10_2 (4_16) | 7,423 | 1,908 | 0 | 0 | 1,093 | 1,419 | 12 | 2,524 | 13 | 29.9 | 6.5 | 434.6 | 236.4 | 55.1 | 76.6 |
| SIG+gFOBT 50-80, 5_2 (7_16) | 6,666 | 3,079 | 0 | 0 | 1,225 | 1,542 | 11 | 2,778 | 14 | 27.5 | 6.0 | 403.1 | 242.6 | 58.7 | 78.3 |
| SIG+gFOBT 50-80, 5_3 (7_11) | 4,963 | 3,362 | 0 | 0 | 1,139 | 1,533 | 11 | 2,683 | 14 | 27.7 | 6.2 | 401.7 | 240.4 | 58.4 | 77.7 |
| SIG+gFOBT 50-85, 10_1 (4_36) | 12,442 | 1,844 | 0 | 0 | 1,475 | 1,558 | 9 | 3,042 | 15 | 26.9 | 5.4 | 406.6 | 249.9 | 59.6 | 80.5 |
| SIG+gFOBT 50-85, 10_2 (4_18) | 7,811 | 1,908 | 0 | 0 | 1,125 | 1,422 | 11 | 2,558 | 13 | 30.0 | 6.3 | 437.0 | 237.1 | 55.0 | 77.2 |
| SIG+gFOBT 50-85, 5_2 (8_18) | 7,009 | 3,248 | 0 | 0 | 1,284 | 1,550 | 10 | 2,844 | 14 | 27.4 | 5.8 | 405.1 | 243.5 | 58.8 | 79.0 |
| SIG+gFOBT 50-85, 5_3 (8_12) | 5,154 | 3,526 | 0 | 0 | 1,183 | 1,539 | 11 | 2,733 | 14 | 27.7 | 6.1 | 403.3 | 241.1 | 58.4 | 78.2 |
| SIG+gFOBT 55-75, 10_1 (3_21) | 8,346 | 1,506 | 0 | 0 | 1,100 | 1,348 | 13 | 2,461 | 13 | 29.7 | 7.1 | 429.3 | 221.9 | 55.4 | 74.4 |
| SIG+gFOBT 55-75, 10_2 (3_11) | 5,368 | 1,544 | 0 | 0 | 871 | 1,240 | 15 | 2,126 | 12 | 32.2 | 8.0 | 451.6 | 211.7 | 51.6 | 71.2 |
| SIG+gFOBT 55-75, 5_2 (5_11) | 4,866 | 2,339 | 0 | 0 | 964 | 1,330 | 14 | 2,308 | 13 | 30.2 | 7.5 | 428.5 | 217.0 | 54.6 | 72.9 |
| SIG+gFOBT 55-75, 5_3 (5_7) | 3,459 | 2,549 | 0 | 0 | 888 | 1,321 | 15 | 2,225 | 12 | 30.5 | 7.8 | 426.7 | 214.5 | 54.1 | 72.0 |
| SIG+gFOBT 55-80, 10_1 (3_26) | 9,391 | 1,506 | 0 | 0 | 1,184 | 1,358 | 12 | 2,554 | 13 | 29.4 | 6.8 | 431.6 | 223.9 | 55.8 | 75.6 |
| SIG+gFOBT 55-80, 10_2 (3_13) | 5,901 | 1,544 | 0 | 0 | 915 | 1,247 | 14 | 2,176 | 12 | 32.1 | 7.7 | 455.0 | 213.5 | 51.8 | 72.4 |
| SIG+gFOBT 55-80, 5_2 (6_13) | 5,334 | 2,588 | 0 | 0 | 1,053 | 1,351 | 13 | 2,417 | 14 | 29.5 | 7.0 | 430.4 | 220.0 | 55.6 | 74.9 |
| SIG+gFOBT 55-80, 5_3 (6_9) | 4,010 | 2,822 | 0 | 0 | 990 | 1,345 | 13 | 2,347 | 13 | 29.8 | 7.1 | 430.0 | 218.1 | 55.3 | 74.4 |
| SIG+gFOBT 55-85, 10_1 (4_31) | 10,210 | 1,651 | 0 | 0 | 1,280 | 1,371 | 11 | 2,662 | 14 | 29.2 | 6.5 | 433.7 | 225.3 | 56.2 | 76.7 |
| SIG+gFOBT 55-85, 10_2 (4_16) | 6,506 | 1,703 | 0 | 0 | 999 | 1,262 | 13 | 2,273 | 13 | 31.9 | 7.3 | 458.5 | 215.3 | 52.0 | 73.8 |
| SIG+gFOBT 55-85, 5_2 (7_16) | 5,855 | 2,722 | 0 | 0 | 1,118 | 1,358 | 12 | 2,488 | 14 | 29.5 | 6.8 | 432.2 | 220.8 | 55.7 | 75.6 |
| SIG+gFOBT 55-85, 5_3 (7_11) | 4,368 | 2,969 | 0 | 0 | 1,043 | 1,351 | 12 | 2,406 | 14 | 29.8 | 7.0 | 431.7 | 218.8 | 55.3 | 74.9 |

SIG = flexible sigmoidoscopy; gFOBT = highly-sensitive guaiac-based fecal occult blood test; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 8c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG+gFOBT screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality | Screening tests | | | | Follow-up | Surveillance | COLs for | Total | Compli- | CRC | CRC | LY with | LYG‡ | Reductions‡ (%) | |
| age to begin-age to end, screening interval (# of tests*) | Stool tests | SIGs | CTCs | COLs | COLs | COLs | symptoms | COLs | cations | cases | deaths† | CRC | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| SIG+gFOBT 45-75, 10_1 (4_31) | 13,791 | 2,301 | 2,301 | 0 | 1,519 | 1,419 | 8 | 2,946 | 12 | 11.6 | 3.2 | 136.3 | 275.2 | 83.8 | 88.1 |
| SIG+gFOBT 45-75, 10_2 (4_16) | 9,157 | 2,532 | 2,532 | 0 | 1,191 | 1,253 | 11 | 2,455 | 11 | 15.2 | 4.3 | 173.7 | 261.2 | 78.9 | 84.1 |
| SIG+gFOBT 45-75, 5_2 (7_16) | 8,525 | 3,926 | 3,926 | 0 | 1,315 | 1,306 | 11 | 2,632 | 12 | 14.2 | 4.0 | 162.8 | 263.8 | 80.2 | 84.9 |
| SIG+gFOBT 45-75, 5_3 (7_11) | 6,375 | 4,199 | 4,199 | 0 | 1,176 | 1,221 | 13 | 2,410 | 11 | 16.6 | 4.9 | 181.6 | 253.1 | 76.9 | 81.7 |
| SIG+gFOBT 45-80, 10_1 (4_36) | 14,951 | 2,448 | 2,448 | 0 | 1,639 | 1,447 | 6 | 3,092 | 14 | 10.0 | 2.5 | 132.6 | 278.8 | 86.0 | 90.7 |
| SIG+gFOBT 45-80, 10_2 (4_18) | 9,778 | 2,626 | 2,626 | 0 | 1,261 | 1,272 | 10 | 2,543 | 12 | 14.0 | 3.7 | 171.6 | 264.1 | 80.6 | 86.1 |
| SIG+gFOBT 45-80, 5_2 (8_18) | 9,153 | 4,211 | 4,211 | 0 | 1,411 | 1,333 | 9 | 2,753 | 13 | 12.6 | 3.4 | 157.7 | 267.6 | 82.4 | 87.5 |
| SIG+gFOBT 45-80, 5_3 (8_12) | 6,904 | 4,516 | 4,516 | 0 | 1,269 | 1,246 | 11 | 2,526 | 12 | 14.9 | 4.2 | 177.6 | 256.8 | 79.3 | 84.4 |
| SIG+gFOBT 45-85, 10_1 (5_41) | 15,779 | 2,568 | 2,568 | 0 | 1,729 | 1,460 | 5 | 3,194 | 15 | 9.1 | 2.1 | 130.4 | 280.8 | 87.3 | 92.1 |
| SIG+gFOBT 45-85, 10_2 (5_21) | 10,461 | 2,798 | 2,798 | 0 | 1,350 | 1,287 | 8 | 2,645 | 14 | 12.7 | 3.1 | 169.4 | 267.0 | 82.3 | 88.3 |
| SIG+gFOBT 45-85, 5_2 (9_21) | 9,734 | 4,418 | 4,418 | 0 | 1,493 | 1,346 | 7 | 2,846 | 14 | 11.7 | 2.9 | 156.1 | 269.7 | 83.7 | 89.1 |
| SIG+gFOBT 45-85, 5_3 (9_14) | 7,319 | 4,735 | 4,735 | 0 | 1,339 | 1,261 | 9 | 2,609 | 13 | 13.9 | 3.7 | 176.1 | 259.0 | 80.6 | 86.1 |
| SIG+gFOBT 50-75, 10_1 (3_26) | 11,376 | 1,940 | 1,940 | 0 | 1,288 | 1,283 | 10 | 2,581 | 12 | 13.9 | 3.9 | 178.1 | 257.5 | 80.6 | 85.4 |
| SIG+gFOBT 50-75, 10_2 (3_13) | 7,386 | 2,062 | 2,062 | 0 | 989 | 1,121 | 14 | 2,125 | 11 | 18.3 | 5.3 | 216.8 | 241.4 | 74.5 | 80.0 |
| SIG+gFOBT 50-75, 5_2 (6_13) | 6,949 | 3,297 | 3,297 | 0 | 1,113 | 1,180 | 13 | 2,305 | 12 | 16.6 | 4.8 | 202.3 | 245.9 | 76.9 | 82.0 |
| SIG+gFOBT 50-75, 5_3 (6_9) | 5,314 | 3,531 | 3,531 | 0 | 1,010 | 1,107 | 15 | 2,132 | 11 | 18.6 | 5.6 | 219.6 | 236.5 | 74.1 | 79.2 |
| SIG+gFOBT 50-80, 10_1 (4_31) | 12,537 | 2,115 | 2,115 | 0 | 1,414 | 1,314 | 8 | 2,735 | 13 | 12.1 | 3.2 | 173.0 | 261.3 | 83.2 | 88.2 |
| SIG+gFOBT 50-80, 10_2 (4_16) | 8,339 | 2,318 | 2,318 | 0 | 1,116 | 1,162 | 11 | 2,288 | 12 | 15.7 | 4.2 | 209.1 | 247.7 | 78.2 | 84.3 |
| SIG+gFOBT 50-80, 5_2 (7_16) | 7,774 | 3,585 | 3,585 | 0 | 1,227 | 1,212 | 10 | 2,449 | 13 | 14.6 | 3.9 | 196.4 | 250.8 | 79.7 | 85.2 |
| SIG+gFOBT 50-80, 5_3 (7_11) | 5,837 | 3,836 | 3,836 | 0 | 1,101 | 1,136 | 12 | 2,249 | 12 | 16.8 | 4.8 | 214.9 | 240.8 | 76.6 | 82.1 |
| SIG+gFOBT 50-85, 10_1 (4_36) | 13,372 | 2,220 | 2,220 | 0 | 1,500 | 1,327 | 7 | 2,834 | 15 | 11.3 | 2.8 | 171.9 | 263.4 | 84.3 | 89.6 |
| SIG+gFOBT 50-85, 10_2 (4_18) | 8,790 | 2,386 | 2,386 | 0 | 1,166 | 1,171 | 9 | 2,346 | 13 | 15.0 | 3.9 | 208.4 | 249.6 | 79.1 | 85.6 |
| SIG+gFOBT 50-85, 5_2 (8_18) | 8,228 | 3,786 | 3,786 | 0 | 1,296 | 1,224 | 9 | 2,529 | 14 | 13.8 | 3.6 | 195.1 | 252.2 | 80.8 | 86.5 |
| SIG+gFOBT 50-85, 5_3 (8_12) | 6,218 | 4,056 | 4,056 | 0 | 1,168 | 1,148 | 11 | 2,327 | 13 | 16.0 | 4.4 | 212.9 | 242.4 | 77.8 | 83.5 |
| SIG+gFOBT 55-75, 10_1 (3_21) | 9,070 | 1,642 | 1,642 | 0 | 1,075 | 1,120 | 13 | 2,207 | 12 | 17.2 | 5.0 | 234.2 | 231.4 | 76.1 | 81.4 |
| SIG+gFOBT 55-75, 10_2 (3_11) | 6,061 | 1,815 | 1,815 | 0 | 862 | 991 | 16 | 1,869 | 11 | 20.6 | 6.1 | 264.3 | 218.1 | 71.3 | 77.2 |
| SIG+gFOBT 55-75, 5_2 (5_11) | 5,674 | 2,700 | 2,700 | 0 | 940 | 1,032 | 15 | 1,987 | 11 | 19.7 | 5.9 | 254.7 | 220.9 | 72.6 | 78.1 |
| SIG+gFOBT 55-75, 5_3 (5_7) | 4,183 | 2,881 | 2,881 | 0 | 838 | 961 | 18 | 1,817 | 11 | 22.2 | 6.8 | 271.0 | 210.8 | 69.1 | 74.6 |
| SIG+gFOBT 55-80, 10_1 (3_26) | 10,238 | 1,773 | 1,773 | 0 | 1,194 | 1,147 | 11 | 2,351 | 13 | 15.5 | 4.3 | 229.4 | 235.2 | 78.4 | 84.0 |
| SIG+gFOBT 55-80, 10_2 (3_13) | 6,685 | 1,888 | 1,888 | 0 | 929 | 1,010 | 14 | 1,953 | 12 | 19.5 | 5.5 | 262.6 | 221.5 | 72.9 | 79.3 |
| SIG+gFOBT 55-80, 5_2 (6_13) | 6,289 | 2,980 | 2,980 | 0 | 1,035 | 1,059 | 13 | 2,107 | 12 | 18.1 | 5.2 | 250.3 | 224.5 | 74.8 | 80.7 |
| SIG+gFOBT 55-80, 5_3 (6_9) | 4,815 | 3,191 | 3,191 | 0 | 941 | 994 | 15 | 1,950 | 12 | 20.1 | 5.9 | 265.4 | 215.7 | 72.1 | 77.9 |
| SIG+gFOBT 55-85, 10_1 (4_31) | 11,070 | 1,896 | 1,896 | 0 | 1,284 | 1,161 | 9 | 2,454 | 14 | 14.7 | 3.9 | 228.2 | 236.7 | 79.6 | 85.4 |
| SIG+gFOBT 55-85, 10_2 (4_16) | 7,374 | 2,067 | 2,067 | 0 | 1,020 | 1,025 | 12 | 2,057 | 13 | 18.2 | 4.9 | 260.0 | 224.1 | 74.6 | 81.5 |
| SIG+gFOBT 55-85, 5_2 (7_16) | 6,885 | 3,182 | 3,182 | 0 | 1,117 | 1,073 | 11 | 2,201 | 14 | 17.1 | 4.7 | 248.5 | 226.5 | 76.2 | 82.4 |
| SIG+gFOBT 55-85, 5_3 (7_11) | 5,190 | 3,403 | 3,403 | 0 | 1,006 | 1,006 | 14 | 2,025 | 13 | 19.2 | 5.5 | 264.2 | 217.8 | 73.2 | 79.5 |

