# Individualizing colonoscopy screening by sex and race

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**Background:** There is increasing discussion whether colorectal cancer (CRC) screening guidelines should be individualized by sex and race.

**Objectives:** To determine individualized colonoscopic screening guidelines by sex and race for the average-risk population and to compare the cost-effectiveness of this approach with that of uniform guidelines for all.

**Design:** We used the MISCAN-Colon microsimulation model to estimate life expectancy and lifetime CRC screening and treatment costs in a U.S. cohort of black and white men and women at average risk for CRC. We compared the base-case strategy of no screening and 3 competing colonoscopy strategies: (1) the currently recommended ''uniform 10-yearly colonoscopy from age 50 years,'' (2) a shorter interval ''uniform 8-yearly colonoscopy from age 51 years,'' and (3) ''individualized screening according to sex and race.''

**Results:** The base-case strategy of no screening was the least expensive, yet least effective. The uniform 10-yearly colonoscopy strategy was dominated. The uniform 8-yearly colonoscopy and individualized strategies both increased life expectancy by 0.0433 to 0.0435 years per individual, at a cost of $15,565 to $15,837 per life-year gained. In the individualized strategy, blacks began screening 6 years earlier, with a 1-year shorter interval compared with whites. The individualized policies were essentially the same for men and women, because the higher CRC risk in men was offset by their shorter life expectancy. The results were robust for changes in model assumptions.

**Conclusions:** The improvements in costs and effects of individualizing CRC screening on a population level were only marginal. Individualized guidelines, however, could contribute to decreasing disparities between blacks and whites. The acceptability and feasibility of individualized guidelines, therefore, should be explored. (Gastrointest Endosc 2009;70:96-108.)

For the average-risk population, the U.S. Multi-Society Task Force on Colorectal Cancer and the American Cancer Society recommend starting colorectal cancer (CRC) screening at the age of 50 years, with an identical menu of screening options for men and women of all races.[1,2] There are separate guidelines for individuals at increased risk because of a family history of CRC, a genetic predisposition (eg, familial adenomatous polyposis and hereditary nonpolyposis colorectal cancer), or a personal history of colorectal cancer, adenomas, or inflammatory bowel disease. The U.S. Multi-Society Task Force on Colorectal Cancer and the American Cancer Society recommend that these individuals have colonoscopy screening at earlier ages and with higher frequency than the general population.[1,2] Race or sex is not used as a basis for modifying recommendations.

Given the differences in CRC risk by sex, race, and ethnicity, debate has arisen whether screening guidelines should be individualized accordingly.[3] The American College of Gastroenterology advocates that screening should start earlier in blacks because of the higher incidence and younger age at presentation of CRC in this population subgroup.[4] During the period 1997 to 2001,[5] black men had the highest age-specific CRC mortality, whereas white women had the lowest rate in the United States (Fig. 1). The 4 curves in Figure 1 become nearly indistinguishable when the rates for blacks are shifted 5 years later

*Abbreviations: CI, confidence interval; CRC, colorectal cancer; FOBT, fecal occult blood test; NCI, U.S. National Cancer Institute; SEER, surveillance epidemiology and end results.*

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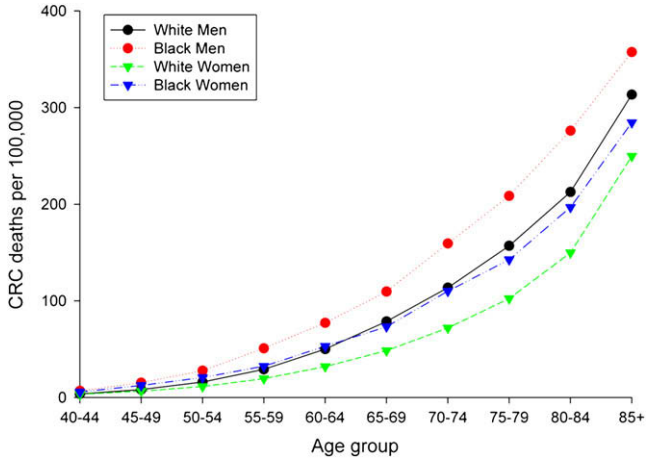


**Figure 1.** U.S. age-specific colorectal cancer mortality rates per 100,000 white men, black men, white women, and black women, 1997-2001 (data from Ries et al[5]).

compared with the whites (including Hispanics) and 5 years earlier for women compared with men.[5] The disparity seems to support individualizing age of screening initiation by sex and race.