SIG = flexible sigmoidoscopy; gFOBT = highly-sensitive guaiac-based fecal occult blood test; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 9a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG+FIT screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy Modality age to begin-age to end, screening interval (# of tests*) | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| SIG+FIT 45-75, 10_1 (4_31) | 16,427 | 2,553 | 0 | 0 | 1,197 | 1,357 | 6 | 2,560 | 12 | 13.3 | 3.0 | 214.2 | 297.9 | 80.9 | 89.4 |
| SIG+FIT 45-75, 10_2 (4_16) | 9,933 | 2,750 | 0 | 0 | 976 | 1,232 | 6 | 2,214 | 11 | 16.1 | 3.5 | 253.4 | 290.4 | 76.9 | 87.3 |
| SIG+FIT 45-75, 5_2 (7_16) | 8,998 | 4,258 | 0 | 0 | 1,154 | 1,352 | 6 | 2,511 | 12 | 14.0 | 3.2 | 222.3 | 294.3 | 80.0 | 88.7 |
| SIG+FIT 45-75, 5_3 (7_11) | 6,508 | 4,422 | 0 | 0 | 1,077 | 1,306 | 6 | 2,389 | 11 | 15.2 | 3.6 | 234.4 | 289.3 | 78.3 | 87.3 |
| SIG+FIT 45-80, 10_1 (4_36) | 17,761 | 2,662 | 0 | 0 | 1,281 | 1,386 | 4 | 2,670 | 13 | 12.4 | 2.5 | 213.6 | 300.4 | 82.3 | 91.2 |
| SIG+FIT 45-80, 10_2 (4_18) | 10,573 | 2,807 | 0 | 0 | 1,020 | 1,249 | 5 | 2,274 | 12 | 15.6 | 3.1 | 254.4 | 292.5 | 77.8 | 88.8 |
| SIG+FIT 45-80, 5_2 (8_18) | 9,635 | 4,546 | 0 | 0 | 1,238 | 1,381 | 4 | 2,623 | 13 | 13.0 | 2.7 | 222.1 | 296.7 | 81.4 | 90.5 |
| SIG+FIT 45-80, 5_3 (8_12) | 6,977 | 4,727 | 0 | 0 | 1,157 | 1,334 | 5 | 2,496 | 13 | 14.2 | 3.0 | 234.8 | 292.0 | 79.6 | 89.2 |
| SIG+FIT 45-85, 10_1 (5_41) | 18,715 | 2,804 | 0 | 0 | 1,355 | 1,405 | 3 | 2,763 | 14 | 12.0 | 2.2 | 214.3 | 301.4 | 82.8 | 92.1 |
| SIG+FIT 45-85, 10_2 (5_21) | 11,285 | 3,001 | 0 | 0 | 1,098 | 1,273 | 3 | 2,374 | 13 | 15.1 | 2.7 | 256.8 | 294.1 | 78.3 | 90.2 |
| SIG+FIT 45-85, 5_2 (9_21) | 10,192 | 4,742 | 0 | 0 | 1,302 | 1,398 | 3 | 2,702 | 14 | 12.8 | 2.4 | 223.3 | 297.6 | 81.7 | 91.3 |
| SIG+FIT 45-85, 5_3 (9_14) | 7,372 | 4,931 | 0 | 0 | 1,215 | 1,350 | 4 | 2,569 | 14 | 14.0 | 2.8 | 236.4 | 292.9 | 79.9 | 90.0 |
| SIG+FIT 50-75, 10_1 (3_26) | 13,393 | 2,097 | 0 | 0 | 1,014 | 1,225 | 8 | 2,248 | 11 | 16.7 | 4.2 | 270.8 | 270.4 | 76.1 | 85.2 |
| SIG+FIT 50-75, 10_2 (3_13) | 7,942 | 2,196 | 0 | 0 | 810 | 1,097 | 10 | 1,917 | 10 | 20.0 | 5.0 | 306.2 | 262.0 | 71.4 | 82.0 |
| SIG+FIT 50-75, 5_2 (6_13) | 7,296 | 3,559 | 0 | 0 | 991 | 1,225 | 8 | 2,224 | 11 | 17.2 | 4.3 | 277.9 | 267.2 | 75.4 | 84.6 |
| SIG+FIT 50-75, 5_3 (6_9) | 5,367 | 3,700 | 0 | 0 | 934 | 1,185 | 8 | 2,127 | 11 | 18.2 | 4.6 | 288.1 | 263.1 | 74.0 | 83.4 |
| SIG+FIT 50-80, 10_1 (4_31) | 14,761 | 2,320 | 0 | 0 | 1,125 | 1,265 | 6 | 2,395 | 13 | 15.4 | 3.5 | 269.7 | 273.8 | 78.0 | 87.6 |
| SIG+FIT 50-80, 10_2 (4_16) | 8,960 | 2,494 | 0 | 0 | 925 | 1,144 | 6 | 2,076 | 12 | 18.2 | 4.0 | 307.1 | 267.2 | 73.9 | 85.6 |
| SIG+FIT 50-80, 5_2 (7_16) | 8,109 | 3,846 | 0 | 0 | 1,085 | 1,257 | 6 | 2,347 | 13 | 16.1 | 3.7 | 278.2 | 270.2 | 76.9 | 86.7 |
| SIG+FIT 50-80, 5_3 (7_11) | 5,887 | 3,997 | 0 | 0 | 1,016 | 1,214 | 6 | 2,237 | 12 | 17.3 | 4.1 | 288.8 | 265.9 | 75.3 | 85.5 |
| SIG+FIT 50-85, 10_1 (4_36) | 15,698 | 2,396 | 0 | 0 | 1,184 | 1,280 | 5 | 2,469 | 14 | 15.1 | 3.3 | 270.3 | 274.6 | 78.4 | 88.4 |
| SIG+FIT 50-85, 10_2 (4_18) | 9,412 | 2,534 | 0 | 0 | 957 | 1,154 | 5 | 2,116 | 13 | 18.1 | 3.8 | 308.5 | 267.9 | 74.1 | 86.2 |
| SIG+FIT 50-85, 5_2 (8_18) | 8,557 | 4,041 | 0 | 0 | 1,143 | 1,272 | 5 | 2,419 | 14 | 15.9 | 3.5 | 279.3 | 271.0 | 77.2 | 87.4 |
| SIG+FIT 50-85, 5_3 (8_12) | 6,217 | 4,202 | 0 | 0 | 1,071 | 1,229 | 6 | 2,305 | 13 | 17.0 | 3.8 | 290.1 | 266.8 | 75.6 | 86.2 |
| SIG+FIT 55-75, 10_1 (3_21) | 10,553 | 1,817 | 0 | 0 | 874 | 1,080 | 10 | 1,965 | 11 | 20.8 | 5.5 | 339.0 | 237.6 | 70.2 | 80.4 |
| SIG+FIT 55-75, 10_2 (3_11) | 6,468 | 1,956 | 0 | 0 | 733 | 981 | 11 | 1,725 | 11 | 23.4 | 6.1 | 368.2 | 230.9 | 66.5 | 78.2 |
| SIG+FIT 55-75, 5_2 (5_11) | 5,893 | 2,893 | 0 | 0 | 846 | 1,071 | 11 | 1,928 | 11 | 21.6 | 5.8 | 345.9 | 233.9 | 69.1 | 79.4 |
| SIG+FIT 55-75, 5_3 (5_7) | 4,200 | 3,003 | 0 | 0 | 789 | 1,031 | 12 | 1,832 | 11 | 22.7 | 6.2 | 353.1 | 229.2 | 67.6 | 77.7 |
| SIG+FIT 55-80, 10_1 (3_26) | 11,892 | 1,902 | 0 | 0 | 954 | 1,107 | 9 | 2,069 | 12 | 19.9 | 5.0 | 338.7 | 240.1 | 71.5 | 82.1 |
| SIG+FIT 55-80, 10_2 (3_13) | 7,111 | 1,997 | 0 | 0 | 774 | 997 | 10 | 1,781 | 11 | 22.9 | 5.7 | 369.6 | 233.0 | 67.2 | 79.6 |
| SIG+FIT 55-80, 5_2 (6_13) | 6,514 | 3,178 | 0 | 0 | 930 | 1,101 | 9 | 2,039 | 12 | 20.7 | 5.3 | 345.9 | 236.4 | 70.5 | 81.2 |
| SIG+FIT 55-80, 5_3 (6_9) | 4,803 | 3,305 | 0 | 0 | 877 | 1,063 | 9 | 1,950 | 12 | 21.7 | 5.6 | 354.4 | 232.5 | 69.0 | 80.0 |
| SIG+FIT 55-85, 10_1 (4_31) | 12,853 | 2,053 | 0 | 0 | 1,030 | 1,128 | 8 | 2,166 | 14 | 19.6 | 4.7 | 339.7 | 241.1 | 72.0 | 83.1 |
| SIG+FIT 55-85, 10_2 (4_16) | 7,830 | 2,197 | 0 | 0 | 854 | 1,022 | 8 | 1,884 | 13 | 22.5 | 5.3 | 372.1 | 234.7 | 67.9 | 81.1 |
| SIG+FIT 55-85, 5_2 (7_16) | 7,087 | 3,372 | 0 | 0 | 994 | 1,118 | 8 | 2,119 | 14 | 20.4 | 5.0 | 347.3 | 237.3 | 70.8 | 82.0 |
| SIG+FIT 55-85, 5_3 (7_11) | 5,168 | 3,505 | 0 | 0 | 933 | 1,079 | 8 | 2,020 | 13 | 21.5 | 5.4 | 356.0 | 233.4 | 69.3 | 80.8 |

SIG = flexible sigmoidoscopy; FIT = fecal immunochemical test; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 9b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG+FIT screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality | Screening tests | | | | Follow-up | Surveillance | COLs for | Total | Compli- | CRC | CRC | LY with | LYG‡ | Reductions‡ (%) | |
| age to begin-age to end, screening interval (# of tests*) | Stool tests | SIGs | CTCs | COLs | COLs | COLs | symptoms | COLs | cations | cases | deaths† | CRC | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| SIG+FIT 45-75, 10_1 (4__31) | 15,711 | 2,397 | 0 | 0 | 1,196 | 1,620 | 10 | 2,826 | 13 | 26.4 | 5.5 | 387.6 | 262.5 | 60.3 | 80.4 |
| SIG+FIT 45-75, 10_2 (4__16) | 9,206 | 2,381 | 0 | 0 | 946 | 1,478 | 12 | 2,436 | 12 | 29.6 | 6.5 | 421.2 | 247.7 | 55.6 | 76.5 |
| SIG+FIT 45-75, 5_2 (7__16) | 8,154 | 3,824 | 0 | 0 | 1,126 | 1,641 | 11 | 2,779 | 13 | 26.9 | 5.9 | 384.1 | 255.3 | 59.6 | 78.6 |
| SIG+FIT 45-75, 5_3 (7__11) | 5,868 | 4,014 | 0 | 0 | 1,068 | 1,630 | 12 | 2,710 | 13 | 27.4 | 6.2 | 385.3 | 251.9 | 58.9 | 77.8 |
| SIG+FIT 45-80, 10_1 (4__36) | 17,016 | 2,397 | 0 | 0 | 1,249 | 1,627 | 9 | 2,885 | 13 | 26.1 | 5.1 | 390.0 | 264.6 | 60.8 | 81.6 |
| SIG+FIT 45-80, 10_2 (4__18) | 9,822 | 2,381 | 0 | 0 | 972 | 1,483 | 11 | 2,467 | 12 | 29.5 | 6.2 | 425.1 | 249.8 | 55.7 | 77.7 |
| SIG+FIT 45-80, 5_2 (8__18) | 8,691 | 4,106 | 0 | 0 | 1,205 | 1,662 | 10 | 2,877 | 14 | 26.2 | 5.4 | 386.4 | 258.5 | 60.7 | 80.7 |
| SIG+FIT 45-80, 5_3 (8__12) | 6,154 | 4,274 | 0 | 0 | 1,131 | 1,647 | 10 | 2,788 | 13 | 26.8 | 5.7 | 387.1 | 254.3 | 59.8 | 79.4 |
| SIG+FIT 45-85, 10_1 (5__41) | 18,030 | 2,585 | 0 | 0 | 1,328 | 1,640 | 8 | 2,976 | 14 | 25.8 | 4.8 | 392.1 | 266.0 | 61.2 | 82.8 |
| SIG+FIT 45-85, 10_2 (5__21) | 10,518 | 2,571 | 0 | 0 | 1,042 | 1,498 | 10 | 2,550 | 13 | 29.3 | 5.8 | 429.0 | 251.6 | 56.0 | 79.2 |
| SIG+FIT 45-85, 5_2 (9__21) | 9,272 | 4,264 | 0 | 0 | 1,255 | 1,668 | 9 | 2,931 | 14 | 26.1 | 5.2 | 388.3 | 259.3 | 60.7 | 81.3 |
| SIG+FIT 45-85, 5_3 (9__14) | 6,588 | 4,476 | 0 | 0 | 1,186 | 1,656 | 9 | 2,851 | 14 | 26.7 | 5.5 | 390.0 | 255.5 | 59.8 | 80.3 |
| SIG+FIT 50-75, 10_1 (3__26) | 12,642 | 1,903 | 0 | 0 | 1,004 | 1,474 | 12 | 2,490 | 12 | 28.2 | 6.3 | 406.2 | 246.2 | 57.6 | 77.4 |
| SIG+FIT 50-75, 10_2 (3__13) | 7,306 | 1,886 | 0 | 0 | 793 | 1,349 | 15 | 2,157 | 11 | 31.2 | 7.4 | 434.4 | 232.5 | 53.1 | 73.4 |
| SIG+FIT 50-75, 5_2 (6__13) | 6,523 | 3,221 | 0 | 0 | 983 | 1,505 | 12 | 2,501 | 13 | 28.0 | 6.4 | 401.9 | 241.1 | 57.9 | 76.8 |
| SIG+FIT 50-75, 5_3 (6__9) | 4,737 | 3,380 | 0 | 0 | 940 | 1,498 | 13 | 2,451 | 13 | 28.3 | 6.6 | 401.9 | 238.8 | 57.5 | 76.2 |
| SIG+FIT 50-80, 10_1 (4__31) | 14,039 | 2,177 | 0 | 0 | 1,121 | 1,504 | 9 | 2,635 | 14 | 27.0 | 5.4 | 407.6 | 250.9 | 59.5 | 80.4 |
| SIG+FIT 50-80, 10_2 (4__16) | 8,260 | 2,164 | 0 | 0 | 898 | 1,383 | 11 | 2,291 | 13 | 30.0 | 6.4 | 438.0 | 238.1 | 54.9 | 77.0 |
| SIG+FIT 50-80, 5_2 (7__16) | 7,328 | 3,453 | 0 | 0 | 1,060 | 1,522 | 11 | 2,592 | 13 | 27.4 | 6.0 | 404.2 | 243.9 | 58.8 | 78.6 |
| SIG+FIT 50-80, 5_3 (7__11) | 5,284 | 3,625 | 0 | 0 | 1,008 | 1,514 | 11 | 2,534 | 13 | 27.8 | 6.2 | 404.0 | 241.2 | 58.3 | 77.8 |
| SIG+FIT 50-85, 10_1 (4__36) | 14,983 | 2,177 | 0 | 0 | 1,159 | 1,507 | 9 | 2,675 | 14 | 26.9 | 5.3 | 409.1 | 251.6 | 59.6 | 81.0 |
| SIG+FIT 50-85, 10_2 (4__18) | 8,706 | 2,164 | 0 | 0 | 917 | 1,385 | 11 | 2,313 | 13 | 30.1 | 6.2 | 440.5 | 238.9 | 54.8 | 77.6 |
| SIG+FIT 50-85, 5_2 (8__18) | 7,717 | 3,646 | 0 | 0 | 1,111 | 1,530 | 10 | 2,650 | 14 | 27.4 | 5.7 | 406.3 | 244.8 | 58.9 | 79.3 |
| SIG+FIT 50-85, 5_3 (8__12) | 5,491 | 3,802 | 0 | 0 | 1,048 | 1,520 | 11 | 2,579 | 14 | 27.7 | 6.0 | 405.6 | 241.9 | 58.3 | 78.4 |
| SIG+FIT 55-75, 10_1 (3__21) | 9,903 | 1,743 | 0 | 0 | 891 | 1,308 | 13 | 2,212 | 12 | 29.7 | 7.0 | 431.3 | 223.0 | 55.3 | 74.7 |
| SIG+FIT 55-75, 10_2 (3__11) | 5,908 | 1,728 | 0 | 0 | 731 | 1,211 | 15 | 1,957 | 12 | 32.3 | 7.9 | 454.3 | 212.7 | 51.4 | 71.4 |
| SIG+FIT 55-75, 5_2 (5__11) | 5,303 | 2,601 | 0 | 0 | 844 | 1,313 | 14 | 2,171 | 12 | 30.3 | 7.5 | 429.5 | 218.1 | 54.5 | 73.1 |
| SIG+FIT 55-75, 5_3 (5__7) | 3,653 | 2,729 | 0 | 0 | 799 | 1,306 | 15 | 2,121 | 12 | 30.6 | 7.8 | 428.0 | 215.0 | 54.0 | 72.1 |
| SIG+FIT 55-80, 10_1 (3__26) | 11,214 | 1,743 | 0 | 0 | 944 | 1,316 | 12 | 2,272 | 13 | 29.4 | 6.7 | 433.7 | 225.1 | 55.8 | 75.9 |
| SIG+FIT 55-80, 10_2 (3__13) | 6,524 | 1,728 | 0 | 0 | 757 | 1,217 | 14 | 1,988 | 12 | 32.2 | 7.6 | 458.2 | 214.8 | 51.6 | 72.6 |
| SIG+FIT 55-80, 5_2 (6__13) | 5,839 | 2,884 | 0 | 0 | 924 | 1,334 | 12 | 2,270 | 13 | 29.5 | 6.9 | 431.6 | 221.3 | 55.7 | 75.2 |
| SIG+FIT 55-80, 5_3 (6__9) | 4,251 | 3,027 | 0 | 0 | 885 | 1,330 | 13 | 2,228 | 13 | 29.8 | 7.1 | 431.6 | 218.9 | 55.2 | 74.6 |
| SIG+FIT 55-85, 10_1 (4__31) | 12,233 | 1,931 | 0 | 0 | 1,024 | 1,329 | 11 | 2,364 | 14 | 29.2 | 6.3 | 435.9 | 226.6 | 56.2 | 77.2 |
| SIG+FIT 55-85, 10_2 (4__16) | 7,222 | 1,919 | 0 | 0 | 828 | 1,232 | 12 | 2,072 | 13 | 32.0 | 7.2 | 461.8 | 216.7 | 51.9 | 74.1 |
| SIG+FIT 55-85, 5_2 (7__16) | 6,422 | 3,043 | 0 | 0 | 974 | 1,340 | 12 | 2,326 | 14 | 29.5 | 6.7 | 433.5 | 222.1 | 55.7 | 75.9 |
| SIG+FIT 55-85, 5_3 (7__11) | 4,641 | 3,194 | 0 | 0 | 929 | 1,335 | 12 | 2,277 | 14 | 29.8 | 6.9 | 433.4 | 219.6 | 55.2 | 75.1 |

SIG = flexible sigmoidoscopy; FIT = fecal immunochemical test; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 9c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with SIG+FIT screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality | Screening tests | | | | Follow-up | Surveillance | COLs for | Total | Compli- | CRC | CRC | LY with | LYG‡ | Reductions‡ (%) | |
| age to begin-age to end, screening interval (# of tests*) | Stool tests | SIGs | CTCs | COLs | COLs | COLs | symptoms | COLs | cations | cases | deaths† | CRC | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| SIG+FIT 45-75, 10_1 (4_31) | 16,356 | 2,523 | 2,523 | 0 | 1,188 | 1,409 | 9 | 2,606 | 12 | 12.3 | 3.3 | 148.8 | 274.1 | 82.8 | 87.8 |
| SIG+FIT 45-75, 10_2 (4_16) | 10,007 | 2,741 | 2,741 | 0 | 952 | 1,232 | 12 | 2,196 | 11 | 16.1 | 4.4 | 187.7 | 258.9 | 77.5 | 83.4 |
| SIG+FIT 45-75, 5_2 (7_16) | 9,231 | 4,307 | 4,307 | 0 | 1,109 | 1,289 | 11 | 2,410 | 12 | 15.0 | 4.2 | 173.5 | 262.1 | 79.1 | 84.3 |
| SIG+FIT 45-75, 5_3 (7_11) | 6,720 | 4,506 | 4,506 | 0 | 1,019 | 1,203 | 14 | 2,236 | 11 | 17.5 | 5.1 | 193.2 | 250.6 | 75.7 | 80.9 |
| SIG+FIT 45-80, 10_1 (4_36) | 17,748 | 2,637 | 2,637 | 0 | 1,275 | 1,435 | 6 | 2,717 | 13 | 10.8 | 2.6 | 144.9 | 278.3 | 85.0 | 90.3 |
| SIG+FIT 45-80, 10_2 (4_18) | 10,688 | 2,802 | 2,802 | 0 | 999 | 1,250 | 10 | 2,259 | 12 | 15.0 | 3.9 | 184.8 | 262.4 | 79.1 | 85.4 |
| SIG+FIT 45-80, 5_2 (8_18) | 9,927 | 4,619 | 4,619 | 0 | 1,192 | 1,315 | 9 | 2,516 | 13 | 13.4 | 3.5 | 169.2 | 265.9 | 81.3 | 86.9 |
| SIG+FIT 45-80, 5_3 (8_12) | 7,238 | 4,841 | 4,841 | 0 | 1,097 | 1,228 | 11 | 2,336 | 12 | 15.8 | 4.4 | 188.6 | 255.0 | 78.1 | 83.7 |
| SIG+FIT 45-85, 10_1 (5_41) | 18,755 | 2,786 | 2,786 | 0 | 1,350 | 1,448 | 5 | 2,804 | 14 | 9.9 | 2.2 | 143.1 | 279.9 | 86.2 | 91.9 |
| SIG+FIT 45-85, 10_2 (5_21) | 11,451 | 3,007 | 3,007 | 0 | 1,075 | 1,264 | 8 | 2,347 | 13 | 13.8 | 3.3 | 183.8 | 264.9 | 80.8 | 87.7 |
| SIG+FIT 45-85, 5_2 (9_21) | 10,558 | 4,837 | 4,837 | 0 | 1,259 | 1,328 | 7 | 2,594 | 14 | 12.5 | 3.0 | 168.5 | 268.3 | 82.5 | 88.7 |
| SIG+FIT 45-85, 5_3 (9_14) | 7,695 | 5,071 | 5,071 | 0 | 1,157 | 1,242 | 10 | 2,409 | 13 | 14.8 | 3.9 | 187.3 | 257.7 | 79.4 | 85.6 |
| SIG+FIT 50-75, 10_1 (3_26) | 13,404 | 2,079 | 2,079 | 0 | 1,012 | 1,267 | 11 | 2,289 | 12 | 14.8 | 4.1 | 190.4 | 255.8 | 79.3 | 84.7 |
| SIG+FIT 50-75, 10_2 (3_13) | 8,033 | 2,192 | 2,192 | 0 | 792 | 1,098 | 15 | 1,905 | 11 | 19.4 | 5.6 | 228.5 | 239.0 | 73.0 | 79.0 |
| SIG+FIT 50-75, 5_2 (6_13) | 7,506 | 3,611 | 3,611 | 0 | 949 | 1,163 | 13 | 2,125 | 11 | 17.4 | 5.0 | 212.1 | 244.1 | 75.8 | 81.4 |
| SIG+FIT 50-75, 5_3 (6_9) | 5,559 | 3,780 | 3,780 | 0 | 880 | 1,089 | 15 | 1,984 | 11 | 19.4 | 5.8 | 228.1 | 234.6 | 72.9 | 78.4 |
| SIG+FIT 50-80, 10_1 (4_31) | 14,812 | 2,307 | 2,307 | 0 | 1,120 | 1,300 | 8 | 2,428 | 13 | 12.8 | 3.2 | 184.3 | 260.9 | 82.2 | 88.1 |
| SIG+FIT 50-80, 10_2 (4_16) | 9,098 | 2,500 | 2,500 | 0 | 903 | 1,139 | 11 | 2,053 | 12 | 16.6 | 4.4 | 221.5 | 246.3 | 76.9 | 83.7 |
| SIG+FIT 50-80, 5_2 (7_16) | 8,405 | 3,922 | 3,922 | 0 | 1,044 | 1,193 | 10 | 2,248 | 13 | 15.4 | 4.1 | 207.1 | 249.3 | 78.5 | 84.7 |
| SIG+FIT 50-80, 5_3 (7_11) | 6,144 | 4,108 | 4,108 | 0 | 961 | 1,116 | 13 | 2,090 | 12 | 17.6 | 5.0 | 223.9 | 239.0 | 75.4 | 81.5 |
| SIG+FIT 50-85, 10_1 (4_36) | 15,814 | 2,389 | 2,389 | 0 | 1,183 | 1,313 | 7 | 2,502 | 14 | 12.1 | 2.8 | 184.2 | 262.6 | 83.1 | 89.4 |
| SIG+FIT 50-85, 10_2 (4_18) | 9,591 | 2,544 | 2,544 | 0 | 937 | 1,147 | 10 | 2,094 | 13 | 16.1 | 4.1 | 221.2 | 247.7 | 77.6 | 84.9 |
| SIG+FIT 50-85, 5_2 (8_18) | 8,906 | 4,138 | 4,138 | 0 | 1,103 | 1,205 | 9 | 2,317 | 13 | 14.6 | 3.7 | 206.3 | 250.7 | 79.6 | 86.1 |
| SIG+FIT 50-85, 5_3 (8_12) | 6,516 | 4,338 | 4,338 | 0 | 1,016 | 1,129 | 11 | 2,157 | 13 | 16.8 | 4.6 | 222.9 | 240.9 | 76.5 | 83.0 |
| SIG+FIT 55-75, 10_1 (3_21) | 10,606 | 1,808 | 1,808 | 0 | 868 | 1,105 | 13 | 1,986 | 12 | 17.9 | 5.1 | 244.3 | 230.4 | 75.1 | 81.1 |
| SIG+FIT 55-75, 10_2 (3_11) | 6,569 | 1,961 | 1,961 | 0 | 710 | 970 | 16 | 1,697 | 11 | 21.5 | 6.3 | 274.3 | 216.7 | 70.0 | 76.6 |
| SIG+FIT 55-75, 5_2 (5_11) | 6,100 | 2,945 | 2,945 | 0 | 808 | 1,014 | 16 | 1,838 | 11 | 20.6 | 6.1 | 264.1 | 219.2 | 71.4 | 77.4 |
| SIG+FIT 55-75, 5_3 (5_7) | 4,355 | 3,077 | 3,077 | 0 | 738 | 944 | 18 | 1,700 | 10 | 23.0 | 7.0 | 278.7 | 209.0 | 68.0 | 73.7 |
| SIG+FIT 55-80, 10_1 (3_26) | 12,010 | 1,898 | 1,898 | 0 | 952 | 1,131 | 11 | 2,094 | 13 | 16.4 | 4.4 | 240.3 | 234.1 | 77.2 | 83.5 |
| SIG+FIT 55-80, 10_2 (3_13) | 7,255 | 2,005 | 2,005 | 0 | 756 | 989 | 14 | 1,759 | 11 | 20.4 | 5.8 | 272.5 | 219.9 | 71.6 | 78.5 |
| SIG+FIT 55-80, 5_2 (6_13) | 6,780 | 3,254 | 3,254 | 0 | 891 | 1,041 | 13 | 1,945 | 12 | 18.9 | 5.3 | 259.5 | 223.4 | 73.7 | 80.2 |
| SIG+FIT 55-80, 5_3 (6_9) | 5,033 | 3,409 | 3,409 | 0 | 826 | 977 | 15 | 1,818 | 12 | 20.8 | 6.0 | 272.9 | 215.0 | 71.0 | 77.4 |
| SIG+FIT 55-85, 10_1 (4_31) | 13,025 | 2,056 | 2,056 | 0 | 1,030 | 1,144 | 9 | 2,183 | 14 | 15.4 | 4.0 | 239.0 | 236.2 | 78.5 | 85.2 |
| SIG+FIT 55-85, 10_2 (4_16) | 8,023 | 2,217 | 2,217 | 0 | 835 | 1,003 | 12 | 1,850 | 13 | 19.2 | 5.1 | 271.5 | 222.8 | 73.3 | 81.0 |
| SIG+FIT 55-85, 5_2 (7_16) | 7,427 | 3,468 | 3,468 | 0 | 959 | 1,055 | 12 | 2,025 | 13 | 17.9 | 4.8 | 258.3 | 225.6 | 75.0 | 82.0 |
| SIG+FIT 55-85, 5_3 (7_11) | 5,451 | 3,634 | 3,634 | 0 | 884 | 988 | 14 | 1,886 | 13 | 20.0 | 5.6 | 272.2 | 216.5 | 72.2 | 79.0 |

SIG = flexible sigmoidoscopy; FIT = fecal immunochemical test; CTC = computed tomographic colonography; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 10a. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with CTC screening strategies that vary by the ages to begin and end screening and screening interval: SimCRC**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 70 | 70 | 2 | 69.9 | 28.0 | 608.2 | 0.0 | 0.0 | 0.0 |
| CTC 45-75, 5 (7) | 0 | 0 | 4,879 | 0 | 860 | 1,267 | 6 | 2,133 | 11 | 13.4 | 3.3 | 202.5 | 290.5 | 80.8 | 88.1 |
| CTC 45-75, 10 (4) | 0 | 0 | 3,167 | 0 | 633 | 1,056 | 9 | 1,698 | 10 | 19.0 | 5.0 | 265.9 | 267.4 | 72.8 | 82.1 |
| CTC 45-80, 5 (8) | 0 | 0 | 5,214 | 0 | 927 | 1,295 | 4 | 2,226 | 12 | 12.4 | 2.9 | 201.4 | 292.6 | 82.3 | 89.8 |
| CTC 45-80, 10 (4) | 0 | 0 | 3,167 | 0 | 633 | 1,056 | 9 | 1,698 | 10 | 19.0 | 5.0 | 265.9 | 267.4 | 72.8 | 82.1 |
| CTC 45-85, 5 (9) | 0 | 0 | 5,436 | 0 | 971 | 1,309 | 4 | 2,284 | 13 | 12.1 | 2.7 | 201.8 | 293.1 | 82.7 | 90.4 |
| CTC 45-85, 10 (5) | 0 | 0 | 3,444 | 0 | 703 | 1,085 | 7 | 1,795 | 12 | 18.5 | 4.5 | 268.3 | 269.0 | 73.5 | 83.8 |
| CTC 50-75, 5 (6) | 0 | 0 | 4,069 | 0 | 758 | 1,161 | 8 | 1,927 | 11 | 16.2 | 4.3 | 254.0 | 265.2 | 76.8 | 84.6 |
| CTC 50-75, 10 (3) | 0 | 0 | 2,458 | 0 | 512 | 934 | 14 | 1,460 | 9 | 23.1 | 6.9 | 307.9 | 239.5 | 66.9 | 75.4 |
| CTC 50-80, 5 (7) | 0 | 0 | 4,405 | 0 | 825 | 1,189 | 6 | 2,021 | 12 | 15.2 | 3.8 | 252.9 | 267.3 | 78.3 | 86.3 |
| CTC 50-80, 10 (4) | 0 | 0 | 2,874 | 0 | 617 | 989 | 10 | 1,615 | 11 | 20.9 | 5.6 | 308.0 | 245.4 | 70.2 | 79.9 |
| CTC 50-85, 5 (8) | 0 | 0 | 4,627 | 0 | 870 | 1,203 | 6 | 2,079 | 13 | 14.9 | 3.7 | 253.3 | 267.8 | 78.7 | 86.8 |
| CTC 50-85, 10 (4) | 0 | 0 | 2,874 | 0 | 617 | 989 | 10 | 1,615 | 11 | 20.9 | 5.6 | 308.0 | 245.4 | 70.2 | 79.9 |
| CTC 55-75, 5 (5) | 0 | 0 | 3,295 | 0 | 658 | 1,025 | 11 | 1,694 | 11 | 20.5 | 5.9 | 320.6 | 231.0 | 70.7 | 79.0 |
| CTC 55-75, 10 (3) | 0 | 0 | 2,250 | 0 | 512 | 870 | 14 | 1,396 | 10 | 25.1 | 7.3 | 362.4 | 214.2 | 64.1 | 73.8 |
| CTC 55-80, 5 (6) | 0 | 0 | 3,631 | 0 | 726 | 1,054 | 9 | 1,788 | 12 | 19.5 | 5.4 | 319.5 | 233.2 | 72.1 | 80.7 |
| CTC 55-80, 10 (3) | 0 | 0 | 2,250 | 0 | 512 | 870 | 14 | 1,396 | 10 | 25.1 | 7.3 | 362.4 | 214.2 | 64.1 | 73.8 |
| CTC 55-85, 5 (7) | 0 | 0 | 3,854 | 0 | 770 | 1,068 | 9 | 1,847 | 13 | 19.2 | 5.2 | 319.9 | 233.8 | 72.5 | 81.3 |
| CTC 55-85, 10 (4) | 0 | 0 | 2,528 | 0 | 583 | 899 | 12 | 1,494 | 12 | 24.6 | 6.8 | 365.0 | 215.9 | 64.8 | 75.5 |