Next to mortality, other determinants should be considered for individualizing screening guidelines. Important determinants would be life expectancy, incidence, stage distribution, survival, and costs. A simulation approach can take all these aspects into account and estimate costs and life-years gained, which is a commonly used summary measure for the benefit of cancer screening,[6] for different screening strategies. In this study, we used the MISCAN-Colon microsimulation model to determine individualized colonoscopy screening guidelines by sex and race for the average-risk population and compare their cost-effectiveness to uniform guidelines with the same screening ages and interval for all.

## MATERIALS AND METHODS

We used the MISCAN-Colon microsimulation model to determine the most cost-effective approach for colonoscopy screening in the average-risk population. The base-case strategy was no screening. This strategy was compared with 2 uniform and 1 individualized colonoscopy strategies.

### MISCAN-Colon microsimulation model

The MISCAN microsimulation model was developed at the Department of Public Health, Erasmus MC, the Netherlands, and has been used to evaluate breast, cervical, colon, and prostate cancer screening. MISCAN-Colon, the CRC version of the MISCAN model, was developed in collaboration with the U.S. National Cancer Institute (NCI) and experts in the field of CRC to assess the effect of different interventions on CRC. A graphical representation of the natural history in the model is given in Figure 2, and the main natural history assumptions in the model are listed in Table 1. A detailed description of the model and the data sources that informed the quantification of the model can be found in Appendix 1 (available online at www.giejournal.org), in previous publications,[7,8] and also in a standardized model profiler.[9] In brief, the MISCAN-Colon model simulates the relevant biographies of a large population of individuals from birth to death, first without screening and subsequently with the changes that would occur under the implementation of screening. CRC arises in this population according to the adenoma-carcinoma sequence.[10,11] More than 1 adenoma can occur in an individual, and each adenoma can independently develop into CRC. Adenomas can progress in size from small (1-5 mm) to medium (6-9 mm) to large (10+ mm). Most adenomas will never develop into cancer (nonprogressive adenomas), but some (progressive adenomas) will eventually become a clinical cancer. Diagnosis of cancer occurs on average 10 years after the manifestation of the adenoma from which it developed. This development competes with death from other causes. A preclinical cancer may progress from stage I to stage IV. In every stage, there is a chance of the cancer being diagnosed because of symptoms. The cure rate and survival after diagnosis without cure depend on the stage of the cancer. The model also simulates how screening can interrupt the development of CRC and how it improves prognosis. With screening, adenomas may be detected and removed and preclinical cancers may be found, depending on sensitivity. In this way, screening may prevent CRC incidence or CRC death. The life-years gained by screening are calculated by comparing the model-predicted life expectancy of the population with and without screening. We assumed the sensitivity of colonoscopy is 75% (95% CI, 70%-79%) for small adenomas (1-5 mm), 85% (95% CI, 80%-92%) for medium adenomas (6-9 mm), and 95% (95% CI, 92%-99%) for large adenomas (10+ mm) and cancers, based on back-to-back colonoscopy studies.[12] We assumed a specificity of

### Capsule Summary

**What is already known on this topic**

- Targeted colorectal screening guidelines exist for individuals at increased risk because of a family or personal history or genetic predisposition, but it is not based on race or sex.

**What this study adds to our knowledge**

- A microsimulation model revealed that individualizing colorectal screening guidelines by sex or race in an average-risk population had only marginal effects on lifetime costs and outcomes.