CTC = computed tomographic colonography; SIG = flexible sigmoidoscopy; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 10b. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with CTC screening strategies that vary by the ages to begin and end screening and screening interval: MISCAN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 67 | 67 | 1 | 66.6 | 27.8 | 565.0 | 0.0 | 0.0 | 0.0 |
| CTC 45-75, 5 (7) | 0 | 0 | 4,990 | 0 | 788 | 1,130 | 15 | 1,933 | 10 | 31.6 | 7.4 | 428.0 | 239.2 | 52.5 | 73.4 |
| CTC 45-75, 10 (4) | 0 | 0 | 3,211 | 0 | 561 | 896 | 21 | 1,478 | 9 | 38.8 | 10.4 | 490.4 | 197.1 | 41.7 | 62.7 |
| CTC 45-80, 5 (8) | 0 | 0 | 5,357 | 0 | 846 | 1,148 | 12 | 2,006 | 11 | 30.4 | 6.5 | 429.1 | 243.7 | 54.3 | 76.4 |
| CTC 45-80, 10 (4) | 0 | 0 | 3,211 | 0 | 561 | 896 | 21 | 1,478 | 9 | 38.8 | 10.4 | 490.4 | 197.1 | 41.7 | 62.7 |
| CTC 45-85, 5 (9) | 0 | 0 | 5,609 | 0 | 885 | 1,156 | 11 | 2,052 | 12 | 30.1 | 6.2 | 430.6 | 244.9 | 54.8 | 77.6 |
| CTC 45-85, 10 (5) | 0 | 0 | 3,515 | 0 | 617 | 913 | 18 | 1,548 | 10 | 38.6 | 9.6 | 497.0 | 200.1 | 42.1 | 65.5 |
| CTC 50-75, 5 (6) | 0 | 0 | 4,171 | 0 | 690 | 1,037 | 16 | 1,743 | 10 | 32.7 | 7.9 | 443.3 | 225.6 | 50.8 | 71.5 |
| CTC 50-75, 10 (3) | 0 | 0 | 2,485 | 0 | 456 | 812 | 26 | 1,293 | 8 | 40.9 | 11.7 | 496.4 | 183.8 | 38.5 | 57.9 |
| CTC 50-80, 5 (7) | 0 | 0 | 4,539 | 0 | 747 | 1,056 | 13 | 1,817 | 11 | 31.5 | 7.1 | 444.6 | 230.1 | 52.6 | 74.6 |
| CTC 50-80, 10 (4) | 0 | 0 | 2,927 | 0 | 538 | 847 | 20 | 1,405 | 9 | 39.0 | 9.9 | 504.5 | 193.5 | 41.4 | 64.5 |
| CTC 50-85, 5 (8) | 0 | 0 | 4,792 | 0 | 787 | 1,065 | 12 | 1,864 | 11 | 31.2 | 6.7 | 446.0 | 231.4 | 53.1 | 75.8 |
| CTC 50-85, 10 (4) | 0 | 0 | 2,927 | 0 | 538 | 847 | 20 | 1,405 | 9 | 39.0 | 9.9 | 504.5 | 193.5 | 41.4 | 64.5 |
| CTC 55-75, 5 (5) | 0 | 0 | 3,388 | 0 | 594 | 911 | 18 | 1,523 | 10 | 34.8 | 8.9 | 465.6 | 203.5 | 47.8 | 67.9 |
| CTC 55-75, 10 (3) | 0 | 0 | 2,284 | 0 | 446 | 750 | 24 | 1,220 | 9 | 40.9 | 11.4 | 511.3 | 172.2 | 38.5 | 58.9 |
| CTC 55-80, 5 (6) | 0 | 0 | 3,759 | 0 | 653 | 930 | 15 | 1,598 | 11 | 33.5 | 8.0 | 466.7 | 208.0 | 49.7 | 71.1 |
| CTC 55-80, 10 (3) | 0 | 0 | 2,284 | 0 | 446 | 750 | 24 | 1,220 | 9 | 40.9 | 11.4 | 511.3 | 172.2 | 38.5 | 58.9 |
| CTC 55-85, 5 (7) | 0 | 0 | 4,014 | 0 | 692 | 939 | 14 | 1,646 | 11 | 33.2 | 7.7 | 468.3 | 209.3 | 50.2 | 72.3 |
| CTC 55-85, 10 (4) | 0 | 0 | 2,590 | 0 | 503 | 768 | 21 | 1,292 | 10 | 40.7 | 10.6 | 518.0 | 175.3 | 38.9 | 61.7 |

CTC = computed tomographic colonography; SIG = flexible sigmoidoscopy; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 10c. Outcomes per 1,000 persons free of diagnosed colorectal cancer at age 40 with no colorectal cancer screening and with CTC screening strategies that vary by the ages to begin and end screening and screening interval: CRC-SPIN**

| Strategy | Outcomes per 1,000 persons free of diagnosed cancer at age 40 | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Modality age to begin-age to end, screening interval (# of tests*) | Screening tests | | | | Follow-up COLs | Surveillance COLs | COLs for symptoms | Total COLs | Compli-cations | CRC cases | CRC deaths† | LY with CRC | LYG‡ | Reductions‡ (%) | |
| | Stool tests | SIGs | CTCs | COLs | | | | | | | | | | Incidence | Mortality |
| No screening | 0 | 0 | 0 | 0 | 0 | 0 | 72 | 72 | 2 | 71.8 | 26.8 | 610.2 | 0.0 | 0.0 | 0.0 |
| CTC 45-75, 5 (7) | 0 | 0 | 5,106 | 0 | 769 | 1,027 | 11 | 1,807 | 10 | 13.9 | 4.2 | 142.1 | 263.9 | 80.7 | 84.3 |
| CTC 45-75, 10 (4) | 0 | 0 | 3,239 | 0 | 569 | 905 | 15 | 1,488 | 10 | 17.7 | 5.5 | 186.1 | 243.8 | 75.3 | 79.3 |
| CTC 45-80, 5 (8) | 0 | 0 | 5,491 | 0 | 832 | 1,052 | 9 | 1,892 | 11 | 11.8 | 3.4 | 136.2 | 267.9 | 83.5 | 87.3 |
| CTC 45-80, 10 (4) | 0 | 0 | 3,239 | 0 | 569 | 905 | 15 | 1,488 | 10 | 17.7 | 5.5 | 186.1 | 243.8 | 75.3 | 79.3 |
| CTC 45-85, 5 (9) | 0 | 0 | 5,753 | 0 | 875 | 1,065 | 7 | 1,948 | 12 | 10.9 | 3.0 | 134.0 | 269.4 | 84.9 | 88.8 |
| CTC 45-85, 10 (5) | 0 | 0 | 3,545 | 0 | 636 | 932 | 12 | 1,579 | 12 | 15.6 | 4.7 | 181.5 | 247.3 | 78.2 | 82.5 |
| CTC 50-75, 5 (6) | 0 | 0 | 4,254 | 0 | 674 | 967 | 13 | 1,654 | 10 | 15.5 | 4.7 | 175.9 | 248.4 | 78.4 | 82.2 |
| CTC 50-75, 10 (3) | 0 | 0 | 2,500 | 0 | 460 | 825 | 19 | 1,304 | 9 | 22.0 | 7.2 | 222.5 | 224.1 | 69.4 | 73.2 |
| CTC 50-80, 5 (7) | 0 | 0 | 4,638 | 0 | 737 | 992 | 10 | 1,739 | 11 | 13.5 | 4.0 | 169.4 | 252.2 | 81.2 | 85.2 |
| CTC 50-80, 10 (4) | 0 | 0 | 2,948 | 0 | 555 | 874 | 14 | 1,442 | 11 | 17.5 | 5.3 | 209.9 | 233.7 | 75.6 | 80.0 |
| CTC 50-85, 5 (8) | 0 | 0 | 4,900 | 0 | 781 | 1,006 | 9 | 1,795 | 12 | 12.5 | 3.5 | 168.0 | 254.1 | 82.6 | 86.8 |
| CTC 50-85, 10 (4) | 0 | 0 | 2,948 | 0 | 555 | 874 | 14 | 1,442 | 11 | 17.5 | 5.3 | 209.9 | 233.7 | 75.6 | 80.0 |
| CTC 55-75, 5 (5) | 0 | 0 | 3,438 | 0 | 583 | 877 | 15 | 1,475 | 10 | 18.4 | 5.8 | 225.4 | 223.9 | 74.4 | 78.4 |
| CTC 55-75, 10 (3) | 0 | 0 | 2,296 | 0 | 459 | 788 | 18 | 1,265 | 9 | 21.6 | 6.9 | 255.4 | 208.8 | 69.9 | 74.1 |
| CTC 55-80, 5 (6) | 0 | 0 | 3,822 | 0 | 646 | 902 | 13 | 1,560 | 11 | 16.3 | 5.0 | 219.8 | 228.2 | 77.2 | 81.5 |
| CTC 55-80, 10 (3) | 0 | 0 | 2,296 | 0 | 459 | 788 | 18 | 1,265 | 9 | 21.6 | 6.9 | 255.4 | 208.8 | 69.9 | 74.1 |
| CTC 55-85, 5 (7) | 0 | 0 | 4,084 | 0 | 689 | 915 | 11 | 1,616 | 12 | 15.3 | 4.6 | 217.3 | 229.8 | 78.6 | 82.9 |
| CTC 55-85, 10 (4) | 0 | 0 | 2,602 | 0 | 525 | 815 | 15 | 1,356 | 11 | 19.5 | 6.1 | 251.7 | 212.3 | 72.8 | 77.3 |

CTC = computed tomographic colonography; SIG = flexible sigmoidoscopy; COL = colonoscopy; CRC = colorectal cancer; LY = life-years; LYG = life-years gained compared with no screening.

* Maximum possible number with this strategy.

† Including deaths from complications of screening.

‡ Compared with no screening.

**Appendix Table 11. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 75, and the set of recommended strategies assuming the colonoscopy strategy with a 5-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,187 | 260 | 22.8 | 220 | 27 | 8 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,007 | 275 | 24.4 | 820 | 15 | 55 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,959 | 285 | 25.5 | 1,554 | 8 | 188 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,887 | 0 | 0 | 971 | 212 | 18.2 | 164 | 34 | 5 |
| FIT 50-75, 2 | 9,326 | 0 | 0 | 1,215 | 234 | 20.2 | 160 | 14 | 12 |
| gFOBT 50-75, 3 | 6,456 | 0 | 0 | 1,286 | 212 | 18.4 | | | Dominated |
| FIT-DNA 50-75, 5 | 4,391 | 0 | 0 | 1,364 | 224 | 19.7 | | | Dominated |
| gFOBT 50-75, 2 | 8,388 | 0 | 0 | 1,597 | 235 | 20.5 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,990 | 0 | 0 | 1,701 | 250 | 21.8 | | | Dominated |
| FIT 50-75, 1* | 15,778 | 0 | 0 | 1,739 | 260 | 22.7 | 413 | 17 | 24* |
| gFOBT 50-75, 1 | 12,914 | 0 | 0 | 2,230 | 261 | 22.9 | | | Dominated |
| FIT-DNA 50-75, 1* | 11,041 | 0 | 0 | 2,601 | 271 | 23.9 | 664 | 4 | 155* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-75, 10 | 0 | 2,480 | 0 | 1,345 | 200 | 17.9 | 78 | 23 | 3 |
| SIG 50-75, 5 | 0 | 4,111 | 0 | 1,820 | 227 | 20.6 | 475 | 27 | 18 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-75, 10_2 | 7,942 | 2,196 | 0 | 1,917 | 262 | 22.9 | 192 | 31 | 6 |
| SIG+FIT 50-75, 5_3 | 5,367 | 3,700 | 0 | 2,127 | 263 | 23.3 | | | Dominated |
| SIG+gFOBT 50-75, 10_2 | 7,212 | 2,042 | 0 | 2,190 | 262 | 23.1 | | | Dominated |
| SIG+FIT 50-75, 5_2* | 7,296 | 3,559 | 0 | 2,224 | 267 | 23.7 | | | Dominated |
| SIG+FIT 50-75, 10_1* | 13,393 | 2,097 | 0 | 2,248 | 270 | 23.8 | 172 | 3 | 54* |
| SIG+gFOBT 50-75, 5_3 | 5,099 | 3,425 | 0 | 2,294 | 263 | 23.3 | | | Dominated |
| SIG+gFOBT 50-75, 5_2 | 6,689 | 3,211 | 0 | 2,431 | 267 | 23.7 | | | Dominated |
| SIG+gFOBT 50-75, 10_1 | 11,100 | 1,926 | 0 | 2,616 | 271 | 23.9 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-75, 10 | 0 | 0 | 2,458 | 1,460 | 239 | 21.1 | 64 | 25 | 3 |
| CTC 50-75, 5 | 0 | 0 | 4,069 | 1,927 | 265 | 23.7 | 467 | 26 | 18 |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,353 | 228 | 20.2 | 275 | 14 | 19 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,101 | 248 | 21.9 | 747 | 19 | 39 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,948 | 264 | 23.3 | 1,847 | 16 | 114 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,795 | 0 | 0 | 995 | 176 | 15.3 | 162 | 23 | 7 |
| FIT 50-75, 2* | 9,342 | 0 | 0 | 1,243 | 200 | 17.3 | 173 | 15 | 12* |
| gFOBT 50-75, 3 | 6,302 | 0 | 0 | 1,296 | 175 | 15.4 | | | Dominated |
| FIT-DNA 50-75, 5 | 4,380 | 0 | 0 | 1,402 | 192.5 | 17.1 | | | Dominated |
| gFOBT 50-75, 2 | 8,408 | 0 | 0 | 1,636 | 200 | 17.5 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,779 | 0 | 0 | 1,714 | 215 | 18.7 | | | Dominated |
| FIT 50-75, 1* | 15,843 | 0 | 0 | 1,757 | 231 | 20.0 | 383 | 18 | 21* |
| gFOBT 50-75, 1 | 12,927 | 0 | 0 | 2,287 | 232 | 20.3 | | | Dominated |
| FIT-DNA 50-75, 1* | 11,025 | 0 | 0 | 2,662 | 246 | 21.4 | 741 | 6 | 120* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-75, 10 | 0 | 2,356 | 0 | 1,881 | 201 | 18.2 | 144 | 16 | 9 |
| SIG 50-75, 5 | 0 | 3,807 | 0 | 2,287 | 221 | 20.0 | 406 | 20 | 20 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-75, 10_2 | 7,306 | 1,886 | 0 | 2,157 | 232 | 20.4 | 201 | 20 | 10 |
| SIG+gFOBT 50-75, 10_2 | 6,594 | 1,677 | 0 | 2,374 | 231 | 20.4 | | | Dominated |
| SIG+FIT 50-75, 5_3 | 4,737 | 3,380 | 0 | 2,451 | 239 | 21.2 | | | Dominated |
| SIG+FIT 50-75, 10_1 | 12,642 | 1,903 | 0 | 2,490 | 246 | 21.5 | 199 | 8 | 24 |
| SIG+FIT 50-75, 5_2 | 6,523 | 3,221 | 0 | 2,501 | 241 | 21.3 | | | Dominated |
| SIG+gFOBT 50-75, 5_3 | 4,462 | 3,146 | 0 | 2,587 | 238 | 21.2 | | | Dominated |
| SIG+gFOBT 50-75, 5_2 | 5,947 | 2,882 | 0 | 2,667 | 240 | 21.3 | | | Dominated |
| SIG+gFOBT 50-75, 10_1 | 10,562 | 1,633 | 0 | 2,814 | 245 | 21.5 | | | Dominated |

**Appendix Table 11. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 75, and the set of recommended strategies assuming the colonoscopy strategy with a 5-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-75, 10 | 0 | 0 | 2,485 | 1,293 | 184 | 16.1 | 73 | 12 | 6 |
| CTC 50-75, 5 | 0 | 0 | 4,171 | 1,743 | 226 | 19.9 | 450 | 42 | 11 |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,258 | 257 | 22.7 | 243 | 21 | 12 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,049 | 270 | 24.1 | 792 | 12 | 65 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,995 | 279 | 25.0 | 1,532 | 6 | 273 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,857 | 0 | 0 | 1,081 | 178 | 15.8 | 186 | 26 | 7 |
| gFOBT 50-75, 3 | 6,498 | 0 | 0 | 1,317 | 183 | 16.4 | | | Dominated |
| FIT 50-75, 2 | 9,241 | 0 | 0 | 1,346 | 207 | 18.3 | 265 | 29 | 9 |
| FIT-DNA 50-75, 5 | 4,370 | 0 | 0 | 1,473 | 195 | 17.8 | | | Dominated |
| gFOBT 50-75, 2 | 8,448 | 0 | 0 | 1,626 | 212 | 18.8 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,927 | 0 | 0 | 1,827 | 226 | 20.2 | | | Dominated |
| FIT 50-75, 1 | 15,444 | 0 | 0 | 1,899 | 244 | 21.6 | 445 | 26 | 17 |
| gFOBT 50-75, 1 | 13,026 | 0 | 0 | 2,253 | 247 | 21.9 | | | Dominated |
| FIT-DNA 50-75, 1* | 10,745 | 0 | 0 | 2,729 | 261 | 23.2 | 638 | 7 | 87* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-75, 10 | 0 | 2,515 | 0 | 1,161 | 165 | 14.7 | 68 | 12 | 6 |
| SIG 50-75, 5 | 0 | 4,298 | 0 | 1,493 | 181 | 16.5 | 220 | 10 | 22 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-75, 10_2 | 8.033 | 2,192 | 0 | 1,905 | 239 | 21.1 | 208 | 22 | 9 |
| SIG+FIT 50-75, 5_3 | 5,559 | 3,780 | 0 | 1,984 | 235 | 21.0 | | | Dominated |
| SIG+FIT 50-75, 5_2 | 7,506 | 3,611 | 0 | 2,125 | 244 | 21.8 | | | Dominated |
| SIG+gFOBT 50-75, 10_2 | 7,386 | 2,062 | 0 | 2,125 | 241 | 21.4 | | | Dominated |
| SIG+gFOBT 50-75, 5_3 | 5,314 | 3,531 | 0 | 2,132 | 237 | 21.2 | | | Dominated |
| SIG+FIT 50-75, 10_1 | 13,404 | 2,079 | 0 | 2,289 | 256 | 22.7 | 237 | 9 | 25 |
| SIG+gFOBT 50-75, 5_2 | 6,949 | 3,297 | 0 | 2,305 | 246 | 21.9 | | | Dominated |
| SIG+gFOBT 50-75, 10_1 | 11,376 | 1,940 | 0 | 2,581 | 258 | 22.9 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-75, 10 | 0 | 0 | 2,500 | 1,304 | 244 | 19.6 | 39 | 15 | 3 |
| CTC 50-75, 5 | 0 | 0 | 4,254 | 1,654 | 248 | 22.0 | 350 | 24 | 14 |

FIT = fecal immunochemical test; gFOBT = highly-sensitive guaiac-based fecal occult blood test; FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; LYG = life-years gained compared with no screening; CRC = colorectal cancer; ΔCOL = incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG = incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

**Appendix Table 12. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 80, and the set of recommended strategies assuming the colonoscopy strategy with a 10-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-80, 15* | 0 | 0 | 0 | 3,656 | 265 | 23.9 | 468 | 5 | 91* |
| COL 50-80, 10 | 0 | 0 | 0 | 4,405 | 277 | 24.9 | 398 | 5 | 166 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,289 | 286 | 25.6 | 330 | <1 | 513 |
| **Stool test** | | | | | | | | | |
| FIT 50-80, 3 | 7,694 | 0 | 0 | 1,055 | 220 | 19.7 | 84 | 9 | 10 |
| FIT 50-80, 2 | 10,572 | 0 | 0 | 1,327 | 243 | 21.7 | 112 | 9 | 13 |
| gFOBT 50-80, 3 | 7,125 | 0 | 0 | 1,383 | 220 | 19.8 | | | Dominated |
| FIT-DNA 50-80, 5 | 4,781 | 0 | 0 | 1,447 | 229 | 20.7 | | | Dominated |
| gFOBT 50-80, 2 | 9,462 | 0 | 0 | 1,738 | 243 | 21.9 | | | Dominated |
| FIT-DNA 50-80, 3 | 6,543 | 0 | 0 | 1,809 | 255 | 22.8 | | | Dominated |
| FIT 50-80, 1 | 17,426 | 0 | 0 | 1,858 | 265 | 23.7 | 531 | 22 | 24 |
| gFOBT 50-80, 1 | 14,193 | 0 | 0 | 2,377 | 265 | 23.8 | | | Dominated |
| FIT-DNA 50-80, 1 | 12,096 | 0 | 0 | 2,763 | 274 | 24.5 | 826 | 7 | 112 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-80, 10* | 0 | 2,910 | 0 | 1,484 | 205 | 18.9 | 139 | 5 | 28* |
| SIG 50-80, 5 | 0 | 4,459 | 0 | 1,910 | 229 | 21.0 | 90 | 2 | 43 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-80, 10_2 | 8,960 | 2,494 | 0 | 2,076 | 267 | 24.0 | 159 | 5 | 31 |
| SIG+FIT 50-80, 5_3 | 5,887 | 3,997 | 0 | 2,237 | 266 | 23.9 | | | Dominated |
| SIG+FIT 50-80, 5_2 | 8,109 | 3,846 | 0 | 2,347 | 270 | 24.3 | | | Dominated |
| SIG+gFOBT 50-80, 10_2 | 8,100 | 2,283 | 0 | 2,360 | 267 | 24.0 | | | Dominated |
| SIG+FIT 50-80, 10_1 | 14,761 | 2,320 | 0 | 2,395 | 274 | 24.5 | 320 | 7 | 48 |
| SIG+gFOBT 50-80, 5_3 | 5,559 | 3,699 | 0 | 2,413 | 265 | 23.9 | | | Dominated |
| SIG+gFOBT 50-80, 5_2 | 7,423 | 3,473 | 0 | 2,576 | 270 | 24.3 | | | Dominated |
| SIG+gFOBT 50-80, 10_1 | 12,172 | 2,091 | 0 | 2,776 | 274 | 24.5 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-80, 10* | 0 | 0 | 2,874 | 1,615 | 245 | 22.4 | 155 | 6 | 26* |
| CTC 50-80, 5 | 0 | 0 | 4,405 | 2,021 | 267 | 24.1 | 94 | 2 | 44 |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-80, 15 | 0 | 0 | 0 | 3,779 | 234 | 21.3 | | | Dominated |
| COL 50-80, 10* | 0 | 0 | 0 | 4,485 | 251 | 22.6 | 384 | 3 | 116* |
| COL 50-80, 5 | 0 | 0 | 0 | 6,296 | 265 | 23.5 | 348 | <1 | 236 |
| **Stool test** | | | | | | | | | |
| FIT 50-80, 3 | 7,693 | 0 | 0 | 1,070 | 186 | 16.9 | 75 | 10 | 8 |
| FIT 50-80, 2 | 10,613 | 0 | 0 | 1,334 | 210 | 18.9 | 264 | 24 | 11 |
| gFOBT 50-80, 3 | 7,106 | 0 | 0 | 1,395 | 184 | 16.9 | | | Dominated |
| FIT-DNA 50-80, 5 | 4,776 | 0 | 0 | 1,472 | 198 | 18.1 | | | Dominated |
| gFOBT 50-80, 2 | 9,497 | 0 | 0 | 1,759 | 209 | 19.0 | | | Dominated |
| FIT-DNA 50-80, 3 | 6,481 | 0 | 0 | 1,828 | 223 | 20.0 | | | Dominated |
| FIT 50-80, 1 | 17,552 | 0 | 0 | 1,855 | 238 | 21.1 | 481 | 25 | 19 |
| gFOBT 50-80, 1 | 14,223 | 0 | 0 | 2,416 | 237 | 21.2 | | | Dominated |
| FIT-DNA 50-80, 1* | 12,108 | 0 | 0 | 2,804 | 250 | 22.2 | 883 | 10 | 85* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-80, 10* | 0 | 2,746 | 0 | 2,001 | 205 | 19.0 | 120 | 4 | 28* |
| SIG 50-80, 5 | 0 | 4,129 | 0 | 2,365 | 223 | 20.4 | 78 | 2 | 37 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-80, 10_2 | 8,260 | 2,164 | 0 | 2,291 | 238 | 21.4 | 134 | 6 | 24 |
| SIG+gFOBT 50-80, 10_2 | 7,423 | 1,908 | 0 | 2,524 | 236 | 21.3 | | | Dominated |
| SIG+FIT 50-80, 5_3 | 5,284 | 3,625 | 0 | 2,534 | 241 | 21.6 | | | Dominated |
| SIG+FIT 50-80, 5_2 | 7,328 | 3,453 | 0 | 2,592 | 244 | 21.8 | | | Dominated |
| SIG+FIT 50-80, 10_1 | 14,039 | 2,177 | 0 | 2,635 | 251 | 22.4 | 144 | 5 | 31 |
| SIG+gFOBT 50-80, 5_3 | 4,963 | 3,362 | 0 | 2,683 | 240 | 21.6 | | | Dominated |
| SIG+gFOBT 50-80, 5_2 | 6,666 | 3,079 | 0 | 2,778 | 243 | 21.8 | | | Dominated |
| SIG+gFOBT 50-80, 10_1 | 11,686 | 1,844 | 0 | 2,977 | 249 | 22.2 | | | Dominated |

**Appendix Table 12. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 80, and the set of recommended strategies assuming the colonoscopy strategy with a 10-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-80, 10* | 0 | 0 | 2,927 | 1,405 | 194 | 17.9 | 112 | 10 | 12* |
| CTC 50-80, 5 | 0 | 0 | 4,539 | 1,817 | 230 | 20.7 | 74 | 4 | 16 |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-80, 15* | 0 | 0 | 0 | 3,728 | 264 | 24.1 | 470 | 7 | 72* |
| COL 50-80, 10 | 0 | 0 | 0 | 4,464 | 273 | 24.8 | 414 | 3 | 126 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,351 | 280 | 25.3 | 356 | 1 | 367 |
| **Stool test** | | | | | | | | | |
| FIT 50-80, 3* | 7,660 | 0 | 0 | 1,163 | 187 | 17.2 | 82 | 9 | 9* |
| gFOBT 50-80, 3 | 7,184 | 0 | 0 | 1,412 | 192 | 17.7 | | | Dominated |
| FIT 50-80, 2 | 10,476 | 0 | 0 | 1,454 | 218 | 19.9 | 108 | 10 | 10 |
| FIT-DNA 50-80, 5 | 4,762 | 0 | 0 | 1,554 | 200 | 18.7 | | | Dominated |
| gFOBT 50-80, 2 | 9,554 | 0 | 0 | 1,763 | 221 | 20.3 | | | Dominated |
| FIT-DNA 50-80, 3 | 6,476 | 0 | 0 | 1,931 | 232 | 21.2 | | | Dominated |
| FIT 50-80, 1 | 17,062 | 0 | 0 | 2,013 | 250 | 22.6 | 114 | 6 | 18 |
| gFOBT 50-80, 1 | 14,364 | 0 | 0 | 2,395 | 252 | 22.8 | | | Dominated |
| FIT-DNA 50-80, 1* | 11,795 | 0 | 0 | 2,886 | 265 | 23.9 | 795 | 11 | 70* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-80, 10 | 0 | 2,983 | 0 | 1,273 | 171 | 16.0 | 113 | 6 | 18 |
| SIG 50-80, 5 | 0 | 4,705 | 0 | 1,567 | 184 | 17.0 | 74 | 3 | 28 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-80, 10_2 | 9,098 | 2,500 | 0 | 2,053 | 246 | 22.4 | 148 | 7 | 20 |
| SIG+FIT 50-80, 5_3 | 6,144 | 4,108 | 0 | 2,090 | 239 | 21.8 | | | Dominated |
| SIG+FIT 50-80, 5_2* | 8,405 | 3,922 | 0 | 2,248 | 249 | 22.7 | 195 | 3 | 65* |
| SIG+gFOBT 50-80, 5_3 | 5,837 | 3,836 | 0 | 2,249 | 241 | 22.0 | | | Dominated |
| SIG+gFOBT 50-80, 10_2 | 8,339 | 2,318 | 0 | 2,288 | 248 | 22.5 | | | Dominated |
| SIG+FIT 50-80, 10_1 | 14,812 | 2,307 | 0 | 2,428 | 261 | 23.6 | 139 | 5 | 27 |
| SIG+gFOBT 50-80, 5_2 | 7,774 | 3,585 | 0 | 2,449 | 251 | 22.8 | | | Dominated |
| SIG+gFOBT 50-80, 10_1 | 12,537 | 2,115 | 0 | 2,735 | 261 | 23.6 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-80, 10* | 0 | 0 | 2,948 | 1,442 | 234 | 21.4 | 138 | 10 | 14* |
| CTC 50-80, 5 | 0 | 0 | 4,638 | 1,739 | 252 | 22.8 | 85 | 4 | 23 |

FIT = fecal immunochemical test; gFOBT = highly-sensitive guaiac-based fecal occult blood test; FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; LYG = life-years gained compared with no screening; CRC = colorectal cancer; ΔCOL = incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG = incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

**Appendix Table 13. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 85, and the set of recommended strategies assuming the colonoscopy strategy with a 10-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-85, 15 | 0 | 0 | 0 | 3,656 | 265 | 23.9 | 468 | 5 | 91 |
| COL 50-85, 10 | 0 | 0 | 0 | 4,405 | 277 | 24.9 | 398 | 5 | 166 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,502 | 286 | 25.7 | 213 | <1 | 1,661 |
| **Stool test** | | | | | | | | | |
| FIT 50-85, 3* | 8,111 | 0 | 0 | 1,095 | 223 | 20.2 | 39 | 2 | 17* |
| FIT 50-85, 2* | 11,165 | 0 | 0 | 1,377 | 245 | 22.2 | 50 | 2 | 24* |
| gFOBT 50-85, 3 | 7,565 | 0 | 0 | 1,441 | 222 | 20.3 | | | Dominated |
| FIT-DNA 50-85, 5 | 5,043 | 0 | 0 | 1,500 | 230 | 21.1 | | | Dominated |
| gFOBT 50-85, 2 | 9,970 | 0 | 0 | 1,801 | 245 | 22.3 | | | Dominated |
| FIT-DNA 50-85, 3 | 6,961 | 0 | 0 | 1,884 | 257 | 23.2 | | | Dominated |
| FIT 50-85, 1 | 18,589 | 0 | 0 | 1,937 | 267 | 24.1 | 79 | 2 | 50 |
| gFOBT 50-85, 1 | 15,090 | 0 | 0 | 2,476 | 266 | 24.1 | | | Dominated |
| FIT-DNA 50-85, 1 | 12,826 | 0 | 0 | 2,870 | 275 | 24.7 | 107 | 1 | 116 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-85, 10* | 0 | 2,910 | 0 | 1,484 | 205 | 18.9 | 139 | 5 | 28* |
| SIG 50-85, 5 | 0 | 4,691 | 0 | 1,965 | 229 | 21.2 | 56 | 1 | 99 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-85, 10_2* | 9,412 | 2,534 | 0 | 2,116 | 268 | 24.1 | 40 | 1 | 56* |
| SIG+FIT 50-85, 5_3 | 6,217 | 4,202 | 0 | 2,305 | 267 | 24.1 | | | Dominated |
| SIG+FIT 50-85, 5_2 | 8,557 | 4,041 | 0 | 2,419 | 271 | 24.5 | | | Dominated |
| SIG+gFOBT 50-85, 10_2* | 8,502 | 2,345 | 0 | 2,420 | 268 | 24.1 | | | Dominated |
| SIG+FIT 50-85, 10_1 | 15,698 | 2,396 | 0 | 2,469 | 275 | 24.7 | 73 | 1 | 92 |
| SIG+gFOBT 50-85, 5_3 | 5,893 | 3,892 | 0 | 2,494 | 266 | 24.1 | | | Dominated |
| SIG+gFOBT 50-85, 5_2 | 7,818 | 3,651 | 0 | 2,658 | 271 | 24.4 | | | Dominated |
| SIG+gFOBT 50-85, 10_1 | 12,922 | 2,188 | 0 | 2,875 | 274 | 24.7 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-85, 10* | 0 | 0 | 2,874 | 1,615 | 245 | 22.4 | 155 | 6 | 26* |
| CTC 50-85, 5 | 0 | 0 | 4,627 | 2,079 | 268 | 24.3 | 58 | 1 | 111 |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-85, 15 | 0 | 0 | 0 | 3,779 | 234 | 21.3 | | | Dominated |
| COL 50-85, 10* | 0 | 0 | 0 | 4,485 | 251 | 22.6 | 384 | 3 | 116* |
| COL 50-85, 5 | 0 | 0 | 0 | 6,525 | 266 | 23.6 | 229 | <1 | 1,146 |
| **Stool test** | | | | | | | | | |
| FIT 50-85, 3* | 8,032 | 0 | 0 | 1,096 | 188 | 17.3 | 26 | 2 | 12* |
| FIT 50-85, 2 | 11,233 | 0 | 0 | 1,375 | 213 | 19.4 | 40 | 3 | 16 |
| gFOBT 50-85, 3 | 7,408 | 0 | 0 | 1,430 | 186 | 17.3 | | | Dominated |
| FIT-DNA 50-85, 5 | 5,048 | 0 | 0 | 1,516 | 200 | 18.5 | | | Dominated |
| gFOBT 50-85, 2 | 10,024 | 0 | 0 | 1,814 | 211 | 19.4 | | | Dominated |
| FIT-DNA 50-85, 3 | 6,745 | 0 | 0 | 1,867 | 224 | 20.3 | | | Dominated |
| FIT 50-85, 1 | 18,796 | 0 | 0 | 1,921 | 240 | 21.6 | 66 | 2 | 27 |
| gFOBT 50-85, 1 | 15,161 | 0 | 0 | 2,505 | 239 | 21.6 | | | Dominated |
| FIT-DNA 50-85, 1 | 12,888 | 0 | 0 | 2,901 | 252 | 22.5 | 980 | 12 | 83 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-85, 10* | 0 | 2,746 | 0 | 2,001 | 205 | 19.0 | 120 | 4 | 28* |
| SIG 50-85, 5 | 0 | 4,349 | 0 | 2,408 | 224 | 20.5 | 42 | <1 | 101 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-85, 10_2* | 8,706 | 2,164 | 0 | 2,313 | 239 | 21.6 | 21 | 1 | 27* |
| SIG+gFOBT 50-85, 10_2 | 7,811 | 1,908 | 0 | 2,558 | 237 | 21.4 | | | Dominated |
| SIG+FIT 50-85, 5_3 | 5,491 | 3,802 | 0 | 2,579 | 242 | 21.8 | | | Dominated |
| SIG+FIT 50-85, 5_2 | 7,717 | 3,646 | 0 | 2,560 | 245 | 22.0 | | | Dominated |
| SIG+FIT 50-85, 10_1 | 14,983 | 2,177 | 0 | 2,675 | 252 | 22.5 | 41 | 1 | 59 |
| SIG+gFOBT 50-85, 5_3 | 5,154 | 3,526 | 0 | 2,733 | 241 | 21.7 | | | Dominated |
| SIG+gFOBT 50-85, 5_2 | 7,009 | 3,248 | 0 | 2,844 | 243 | 22.0 | | | Dominated |
| SIG+gFOBT 50-85, 10_1 | 12,442 | 1,844 | 0 | 3,042 | 250 | 22.4 | | | Dominated |