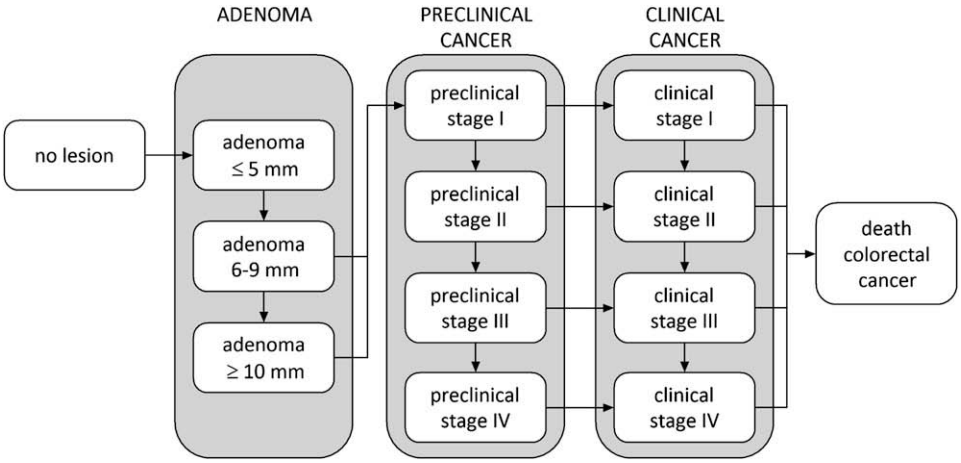


**Figure 2.** Adenoma and cancer stages in the MISCAN-Colon model. Cancer stages correspond to the American Joint Committee on Cancer/International Union Against Cancer staging system for colorectal cancer. Adenomas are categorized by size. The size-specific prevalence of adenomas, as well as the proportion of adenomas that ever develop into cancer, is dependent on age. It is assumed that the proportion of progressive adenomas increases from 16% at age 65 years to 37% at age 75 years, and 96% at age 100 years. It is assumed that 50% of nonprogressive adenomas will remain at the 6-mm to 9-mm stage until death and that 50% will progress to the ≥10-mm stage. For progressive adenomas, it is assumed that 30% will develop through the sequence ≤5-mm adenoma → 6-mm to 9-mm adenoma → preclinical cancer stage I, and that 70% will develop through the sequence ≤5-mm adenoma → 6-mm to 9-mm adenoma → ≥10-mm adenoma → preclinical cancer stage I. The mean duration time for progressive adenoma is assumed to be 16.4 years (with an exponential distribution). The mean duration time for preclinical cancer is assumed to be 2 years (stage I), 1 year (stage II), 1.5 years (stage III), and 0.8 years (stage IV). The model is calibrated to reproduce observed CRC incidence, stage distribution, and survival by sex and race (see Materials and Methods section).

90% of colonoscopy. This percentage was equal to 1 minus the 10% of the population without adenomas or cancer but with hyperplastic polyps, lipomas, or other lesions that lead to polypectomy and pathology after colonoscopy. Specificity was assumed to be independent of the screening round. We assumed a cecal intubation rate of 95%.[13-15] Harms associated with colonoscopy were assumed to be perforations (0.7 per 1000 colonoscopies), serosal burns (0.3 per 1000), bleeds that require transfusion (0.4 per 1000), and bleeds that do not require transfusion (1.1 per 1000), all of which can occur with or without polypectomy.[16-19] We assumed that fatal events occur at a rate of 1 per 10,000 colonoscopies.[20]

The validity of the model is based on observational data before the introduction of screening, such as clinical incidence and mortality from CRC (Surveillance Research Program, surveillance epidemiology and end results [SEER]*Stat Software, version 5.3.1., 2003; NCI, Bethesda, Md) and the size distribution of adenomas in colonoscopy and autopsy studies.[21-25] The external validity has further been tested on the results of large (randomized) screening and surveillance studies, such as the Minnesota Colon Cancer Control Study,[26] the Colon Cancer Prevention Program sigmoidoscopy study,[26] and the National Polyp Study.[27] Also, the model was able to explain observed incidence and mortality trends in the United States when accounting for risk factor trends, screening practice, and chemotherapy treatment.[28]