**Appendix Table 13. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 85, and the set of recommended strategies assuming the colonoscopy strategy with a 10-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-85, 10* | 0 | 0 | 2,927 | 1,405 | 194 | 17.9 | 112 | 10 | 12* |
| CTC 50-85, 5 | 0 | 0 | 4,792 | 1,864 | 231 | 21.1 | 47 | 1 | 37 |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-85, 15* | 0 | 0 | 0 | 3,728 | 264 | 24.1 | 470 | 7 | 72* |
| COL 50-85, 10 | 0 | 0 | 0 | 4,464 | 273 | 24.8 | 414 | 3 | 126 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,586 | 280 | 25.3 | 235 | <1 | 947 |
| **Stool test** | | | | | | | | | |
| FIT 50-85, 3* | 8,084 | 0 | 0 | 1,201 | 191 | 17.9 | 120 | 13 | 10* |
| gFOBT 50-85, 3 | 7,643 | 0 | 0 | 1,466 | 195 | 18.4 | | | Dominated |
| FIT 50-85, 2* | 11,071 | 0 | 0 | 1,504 | 220 | 20.4 | 49 | 2 | 24* |
| FIT-DNA 50-85, 5 | 5,028 | 0 | 0 | 1,606 | 203 | 19.3 | | | Dominated |
| gFOBT 50-85, 2 | 10,089 | 0 | 0 | 1,824 | 223 | 20.8 | | | Dominated |
| FIT-DNA 50-85, 3 | 6,903 | 0 | 0 | 2,005 | 235 | 21.8 | | | Dominated |
| FIT 50-85, 1 | 18,224 | 0 | 0 | 2,091 | 253 | 23.2 | 78 | 3 | 26 |
| gFOBT 50-85, 1* | 15,321 | 0 | 0 | 2,493 | 255 | 23.3 | 402 | 1 | 318* |
| FIT-DNA 50-85, 1 | 12,542 | 0 | 0 | 2,994 | 266 | 24.3 | 903 | 13 | 69 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-85, 10 | 0 | 2,983 | 0 | 1,273 | 171 | 16.0 | 113 | 6 | 18 |
| SIG 50-85, 5 | 0 | 4,987 | 0 | 1,616 | 184 | 17.3 | 49 | 1 | 71 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-85, 10_2* | 9,591 | 2,544 | 0 | 2,094 | 248 | 22.7 | 42 | 1 | 31* |
| SIG+FIT 50-85, 5_3 | 6,516 | 4,338 | 0 | 2,157 | 241 | 22.2 | | | Dominated |
| SIG+FIT 50-85, 5_2 | 8,906 | 4,138 | 0 | 2,317 | 251 | 23.0 | | | Dominated |
| SIG+gFOBT 50-85, 5_3 | 6,218 | 4,056 | 0 | 2,327 | 242 | 22.4 | | | Dominated |
| SIG+gFOBT 50-85, 10_2 | 8,790 | 2,386 | 0 | 2,346 | 250 | 22.9 | | | Dominated |
| SIG+FIT 50-85, 10_1 | 15,814 | 2,389 | 0 | 2,502 | 263 | 23.9 | 74 | 2 | 43 |
| SIG+gFOBT 50-85, 5_2 | 8,228 | 3,786 | 0 | 2,529 | 252 | 23.2 | | | Dominated |
| SIG+gFOBT 50-85, 10_1 | 13,373 | 2,220 | 0 | 2,834 | 263 | 24.0 | 332 | 1 | 449 |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-85, 10* | 0 | 0 | 2,948 | 1,442 | 234 | 21.4 | 138 | 10 | 14* |
| CTC 50-85, 5 | 0 | 0 | 4,900 | 1,795 | 254 | 23.2 | 56 | 2 | 29 |

FIT = fecal immunochemical test; gFOBT = highly-sensitive guaiac-based fecal occult blood test; FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; LYG = life-years gained compared with no screening; CRC = colorectal cancer; ΔCOL = incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG = incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

**Appendix Table 14. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 80, and the set of recommended strategies assuming the colonoscopy strategy with a 5-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-80, 15* | 0 | 0 | 0 | 3,656 | 265 | 23.9 | 468 | 5 | 91* |
| COL 50-80, 10 | 0 | 0 | 0 | 4,405 | 277 | 24.9 | 398 | 5 | 166 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,289 | 286 | 25.6 | 330 | <1 | 513 |
| **Stool test** | | | | | | | | | |
| FIT 50-80, 3 | 7,694 | 0 | 0 | 1,055 | 220 | 19.7 | 84 | 9 | 10 |
| FIT 50-80, 2 | 10,572 | 0 | 0 | 1,327 | 243 | 21.7 | 112 | 9 | 13 |
| gFOBT 50-80, 3 | 7,125 | 0 | 0 | 1,383 | 220 | 19.8 | | | Dominated |
| FIT-DNA 50-80, 5 | 4,781 | 0 | 0 | 1,447 | 229 | 20.7 | | | Dominated |
| gFOBT 50-80, 2 | 9,462 | 0 | 0 | 1,738 | 243 | 21.9 | | | Dominated |
| FIT-DNA 50-80, 3 | 6,543 | 0 | 0 | 1,809 | 255 | 22.8 | | | Dominated |
| FIT 50-80, 1 | 17,426 | 0 | 0 | 1,858 | 265 | 23.7 | 531 | 22 | 24 |
| gFOBT 50-80, 1 | 14,193 | 0 | 0 | 2,377 | 265 | 23.8 | | | Dominated |
| FIT-DNA 50-80, 1 | 12,096 | 0 | 0 | 2,763 | 274 | 24.5 | 826 | 7 | 112 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-80, 10* | 0 | 2,910 | 0 | 1,484 | 205 | 18.9 | 139 | 5 | 28* |
| SIG 50-80, 5 | 0 | 4,459 | 0 | 1,910 | 229 | 21.0 | 90 | 2 | 43 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-80, 10_2 | 8,960 | 2,494 | 0 | 2,076 | 267 | 24.0 | 159 | 5 | 31 |
| SIG+FIT 50-80, 5_3 | 5,887 | 3,997 | 0 | 2,237 | 266 | 23.9 | | | Dominated |
| SIG+FIT 50-80, 5_2 | 8,109 | 3,846 | 0 | 2,347 | 270 | 24.3 | | | Dominated |
| SIG+gFOBT 50-80, 10_2 | 8,100 | 2,283 | 0 | 2,360 | 267 | 24.0 | | | Dominated |
| SIG+FIT 50-80, 10_1 | 14,761 | 2,320 | 0 | 2,395 | 274 | 24.5 | 320 | 7 | 48 |
| SIG+gFOBT 50-80, 5_3 | 5,559 | 3,699 | 0 | 2,413 | 265 | 23.9 | | | Dominated |
| SIG+gFOBT 50-80, 5_2 | 7,423 | 3,473 | 0 | 2,576 | 270 | 24.3 | | | Dominated |
| SIG+gFOBT 50-80, 10_1 | 12,172 | 2,091 | 0 | 2,776 | 274 | 24.5 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-80, 10* | 0 | 0 | 2,874 | 1,615 | 245 | 22.4 | 155 | 6 | 26* |
| CTC 50-80, 5 | 0 | 0 | 4,405 | 2,021 | 267 | 24.1 | 94 | 2 | 44 |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-80, 15 | 0 | 0 | 0 | 3,779 | 234 | 21.3 | | | Dominated |
| COL 50-80, 10* | 0 | 0 | 0 | 4,485 | 251 | 22.6 | 384 | 3 | 116* |
| COL 50-80, 5 | 0 | 0 | 0 | 6,296 | 265 | 23.5 | 348 | <1 | 236 |
| **Stool test** | | | | | | | | | |
| FIT 50-80, 3 | 7,693 | 0 | 0 | 1,070 | 186 | 16.9 | 75 | 10 | 8 |
| FIT 50-80, 2 | 10,613 | 0 | 0 | 1,334 | 210 | 18.9 | 264 | 24 | 11 |
| gFOBT 50-80, 3 | 7,106 | 0 | 0 | 1,395 | 184 | 16.9 | | | Dominated |
| FIT-DNA 50-80, 5 | 4,776 | 0 | 0 | 1,472 | 198 | 18.1 | | | Dominated |
| gFOBT 50-80, 2 | 9,497 | 0 | 0 | 1,759 | 209 | 19.0 | | | Dominated |
| FIT-DNA 50-80, 3 | 6,481 | 0 | 0 | 1,828 | 223 | 20.0 | | | Dominated |
| FIT 50-80, 1 | 17,552 | 0 | 0 | 1,855 | 238 | 21.1 | 481 | 25 | 19 |
| gFOBT 50-80, 1 | 14,223 | 0 | 0 | 2,416 | 237 | 21.2 | | | Dominated |
| FIT-DNA 50-80, 1* | 12,108 | 0 | 0 | 2,804 | 250 | 22.2 | 883 | 10 | 85* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-80, 10* | 0 | 2,746 | 0 | 2,001 | 205 | 19.0 | 120 | 4 | 28* |
| SIG 50-80, 5 | 0 | 4,129 | 0 | 2,365 | 223 | 20.4 | 78 | 2 | 37 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-80, 10_2 | 8,260 | 2,164 | 0 | 2,291 | 238 | 21.4 | 134 | 6 | 24 |
| SIG+gFOBT 50-80, 10_2 | 7,423 | 1,908 | 0 | 2,524 | 236 | 21.3 | | | Dominated |
| SIG+FIT 50-80, 5_3 | 5,284 | 3,625 | 0 | 2,534 | 241 | 21.6 | | | Dominated |
| SIG+FIT 50-80, 5_2 | 7,328 | 3,453 | 0 | 2,592 | 244 | 21.8 | | | Dominated |
| SIG+FIT 50-80, 10_1 | 14,039 | 2,177 | 0 | 2,635 | 251 | 22.4 | 144 | 5 | 31 |
| SIG+gFOBT 50-80, 5_3 | 4,963 | 3,362 | 0 | 2,683 | 240 | 21.6 | | | Dominated |
| SIG+gFOBT 50-80, 5_2 | 6,666 | 3,079 | 0 | 2,778 | 243 | 21.8 | | | Dominated |
| SIG+gFOBT 50-80, 10_1 | 11,686 | 1,844 | 0 | 2,977 | 249 | 22.2 | | | Dominated |

**Appendix Table 14. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 80, and the set of recommended strategies assuming the colonoscopy strategy with a 5-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-80, 10* | 0 | 0 | 2,927 | 1,405 | 194 | 17.9 | 112 | 10 | 12* |
| CTC 50-80, 5 | 0 | 0 | 4,539 | 1,817 | 230 | 20.7 | 74 | 4 | 16 |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-80, 15* | 0 | 0 | 0 | 3,728 | 264 | 24.1 | 470 | 7 | 72* |
| COL 50-80, 10 | 0 | 0 | 0 | 4,464 | 273 | 24.8 | 414 | 3 | 126 |
| COL 50-80, 5 | 0 | 0 | 0 | 6,351 | 280 | 25.3 | 356 | 1 | 367 |
| **Stool test** | | | | | | | | | |
| FIT 50-80, 3* | 7,660 | 0 | 0 | 1,163 | 187 | 17.2 | 82 | 9 | 9* |
| gFOBT 50-80, 3 | 7,184 | 0 | 0 | 1,412 | 192 | 17.7 | | | Dominated |
| FIT 50-80, 2 | 10,476 | 0 | 0 | 1,454 | 218 | 19.9 | 108 | 10 | 10 |
| FIT-DNA 50-80, 5 | 4,762 | 0 | 0 | 1,554 | 200 | 18.7 | | | Dominated |
| gFOBT 50-80, 2 | 9,554 | 0 | 0 | 1,763 | 221 | 20.3 | | | Dominated |
| FIT-DNA 50-80, 3 | 6,476 | 0 | 0 | 1,931 | 232 | 21.2 | | | Dominated |
| FIT 50-80, 1 | 17,062 | 0 | 0 | 2,013 | 250 | 22.6 | 114 | 6 | 18 |
| gFOBT 50-80, 1 | 14,364 | 0 | 0 | 2,395 | 252 | 22.8 | | | Dominated |
| FIT-DNA 50-80, 1* | 11,795 | 0 | 0 | 2,886 | 265 | 23.9 | 795 | 11 | 70* |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-80, 10 | 0 | 2,983 | 0 | 1,273 | 171 | 16.0 | 113 | 6 | 18 |
| SIG 50-80, 5 | 0 | 4,705 | 0 | 1,567 | 184 | 17.0 | 74 | 3 | 28 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-80, 10_2 | 9,098 | 2,500 | 0 | 2,053 | 246 | 22.4 | 148 | 7 | 20 |
| SIG+FIT 50-80, 5_3 | 6,144 | 4,108 | 0 | 2,090 | 239 | 21.8 | | | Dominated |
| SIG+FIT 50-80, 5_2* | 8,405 | 3,922 | 0 | 2,248 | 249 | 22.7 | 195 | 3 | 65* |
| SIG+gFOBT 50-80, 5_3 | 5,837 | 3,836 | 0 | 2,249 | 241 | 22.0 | | | Dominated |
| SIG+gFOBT 50-80, 10_2 | 8,339 | 2,318 | 0 | 2,288 | 248 | 22.5 | | | Dominated |
| SIG+FIT 50-80, 10_1 | 14,812 | 2,307 | 0 | 2,428 | 261 | 23.6 | 139 | 5 | 27 |
| SIG+gFOBT 50-80, 5_2* | 7,774 | 3,585 | 0 | 2,449 | 251 | 22.8 | | | Dominated |
| SIG+gFOBT 50-80, 10_1 | 12,537 | 2,115 | 0 | 2,735 | 261 | 23.6 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-80, 10* | 0 | 0 | 2,948 | 1,442 | 234 | 21.4 | 138 | 10 | 14* |
| CTC 50-80, 5 | 0 | 0 | 4,638 | 1,739 | 252 | 22.8 | 85 | 4 | 23 |