In this study, the model was used to simulate a U.S. cohort born in 1967, subdivided by sex and race (blacks and whites, including Hispanics).[29] Age-specific adenoma onset, distribution of cancer localization over the colorectum, distribution of CRC stages, stage-specific CRC survival, and all-cause mortality rates were adjusted for all sex and race combinations to reflect observed CRC incidence and mortality and other-cause mortality in the period 1997 to 2001 (SEER*Stat Software, version 5.3.1., 2003; NCI). Adenoma and cancer progression were assumed to be the same for all sexes and races. Subsequently, the model was used to predict costs and life expectancy for different screening strategies.

According to our model, the current recommendation of colonoscopy screening every 10 years from age 50 years was not optimally cost effective, although it was close. To enable a fair and interpretable comparison between uniform and individualized guidelines, we also determined a cost-effective uniform colonoscopy strategy. To obtain this cost-effective uniform strategy, we simulated more than 1000 colonoscopy screening policies that differed with respect to age to begin screening, screening interval, and total number of screenings. Policies that were more costly and less effective than other policies were ruled out as nonefficient by simple dominance. Policies that were more costly and less effective than a combination of other strategies were ruled out as nonefficient by extended dominance. Of the remaining policies (Appendix 2, available online at www.giejournal.org), we selected the policy that was closest to the current recommendation with respect to the number of screenings and the age to begin screening as the alternative uniform strategy (the result was strategy 2).

To obtain individualized guidelines, we first determined the cost-effective colonoscopy policies by population

**TABLE 1. Main natural history assumptions in the MISCAN-Colon model**

| Model parameter | Value | Source |
|---|---|---|
| Distribution of risk for adenomas over the general population | Gamma distributed, mean 1, variance 2 | Fit to multiplicity distribution of adenomas in colonoscopy and autopsy studies[21-25]: |
| | | Age 60: |
| | | 1 or more 20% |
| | | 2 or more 6% |
| | | 3 or more 2% |
| | | Age 90: |
| | | 1 or more 37% |
| | | 2 or more 17% |
| | | 3 or more 9% |
| Adenoma incidence per year | Age, sex, and race dependent | Fit to adenoma prevalence in autopsy and colonoscopy studies of 15% in age group 50–59 to 33% in age group 70+,[21-25] and to cancer incidence per 100,000 in 1997-2001 in SEER registry*: |

| | White | | Black | | | White | | Black | |
|---|---|---|---|---|---|---|---|---|---|
| Age: | Men | Women | Men | Women | Age (y) | Men | Women | Men | Women |
| 0-30 years: | 0.0% | 0.0% | 0.0% | 0.0% | 0-20: | 0.1 | 0.1 | 0.1 | 0.0 |
| 30-39 y: | 0.2% | 0.1% | 0.2% | 0.2% | 20-24: | 0.7 | 0.6 | 0.4 | 1.3 |
| 40-44 y: | 0.4% | 0.4% | 1.0% | 0.6% | 25-29: | 1.5 | 1.8 | 2.1 | 1.9 |
| 45-49 y: | 0.9% | 0.6% | 1.3% | 1.2% | 30-34: | 3.6 | 3.5 | 3.1 | 3.8 |
| 50-54 y: | 1.6% | 1.0% | 2.0% | 1.5% | 35-39: | 7.1 | 5.8 | 8.5 | 8.1 |
| 55-59 y: | 2.9% | 1.8% | 3.0% | 2.3% | 40-44: | 12.9 | 11.1 | 17.5 | 14.8 |
| 60-64 y: | 3.2% | 2.2% | 3.3% | 2.4% | 45-49: | 26.3 | 22.2 | 36.9 | 33.1 |
| 65-69 y: | 3.2% | 2.2% | 3.7% | 2.5% | 50-54: | 51.5 | 37.8 | 74.1 | 57.3 |
| 70-74 y: | 3.2% | 2.3% | 4.3% | 2.5% | 55-59: | 91.4 | 60.5 | 111.4 | 97.3 |
| 75-84 y: | 1.8% | 1.2% | 1.3% | 1.0% | 60-64: | 150.0 | 103.5 | 198.4 | 140.1 |
| 85-100 y: | 1.4% | 1.1% | 1.1% | 0.5% | 65-69: | 226.5 | 151.8 | 231.9 | 193.9 |
| | | | | | 70-74: | 302.8 | 212.8 | 315.3 | 237.8 |
| | | | | | 75-79: | 378.1 | 279.9 | 435.7 | 309.0 |
| | | | | | 80-84: | 457.4 | 338.4 | 488.1 | 361.2 |
| | | | | | 85-100: | 500.9 | 391.6 | 469.1 | 335.6 |