FIT = fecal immunochemical test; gFOBT = highly-sensitive guaiac-based fecal occult blood test; FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; LYG = life-years gained compared with no screening; CRC = colorectal cancer; ΔCOL = incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG = incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

**Appendix Table 15. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 85, and the set of recommended strategies assuming the colonoscopy strategy with a 5-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-85, 15 | 0 | 0 | 0 | 3,656 | 265 | 23.9 | 468 | 5 | 91 |
| COL 50-85, 10 | 0 | 0 | 0 | 4,405 | 277 | 24.9 | 398 | 5 | 166 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,502 | 286 | 25.7 | 213 | <1 | 1,661 |
| **Stool test** | | | | | | | | | |
| FIT 50-85, 3* | 8,111 | 0 | 0 | 1,095 | 223 | 20.2 | 39 | 2 | 17* |
| FIT 50-85, 2* | 11,165 | 0 | 0 | 1,377 | 245 | 22.2 | 50 | 2 | 24* |
| gFOBT 50-85, 3 | 7,565 | 0 | 0 | 1,441 | 222 | 20.3 | | | Dominated |
| FIT-DNA 50-85, 5 | 5,043 | 0 | 0 | 1,500 | 230 | 21.1 | | | Dominated |
| gFOBT 50-85, 2 | 9,970 | 0 | 0 | 1,801 | 245 | 22.3 | | | Dominated |
| FIT-DNA 50-85, 3 | 6,961 | 0 | 0 | 1,884 | 257 | 23.2 | | | Dominated |
| FIT 50-85, 1 | 18,589 | 0 | 0 | 1,937 | 267 | 24.1 | 79 | 2 | 50 |
| gFOBT 50-85, 1 | 15,090 | 0 | 0 | 2,476 | 266 | 24.1 | | | Dominated |
| FIT-DNA 50-85, 1 | 12,826 | 0 | 0 | 2,870 | 275 | 24.7 | 107 | 1 | 116 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-85, 10* | 0 | 2,910 | 0 | 1,484 | 205 | 18.9 | 139 | 5 | 28* |
| SIG 50-85, 5 | 0 | 4,691 | 0 | 1,965 | 229 | 21.2 | 56 | 1 | 99 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-85, 10_2* | 9,412 | 2,534 | 0 | 2,116 | 268 | 24.1 | 40 | 1 | 56* |
| SIG+FIT 50-85, 5_3 | 6,217 | 4,202 | 0 | 2,305 | 267 | 24.1 | | | Dominated |
| SIG+FIT 50-85, 5_2 | 8,557 | 4,041 | 0 | 2,419 | 271 | 24.5 | | | Dominated |
| SIG+gFOBT 50-85, 10_2 | 8,502 | 2,345 | 0 | 2,420 | 268 | 24.1 | | | Dominated |
| SIG+FIT 50-85, 10_1 | 15,698 | 2,396 | 0 | 2,469 | 275 | 24.7 | 73 | 1 | 92 |
| SIG+gFOBT 50-85, 5_3 | 5,893 | 3,892 | 0 | 2,494 | 266 | 24.1 | | | Dominated |
| SIG+gFOBT 50-85, 5_2 | 7,818 | 3,651 | 0 | 2,658 | 271 | 24.4 | | | Dominated |
| SIG+gFOBT 50-85, 10_1 | 12,922 | 2,188 | 0 | 2,875 | 274 | 24.7 | | | Dominated |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-85, 10* | 0 | 0 | 2,874 | 1,615 | 245 | 22.4 | 155 | 6 | 26* |
| CTC 50-85, 5 | 0 | 0 | 4,627 | 2,079 | 268 | 24.3 | 58 | 1 | 111 |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-85, 15 | 0 | 0 | 0 | 3,779 | 234 | 21.3 | | | Dominated |
| COL 50-85, 10* | 0 | 0 | 0 | 4,485 | 251 | 22.6 | 384 | 3 | 116* |
| COL 50-85, 5 | 0 | 0 | 0 | 6,525 | 266 | 23.6 | 229 | <1 | 1,146 |
| **Stool test** | | | | | | | | | |
| FIT 50-85, 3* | 8,032 | 0 | 0 | 1,096 | 188 | 17.3 | 26 | 2 | 12* |
| FIT 50-85, 2 | 11,233 | 0 | 0 | 1,375 | 213 | 19.4 | 40 | 3 | 16 |
| gFOBT 50-85, 3 | 7,408 | 0 | 0 | 1,430 | 186 | 17.3 | | | Dominated |
| FIT-DNA 50-85, 5 | 5,048 | 0 | 0 | 1,516 | 200 | 18.5 | | | Dominated |
| gFOBT 50-85, 2 | 10,024 | 0 | 0 | 1,814 | 211 | 19.4 | | | Dominated |
| FIT-DNA 50-85, 3 | 6,745 | 0 | 0 | 1,867 | 224 | 20.3 | | | Dominated |
| FIT 50-85, 1 | 18,796 | 0 | 0 | 1,921 | 240 | 21.6 | 66 | 2 | 27 |
| gFOBT 50-85, 1 | 15,161 | 0 | 0 | 2,505 | 239 | 21.6 | | | Dominated |
| FIT-DNA 50-85, 1 | 12,888 | 0 | 0 | 2,901 | 252 | 22.5 | 980 | 12 | 83 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-85, 10* | 0 | 2,746 | 0 | 2,001 | 205 | 19.0 | 120 | 4 | 28* |
| SIG 50-85, 5 | 0 | 4,349 | 0 | 2,408 | 224 | 20.5 | 42 | <1 | 101 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-85, 10_2* | 8,706 | 2,164 | 0 | 2,313 | 239 | 21.6 | 21 | 1 | 27* |
| SIG+gFOBT 50-85, 10_2 | 7,811 | 1,908 | 0 | 2,558 | 237 | 21.4 | | | Dominated |
| SIG+FIT 50-85, 5_3 | 5,491 | 3,802 | 0 | 2,579 | 242 | 21.8 | | | Dominated |
| SIG+FIT 50-85, 5_2 | 7,717 | 3,646 | 0 | 2,560 | 245 | 22.0 | | | Dominated |
| SIG+FIT 50-85, 10_1 | 14,983 | 2,177 | 0 | 2,675 | 252 | 22.5 | 41 | 1 | 59 |
| SIG+gFOBT 50-85, 5_3 | 5,154 | 3,526 | 0 | 2,733 | 241 | 21.7 | | | Dominated |
| SIG+gFOBT 50-85, 5_2 | 7,009 | 3,248 | 0 | 2,844 | 243 | 22.0 | | | Dominated |
| SIG+gFOBT 50-85, 10_1 | 12,442 | 1,844 | 0 | 3,042 | 250 | 22.4 | | | Dominated |

**Appendix Table 15. Outcomes for colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 85, and the set of recommended strategies assuming the colonoscopy strategy with a 5-year interval is chosen**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-85, 10* | 0 | 0 | 2,927 | 1,405 | 194 | 17.9 | 112 | 10 | 12* |
| CTC 50-85, 5 | 0 | 0 | 4,792 | 1,864 | 231 | 21.1 | 47 | 1 | 37 |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-85, 15* | 0 | 0 | 0 | 3,728 | 264 | 24.1 | 470 | 7 | 72* |
| COL 50-85, 10 | 0 | 0 | 0 | 4,464 | 273 | 24.8 | 414 | 3 | 126 |
| COL 50-85, 5 | 0 | 0 | 0 | 6,586 | 280 | 25.3 | 235 | <1 | 947 |
| **Stool test** | | | | | | | | | |
| FIT 50-85, 3* | 8,084 | 0 | 0 | 1,201 | 191 | 17.9 | 120 | 13 | 10* |
| gFOBT 50-85, 3 | 7,643 | 0 | 0 | 1,466 | 195 | 18.4 | | | Dominated |
| FIT 50-85, 2* | 11,071 | 0 | 0 | 1,504 | 220 | 20.4 | 49 | 2 | 24* |
| FIT-DNA 50-85, 5 | 5,028 | 0 | 0 | 1,606 | 203 | 19.3 | | | Dominated |
| gFOBT 50-85, 2 | 10,089 | 0 | 0 | 1,824 | 223 | 20.8 | | | Dominated |
| FIT-DNA 50-85, 3 | 6,903 | 0 | 0 | 2,005 | 235 | 21.8 | | | Dominated |
| FIT 50-85, 1 | 18,224 | 0 | 0 | 2,091 | 253 | 23.2 | 78 | 3 | 26 |
| gFOBT 50-85, 1* | 15,321 | 0 | 0 | 2,493 | 255 | 23.3 | 402 | 1 | 318* |
| FIT-DNA 50-85, 1 | 12,542 | 0 | 0 | 2,994 | 266 | 24.3 | 903 | 13 | 69 |
| **Sigmoidoscopy** | | | | | | | | | |
| SIG 50-85, 10 | 0 | 2,983 | 0 | 1,273 | 171 | 16.0 | 113 | 6 | 18 |
| SIG 50-85, 5 | 0 | 4,987 | 0 | 1,616 | 184 | 17.3 | 49 | 1 | 71 |
| **Sigmoidoscopy + stool test** | | | | | | | | | |
| SIG+FIT 50-85, 10_2* | 9,591 | 2,544 | 0 | 2,094 | 248 | 22.7 | 42 | 1 | 31* |
| SIG+FIT 50-85, 5_3 | 6,516 | 4,338 | 0 | 2,157 | 241 | 22.2 | | | Dominated |
| SIG+FIT 50-85, 5_2 | 8,906 | 4,138 | 0 | 2,317 | 251 | 23.0 | | | Dominated |
| SIG+gFOBT 50-85, 5_3 | 6,218 | 4,056 | 0 | 2,327 | 242 | 22.4 | | | Dominated |
| SIG+gFOBT 50-85, 10_2 | 8,790 | 2,386 | 0 | 2,346 | 250 | 22.9 | | | Dominated |
| SIG+FIT 50-85, 10_1 | 15,814 | 2,389 | 0 | 2,502 | 263 | 23.9 | 74 | 2 | 43 |
| SIG+gFOBT 50-85, 5_2 | 8,228 | 3,786 | 0 | 2,529 | 252 | 23.2 | | | Dominated |
| SIG+gFOBT 50-85, 10_1 | 13,373 | 2,220 | 0 | 2,834 | 263 | 24.0 | 332 | 9 | 448 |
| **Computed tomographic colonography** | | | | | | | | | |
| CTC 50-85, 10* | 0 | 0 | 2,948 | 1,442 | 234 | 21.4 | 138 | 10 | 14* |
| CTC 50-85, 5 | 0 | 0 | 4,900 | 1,795 | 254 | 23.2 | 56 | 2 | 29 |

FIT = fecal immunochemical test; gFOBT = highly-sensitive guaiac-based fecal occult blood test; FIT-DNA = fecal immunochemical test with a DNA stool test; SIG = flexible sigmoidoscopy; CTC = computed tomographic colonography; COL = colonoscopy; LYG = life-years gained compared with no screening; CRC = colorectal cancer; ΔCOL = incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG = incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

**Appendix Table 16. Sensitivity analysis: percent change in outcomes compared to the base-case analysis for the set of model-recommended strategies* using the worst-case and best-case sets of test characteristics,† by model**

| Model/strategy | Percent change in outcomes from base-case assumptions | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Colonoscopies | | Non-colonoscopy tests | | Life-years gained | | CRC deaths averted | |
| | Worst case | Best case | Worst case | Best case | Worst case | Best case | Worst case | Best case |
| ***SimCRC*** | | | | | | | | |
| COL 50-75, 10 | -1% | 1% | 0% | 0% | -1% | 2% | -1% | 2% |
| FIT 50-75, 1 | -5% | 5% | 1% | -1% | -4% | 4% | -4% | 4% |
| SIG+FIT 50-75, 10_1 | -3% | 3% | 1% | -1% | -2% | 3% | -2% | 3% |
| CTC 50-75, 5 | -4% | 5% | 1% | -1% | -4% | 4% | -3% | 4% |
| ***MISCAN*** | | | | | | | | |
| COL 50-75, 10 | -1% | 1% | 0% | 0% | -2% | 3% | -2% | 2% |
| FIT 50-75, 1 | -4% | 3% | 1% | -1% | -6% | 6% | -5% | 5% |
| SIG+FIT 50-75, 10_1 | -2% | 2% | 1% | -1% | -4% | 4% | -3% | 5% |
| CTC 50-75, 5 | -3% | 3% | 1% | -1% | -5% | 7% | -5% | 6% |
| ***CRC-SPIN*** | | | | | | | | |
| COL 50-75, 10 | -1% | 1% | 0% | 0% | -2% | 2% | -1% | 1% |
| FIT 50-75, 1 | -5% | 5% | 2% | -2% | -5% | 5% | -4% | 4% |
| SIG+FIT 50-75, 10_1 | -4% | 4% | 2% | -2% | -3% | 3% | -3% | 3% |
| CTC 50-75, 5 | -3% | 3% | 1% | -1% | -4% | 4% | -4% | 3% |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; FIT – fecal immunochemical test; SIG – flexible sigmoidoscopy.

* With age to begin screening of 50 and age to end screening of 75 and assuming colonoscopy strategy with a 10-year interval is selected.

† See **Table 4** for base-case, best-case, and worst-case sets of test characteristics.