| | | |
|---|---|---|
| Probability that a new adenoma is progressive | Dependent on age at onset:<br>0–65 y: 14%<br>65–100 y: linearly increasing from 14% to 96% | Fit to adenoma prevalence in autopsy studies,[21-25] cancer incidence in SEER registry in 1978.* |
| Regression of adenomas | No significant regression of adenomas | Expert opinion |
| Mean duration of development of progressive adenomas to clinical cancer | 20 y | Expert opinion† |

(*continued on next page*)

**TABLE 1 (*continued*)**

| | | | | | |
|---|---|---|---|---|---|
| Mean duration of preclinical cancer | 3.6 y | | | | Estimated from cancer detection rate at first screening and background cancer incidence in FOBT trials.[76,77] |
| Mean duration of adenoma | 16.4 y | | | | 20–3.6 y |
| Percentage of non-]progressive adenomas that stay at 6-9 mm | 50% | | | | Fit to size distribution of adenomas in autopsy studies[21-25]:<br>1-5 mm: 56%<br>6-9 mm: 24%<br>10+ mm: 20% |
| Percentage of nonprogressive adenoma that become 10 mm or larger | 50% | | | | Fit to size distribution of adenomas in autopsy studies[21-25]:<br>1-5 mm: 56%<br>6-9 mm: 24%<br>10+ mm: 20% |
| Percentage of cancers that develops from 6-9 mm adenoma and from 10+ mm adenoma | 30% of cancer develops from 6-9 mm, 70% from 10+ mm | | | | Expert opinion |
| Localization distribution of adenomas and cancer | Dependent on sex and race: | | | | Directly estimated from SEER 1997-2001.* |
| | | White | | Black | |
| | Men | Women | Men | Women | |
| Rectum: | 22% | 17% | 19% | 15% | |
| Rectosigmoid junction: | 9% | 7% | 8% | 8% | |
| Sigmoid colon: | 23% | 21% | 20% | 20% | |
| Descending colon: | 4% | 4% | 6% | 6% | |
| Transverse colon (including flexures): | 14% | 15% | 16% | 16% | |
| Ascending colon: | 12% | 14% | 13% | 15% | |
| Cecum: | 16% | 21% | 18% | 21% | |
| 10-y survival after clinical diagnosis of CRC | Dependent on stage, sex, and race: | | | | Directly estimated from SEER 1997-2001.* |
| | | White | | Black | |
| | Men | Women | Men | Women | |
| Stage I: | 95% | 96% | 71% | 89% | |
| Stage II: | 76% | 80% | 73% | 68% | |
| Stage III: | 58% | 52% | 40% | 43% | |
| Stage IV: | 7% | 4% | 5% | 3% | |
| Sensitivity colonoscopy | | | | | |
| Adenoma <5 mm: | 75% | | | | Van Rijn et al,[12] 2007 |
| Adenoma 6-9 mm: | 85% | | | | |
| Adenoma 10+ mm: | 95% | | | | |
| Cancer: | 95% | | | | |

(*continued on next page*)

**TABLE 1 (*continued*)**

| | | |
|---|---|---|
| Cecal intubation rate with colonoscopy | 95% | Aslinia et al,[13] 2006; Cotterill et al,[14] 2005; Rex et al,[15] 2002 |
| Complications with colonoscopy | Per 1000 colonoscopies: | Levin et al,[16] 2006; Lieberman et al,[17] 2000; Pox et al,[18] 2007; Regula et al,[19] 2006; Jentschura et al,[20] 1994 |
| Perforations | 0.7 | |
| Fatal perforations | 0.1 | |
| Serosal burn | 0.3 | |
| Bleeds with transfusion | 0.4 | |
| Bleeds without transfusion | 1.1 | |

*Surveillance Research Program, SEER*Stat Software, version 5.3.1., 2003; NCI.
†To be estimated from randomized controlled endoscopy trials, data not yet available.

subgroup, as described above (see Appendix 2 for an overview of strategies). For each cost-effective policy, we calculated the incremental cost-effectiveness ratio, defined as the additional cost of a specific policy divided by its additional clinical benefit compared with the closest less-expensive cost-effective policy. Next, we combined cost-effective policies, one for each population subgroup, with the same threshold for the incremental cost-effectiveness ratio.[30,31] For each of the resulting individualized strategies, the costs and life-years of the 4 population subgroups were summed. The strategy with total costs closest to that of the alternative uniform strategy was used as the individualized strategy (the result was strategy 3).

## Base case

The base case for the analysis was the absence of screening for CRC. All diagnoses of CRC occurred because of symptoms, after which patients received treatment according to current practice.

## Competing screening strategies

1. Uniform 10-yearly colonoscopy at age 50 years. In this strategy, all individuals were oered colonoscopy screening at age 50 years and every 10 years thereafter up to age 80 years, according to guidelines.[1]
2. Uniform 8-yearly colonoscopy at age 51 years. In this strategy (resulting from the modeling analysis described before), all individuals were oered colonoscopy screening at age 51 years and every 8 years thereafter up to age 75 years.
3. Individualized screening according to sex and race. In this strategy, each population subgroup (black and white men and women) was allowed to have a dierent colonoscopy policy. The policies, which resulted from the modeling analysis described before, were.
   - White men: 4 screenings from age 53 to 74 years every 7 years.
   - Black men: 5 screenings from age 47 to 75 years every 7 years.
   - White women: 4 screenings from age 53 to 77 years every 8 years.
   - Black women: 5 screenings from age 47 to 75 years every 7 years.

As part of all simulated screening strategies, patients with adenoma (in whom adenomas had been detected and consequently removed) were kept under colonoscopy surveillance according to the guidelines of the U.S. Multi-Society Task Force on Colorectal Cancer.[32]

## Costs

Screening costs were based on Medicare payments of 2007 for procedures and tests associated with CRC screening and complications of screening.[33] The costs of complications were based on the relevant Diagnostic Related Group codes.[33] The phase-specific costs of CRC (Table 2, footnote ‡) were derived by comparing medical costs of CRC cases relative to matched controls in the SEER-Medicare files.[34] The results were reported in 2004 dollars and subsequently updated to 2007 dollars by using the medical care component of the Consumer Price Index. A detailed overview of the derivation of the costs is shown in Appendix 3 (available online at www.giejournal.org). The final cost inputs used in the model are summarized in Table 2.

## Outcomes

We projected lifetime costs and life expectancy for a cohort of 40-year old black and white men and women in the

**TABLE 2. Unit costs in 2007 U.S. dollars (95% CI) for screening and CRC treatment, used as inputs for the MISCAN-Colon model**

| Screening costs* | | CRC treatment costs† ($) | | | | |
|---|---|---|---|---|---|---|
| Procedure | Cost ($) | Stage | Initial‡ | Continuous‡ | Terminal care, death CRC‡ | Terminal care, death other cause‡ |
| Colonoscopy | 662 | I | 28,668 (27,905-29,432) | 2395 (2179-2612) | 51,935 (49,690-54,181) | 12,703 (10,533-14,870) |
| Colonoscopy with polypectomy | 846 | II | 39,700 (38,876-40,525) | 2237 (2036-2440) | 51,712 (49,989-53,434) | 11,035 (9214-12,856) |
| Treatment of perforation | 12,446 | III | 48,951 (47,924-49,976) | 3249 (2966-3531) | 54,776 (53,204-56,348) | 14,708 (11,993-17,422) |
| Treatment of serosal burn | 5208 | IV | 64,801 (62,420-67,181) | 10,419 (9249-11,590) | 73,522 (71,800-75,243) | 39,679 (31,826-47,532) |
| Treatment of bleed with transfusion | 5208 | | | | | |
| Treatment of bleed without transfusion | 320 | | | | | |