**Appendix Table 17. Sensitivity analysis: efficient and near-efficient stool-based screening strategies* with age to begin of 50 or 55, by model, with the inclusion of FIT strategies with a lower cutoff for positivity of 50 ng of hemoglobin per mL of buffer (i.e., 10 µg of hemoglobin per g of feces)**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL/ΔLYG) |
| **SimCRC** | | | | | | | | | |
| FIT 55-75, 3 | 5,306 | 0 | 0 | 807 | 178 | 16.1 | -- | -- | -- |
| FIT 50-75, 3 | 6,887 | 0 | 0 | 971 | 212 | 18.2 | 164 | 34 | 5 |
| FIT 50-80, 3 | 7,694 | 0 | 0 | 1,055 | 220 | 19.7 | 84 | 9 | 10 |
| FIT 50-85, 3 | 8,111 | 0 | 0 | 1,095 | 223 | 20.2 | | | Near-efficient† |
| FIT 50-75, 2 | 9,326 | 0 | 0 | 1,215 | 234 | 20.2 | 160 | 14 | 12 |
| FIT 50-80, 2 | 10,572 | 0 | 0 | 1,327 | 243 | 21.7 | 112 | 9 | 13 |
| FIT 50-85, 2 | 11,165 | 0 | 0 | 1,377 | 245 | 22.2 | | | Near-efficient† |
| FIT 50-75, 1 | 15,778 | 0 | 0 | 1,739 | 260 | 22.7 | | | Near-efficient† |
| FIT 50-80, 1 | 17,426 | 0 | 0 | 1,858 | 265 | 23.7 | 531 | 22 | 24 |
| FIT 50-85, 1 | 18,589 | 0 | 0 | 1,937 | 267 | 24.1 | 79 | 2 | 50 |
| FIT50 50-75, 1 | 12,485 | 0 | 0 | 2,326 | 268 | 23.5 | | | Near-efficient† |
| FIT50 50-80, 1 | 13,711 | 0 | 0 | 2,477 | 272 | 24.3 | | | Near-efficient† |
| FIT50 50-85, 1 | 14,568 | 0 | 0 | 2,577 | 273 | 24.6 | 640 | 6 | 100 |
| FIT-DNA 50-80, 1 | 12,096 | 0 | 0 | 2,763 | 274 | 24.5 | | | Near-efficient† |
| FIT-DNA 50-85, 1 | 12,826 | 0 | 0 | 2,870 | 275 | 24.7 | 292 | 2 | 151 |
| **MISCAN** | | | | | | | | | |
| FIT 55-75, 3 | 5,250 | 0 | 0 | 833 | 153 | 13.9 | -- | -- | -- |
| FIT 55-80, 3 | 6,204 | 0 | 0 | 917 | 165 | 15.8 | | | Near-efficient† |
| FIT 55-85, 3 | 6,859 | 0 | 0 | 967 | 169 | 16.6 | | | Near-efficient† |
| FIT 50-75, 3 | 6,795 | 0 | 0 | 995 | 176 | 15.3 | 162 | 23 | 7 |
| FIT 50-80, 3 | 7,693 | 0 | 0 | 1,070 | 186 | 16.9 | 75 | 10 | 8 |
| FIT 50-85, 3 | 8,032 | 0 | 0 | 1,096 | 188 | 17.3 | | | Near-efficient† |
| FIT 50-75, 2 | 9,342 | 0 | 0 | 1,243 | 200 | 17.3 | | | Near-efficient† |
| FIT 50-80, 2 | 10,613 | 0 | 0 | 1,334 | 210 | 18.9 | 264 | 24 | 11 |
| FIT 50-85, 2 | 11,233 | 0 | 0 | 1,375 | 213 | 19.4 | 40 | 3 | 16 |
| FIT 50-75, 1 | 15,843 | 0 | 0 | 1,757 | 231 | 20.0 | | | Near-efficient† |
| FIT 50-80, 1 | 17,552 | 0 | 0 | 1,855 | 238 | 21.1 | 481 | 25 | 19 |
| FIT 50-85, 1 | 18,796 | 0 | 0 | 1,921 | 240 | 21.6 | 66 | 2 | 27 |
| FIT50 50-75, 1 | 12,425 | 0 | 0 | 2,399 | 242 | 21.0 | | | Near-efficient† |
| FIT50 50-80, 1 | 13,666 | 0 | 0 | 2,530 | 247 | 21.9 | | | Near-efficient† |
| FIT50 50-85, 1 | 14,564 | 0 | 0 | 2,620 | 249 | 22.2 | 699 | 9 | 81 |
| FIT-DNA 50-80, 1 | 12,108 | 0 | 0 | 2,804 | 250 | 22.2 | | | Near-efficient† |
| FIT-DNA 50-85, 1 | 12,888 | 0 | 0 | 2,901 | 252 | 22.5 | 281 | 3 | 88 |
| **CRC-SPIN** | | | | | | | | | |
| FIT 55-75, 3 | 5,301 | 0 | 0 | 895 | 152 | 14.0 | -- | -- | -- |
| FIT 55-80, 3 | 6,254 | 0 | 0 | 995 | 164 | 15.9 | | | Near-efficient† |
| FIT 50-75, 3 | 6,857 | 0 | 0 | 1,081 | 178 | 15.8 | 186 | 26 | 7 |
| FIT 55-75, 2 | 7,575 | 0 | 0 | 1,160 | 183 | 17.1 | | | Near-efficient† |
| FIT 50-80, 3 | 7,660 | 0 | 0 | 1,163 | 187 | 17.2 | | | Near-efficient† |
| FIT 50-85, 3 | 8,084 | 0 | 0 | 1,201 | 191 | 17.9 | | | Near-efficient† |
| FIT 50-75, 2 | 9,241 | 0 | 0 | 1,346 | 207 | 18.3 | 265 | 29 | 9 |
| FIT 50-80, 2 | 10,476 | 0 | 0 | 1,454 | 218 | 19.9 | 108 | 10 | 10 |
| FIT 50-85, 2 | 11,071 | 0 | 0 | 1,504 | 220 | 20.4 | | | Near-efficient† |
| FIT 50-75, 1 | 15,444 | 0 | 0 | 1,899 | 244 | 21.6 | 445 | 26 | 17 |
| FIT 50-80, 1 | 17,062 | 0 | 0 | 2,013 | 250 | 22.6 | 114 | 6 | 18 |
| FIT 50-85, 1 | 18,224 | 0 | 0 | 2,091 | 253 | 23.2 | 78 | 3 | 26 |
| FIT50 50-75, 1 | 12,339 | 0 | 0 | 2,392 | 255 | 22.5 | | | Near-efficient† |
| FIT50 50-80, 1 | 13,575 | 0 | 0 | 2,537 | 260 | 23.4 | | | Near-efficient† |
| FIT50 50-85, 1 | 14,460 | 0 | 0 | 2,638 | 262 | 23.8 | 547 | 9 | 62 |
| FIT-DNA 50-80, 1 | 11,795 | 0 | 0 | 2,886 | 265 | 23.9 | | | Near-efficient† |
| FIT-DNA 50-85, 1 | 12,542 | 0 | 0 | 2,994 | 266 | 24.3 | 357 | 4 | 83 |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed-tomographic colonography; FIT – fecal immunochemical test (positivity cutoff of ≥ 100 ng of hemoglobin per ml of buffer (i.e., 20 µg of hemoglobin per g of feces); FIT50 – fecal immunochemical test (positivity cutoff of ≥ 50 ng of hemoglobin per ml of buffer (i.e., 10 µg of hemoglobin per g of feces); FIT-DNA – multi-target stool DNA test (fecal immunochemical test with a DNA stool test); gFOBT – sensitive guaiac-based fecal occult blood test; LYG – life-years gained compared with no screening; SIG –

**Appendix Table 17. Sensitivity analysis: efficient and near-efficient stool-based screening strategies* with age to begin of 50 or 55, by model, with the inclusion of FIT strategies with a lower cutoff for positivity of 50 ng of hemoglobin per mL of buffer (i.e., 10 µg of hemoglobin per g of feces)**

flexible sigmoidoscopy; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* FIT, FIT50, FIT-DNA, and gFOBT.

† Strategy yields life-years gained within 98% of the efficient frontier.

**Appendix Table 18. Sensitivity analysis: outcomes for colonoscopy and stool-based colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 75, and the recommended stool-based strategies (assuming the colonoscopy strategy with a 10-year interval is chosen) after the inclusion of FIT strategies with a lower cutoff for positivity**

| Model/strategy | Outcomes per 1,000 40-year-olds | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Screening modality, age to begin-age to end, interval | Stool tests | SIGs | CTCs | COLs | LYG | CRC deaths averted | ΔCOL | ΔLYG | Efficiency ratio (ΔCOL / ΔLYG) |
| ***SimCRC*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,187 | 260 | 22.8 | 220 | 27 | 8 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,007 | 275 | 24.4 | 820 | 15 | 55 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,959 | 285 | 25.5 | 1,554 | 8 | 188 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,887 | 0 | 0 | 971 | 212 | 18.2 | 164 | 34 | 5 |
| FIT 50-75, 2 | 9,326 | 0 | 0 | 1,215 | 234 | 20.2 | 160 | 14 | 12 |
| gFOBT 50-75, 3 | 6,456 | 0 | 0 | 1,286 | 212 | 18.4 | | | Dominated |
| FIT-DNA 50-75, 5 | 4,391 | 0 | 0 | 1,364 | 224 | 19.7 | | | Dominated |
| FIT50 50-75, 3 | 6,339 | 0 | 0 | 1,404 | 237 | 20.5 | | | Dominated |
| gFOBT 50-75, 2 | 8,388 | 0 | 0 | 1,597 | 235 | 20.5 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,990 | 0 | 0 | 1,701 | 250 | 21.8 | | | Dominated |
| FIT50 50-75, 2 | 8,189 | 0 | 0 | 1,711 | 253 | 21.9 | | | Dominated |
| FIT 50-75, 1* | 15,778 | 0 | 0 | 1,739 | 260 | 22.7 | 413 | 17 | 24* |
| gFOBT 50-75, 1 | 12,914 | 0 | 0 | 2,230 | 261 | 22.9 | | | Dominated |
| FIT50 50-75, 1* | 12,485 | 0 | 0 | 2,326 | 268 | 23.5 | 389 | 1 | 289* |
| FIT-DNA 50-75, 1 | 11,041 | 0 | 0 | 2,601 | 271 | 23.9 | | | Dominated |
| ***MISCAN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,353 | 228 | 20.2 | 275 | 14 | 19 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,101 | 248 | 21.9 | 747 | 19 | 39 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,948 | 264 | 23.3 | 1,847 | 16 | 114 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,795 | 0 | 0 | 995 | 176 | 15.3 | 162 | 23 | 7 |
| FIT 50-75, 2* | 9,342 | 0 | 0 | 1,243 | 200 | 17.3 | 173 | 15 | 12* |
| gFOBT 50-75, 3 | 6,302 | 0 | 0 | 1,296 | 175 | 15.4 | | | Dominated |
| FIT-DNA 50-75, 5 | 4,380 | 0 | 0 | 1,402 | 193 | 17.1 | | | Dominated |
| FIT50 50-75, 3 | 6,148 | 0 | 0 | 1,437 | 200 | 17.3 | | | Dominated |
| gFOBT 50-75, 2 | 8,408 | 0 | 0 | 1,636 | 200 | 17.5 | | | Dominated |
| FIT-DNA 50-75, 3 | 5,779 | 0 | 0 | 1,714 | 215 | 18.7 | | | Dominated |
| FIT 50-75, 1* | 15,843 | 0 | 0 | 1,757 | 231 | 20.0 | 383 | 18 | 21* |
| FIT50 50-75, 2 | 8,164 | 0 | 0 | 1,774 | 220 | 19.0 | | | Dominated |
| gFOBT 50-75, 1 | 12,927 | 0 | 0 | 2,287 | 232 | 20.3 | | | Dominated |
| FIT50 50-75, 1* | 12,425 | 0 | 0 | 2,399 | 242 | 21.0 | 477 | 2 | 265* |
| FIT-DNA 50-75, 1 | 11,025 | 0 | 0 | 2,662 | 246 | 21.4 | | | Dominated |
| ***CRC-SPIN*** | | | | | | | | | |
| **Colonoscopy** | | | | | | | | | |
| COL 50-75, 15 | 0 | 0 | 0 | 3,258 | 257 | 22.7 | 243 | 21 | 12 |
| COL 50-75, 10 | 0 | 0 | 0 | 4,049 | 270 | 24.1 | 792 | 12 | 65 |
| COL 50-75, 5 | 0 | 0 | 0 | 5,995 | 279 | 25.0 | 1,532 | 6 | 273 |
| **Stool test** | | | | | | | | | |
| FIT 50-75, 3 | 6,857 | 0 | 0 | 1,081 | 178 | 15.8 | 186 | 26 | 7 |
| gFOBT 50-75, 3 | 6,498 | 0 | 0 | 1,317 | 183 | 16.4 | | | Dominated |
| FIT 50-75, 2 | 9,241 | 0 | 0 | 1,346 | 207 | 18.3 | 265 | 29 | 9 |
| FIT-DNA 50-75, 5 | 4,370 | 0 | 0 | 1,473 | 195 | 17.8 | | | Dominated |
| FIT50 50-75, 3 | 6,322 | 0 | 0 | 1,478 | 208 | 18.4 | | | |
| gFOBT 50-75, 2 | 8,448 | 0 | 0 | 1,626 | 212 | 18.8 | | | Dominated |
| FIT50 50-75, 2 | 8,143 | 0 | 0 | 1,784 | 230 | 20.3 | | | |
| FIT-DNA 50-75, 3 | 5,927 | 0 | 0 | 1,827 | 226 | 20.2 | | | Dominated |
| FIT 50-75, 1 | 15,444 | 0 | 0 | 1,899 | 244 | 21.6 | 445 | 26 | 17 |
| gFOBT 50-75, 1 | 13,026 | 0 | 0 | 2,253 | 247 | 21.9 | | | Dominated |
| FIT50 50-75, 1* | 12,339 | 0 | 0 | 2,392 | 255 | 22.5 | 301 | 1 | 208* |
| FIT-DNA 50-75, 1 | 10,745 | 0 | 0 | 2,729 | 261 | 23.2 | | | Dominated |

COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; FIT – fecal immunochemical test (positivity cutoff of ≥ 100 ng of hemoglobin per ml of buffer (i.e., 20 µg of hemoglobin per g of feces); FIT50 – fecal immunochemical test (positivity cutoff of ≥ 50 ng of hemoglobin per ml of buffer (i.e., 10 µg of

**Appendix Table 18. Sensitivity analysis: outcomes for colonoscopy and stool-based colorectal cancer screening strategies with age to begin screening of 50 and age to end screening of 75, and the recommended stool-based strategies (assuming the colonoscopy strategy with a 10-year interval is chosen) after the inclusion of FIT strategies with a lower cutoff for positivity**

hemoglobin per g of feces); FIT-DNA – multi-target stool DNA test (fecal immunochemical test with a DNA stool test); gFOBT – sensitive guaiac-based fecal occult blood test; SIG – flexible sigmoidoscopy; LYG – life-years gained compared with no screening; ΔCOL – incremental number of colonoscopies compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Indicates the strategy is nearly efficient (i.e. life-years gained within 98% of the within-test efficient frontier).

**Appendix Table 19. Sensitivity analysis: efficient and near-efficient CTC screening strategies with age to begin screening of 50 or 55, by model, using the number of cathartic bowel preparations as the proxy for burden and harms of screening**

| Model/strategy<br>Screening modality, age to begin-age to end, interval | Outcomes per 1,000 40-year-olds | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | CTCs | COLs | cPREPs | LYG | CRC deaths averted | ΔcPREPs | ΔLYG | Efficiency ratio (ΔcPREPs/ΔLYG) |
| **SimCRC** | | | | | | | | |
| CTC 55-75, 10 | 2,250 | 1,396 | 3,646 | 214 | 20.7 | -- | -- | -- |
| CTC 50-75, 10 | 2,458 | 1,460 | 3,918 | 239 | 21.1 | 272 | 25 | 11 |
| CTC 50-80, 10 | 2,874 | 1,615 | 4,489 | 245 | 22.4 | | | Near-efficient* |
| CTC 50-75, 5 | 4,069 | 1,927 | 5,996 | 265 | 23.7 | 2,077 | 26 | 81 |
| CTC 50-80, 5 | 4,405 | 2,021 | 6,425 | 267 | 24.1 | 430 | 2 | 200 |
| CTC 50-85, 5 | 4,627 | 2,079 | 6,706 | 268 | 24.3 | 280 | 1 | 536 |
| **MISCAN** | | | | | | | | |
| CTC 55-75, 10 | 2,284 | 1,220 | 3,504 | 172 | 16.4 | -- | -- | -- |
| CTC 50-75, 10 | 2,485 | 1,293 | 3,778 | 184 | 16.1 | 274 | 12 | 24 |
| CTC 50-80, 10 | 2,927 | 1,405 | 4,331 | 194 | 17.9 | | | Near-efficient* |
| CTC 55-75, 5 | 3,388 | 1,523 | 4,912 | 204 | 18.9 | | | Near-efficient* |
| CTC 50-75, 5 | 4,171 | 1,743 | 5,914 | 226 | 19.9 | 2,135 | 42 | 51 |
| CTC 50-80, 5 | 4,539 | 1,817 | 6,355 | 230 | 20.7 | 442 | 4 | 98 |
| CTC 50-85, 5 | 4,792 | 1,864 | 6,655 | 231 | 21.1 | 300 | 1 | 238 |
| **CRC-SPIN** | | | | | | | | |
| CTC 55-75, 10 | 2,296 | 1,265 | 3,561 | 209 | 19.8 | -- | -- | -- |
| CTC 50-75, 10 | 2,500 | 1,304 | 3,804 | 224 | 19.6 | 244 | 15 | 16 |
| CTC 50-80, 10 | 2,948 | 1,442 | 4,391 | 234 | 21.4 | 586 | 10 | 61 |
| CTC 50-75, 5 | 4,254 | 1,654 | 5,908 | 248 | 22.0 | 1,518 | 15 | 103 |
| CTC 50-80, 5 | 4,638 | 1,739 | 6,378 | 252 | 22.8 | 469 | 4 | 125 |
| CTC 50-85, 5 | 4,900 | 1,795 | 6,695 | 254 | 23.2 | 317 | 2 | 164 |

cPREPs – procedures with cathartic bowel preparation (i.e., CT colonographies and colonoscopies); COL – colonoscopy; CRC – colorectal cancer; CTC – computed tomographic colonography; LYG – life-years gained compared with no screening; ΔcPREP – incremental number of procedures requiring cathartic bowel preparation compared with the next-best non-dominated strategy; ΔLYG – incremental number of life-years gained compared with the next best non-dominated strategy.

* Strategy yields life-years gained within 98% of the efficient frontier.