*From Ref. 33.
†From Ref. 34.
‡Costs for cancer care were divided into 3 clinically relevant phases of care: initial, continuing, and terminal care. The initial phase was defined as the first 12 mo after diagnosis, the terminal phase was defined as the final 12 mo of life, and the continuing phase was defined as all months between the initial and last year of life phases of care. For patients who survive fewer than 24 mo after diagnosis, the final 12 mo of observation and costs of care were then allocated first to the last year of life phase, because the content of care for patients with short survival is more similar to the last year of life phase than the initial phase. The remainder of months of observation and costs were allocated to the initial phase, with no contribution to the continuing phase.

United States. Costs and future life-years were discounted at an annual rate of 3%.[35]

## Sensitivity and uncertainty analysis

We performed a 1-way sensitivity and a multivariate uncertainty analysis on influential model assumptions:

- The assumption of a higher incidence of adenomas versus faster progression of adenomas, which explained the risk dierences between population subgroups.
- The duration of the adenoma-carcinoma sequence.
- The CRC risk in blacks.
- Sensitivity, specificity, and complication rate of colonoscopy.
- Costs of colonoscopy, polypectomy, complications, and CRC treatment.

Because the focus of the analysis was to assess the cost-effectiveness of individualized guidelines compared with uniform guidelines, we restricted the sensitivity analysis to comparing strategies 2 and 3.

In the 1-way sensitivity analysis, each parameter was varied from its original value to a low and high value. For colonoscopy sensitivity and treatment costs, these values were set at the boundaries of the 95% CIs. Ranges reported in the literature were used for colonoscopy reach[13,17,36-42]; specificity[17,41,43-45]; perforation rates[45-54]; and the costs of colonoscopy, polypectomy, and complications.[43-55] The average duration between the manifestation of an adenoma and the diagnosis of CRC (base assumption 10 years) was decreased and increased by 50%, whereas the CRC risk in blacks was decreased and increased by 10%.

In the multivariate uncertainty analysis, we simulated the uniform 8-yearly colonoscopy and individualized strategies 1000 times, with different sets of parameters. The test characteristic parameters (sensitivity, specificity, reach, and complication rate) were drawn from a beta distribution, with the mean equal to the base value. For the cost parameters and the CRC risk in blacks, we assumed log-normal distributions, with the median equal to the base value. For all parameters varied, the standard deviation was chosen such that the 95% probability mass overlapped with the low and high values used in the 1-way sensitivity analysis. In 50% of the runs, we assumed a duration of the development of CRC of 20 years, whereas 10 and 30 years were used in 25% of the runs each. In 75% of the runs, we assumed that the difference in CRC risk between population subgroups was because of a different adenoma incidence, whereas, in 25%, we assumed the difference was caused by different adenoma progression rates. For each of the 1000 simulations, the difference in costs and life expectancy between the uniform 8-yearly colonoscopy strategy and the individualized strategy were plotted in a scatterplot.[56]

## RESULTS

The life expectancy and lifetime costs of the no screening, uniform 8-yearly colonoscopy, uniform 10-yearly colonoscopy, and individualized strategies are displayed in Table 3. The no-screening strategy was the least-expensive

**TABLE 3. Results from cost-effectiveness analysis**

| Strategy | CRC cases/100,000 from age 40 y to age 100 y | CRC deaths/100,000 from age 40 y to age 100 y* | Life-expectancy at age 40 y† | Lifetime per person cost for CRC screening and treatment after age 40 y ($)† | ICER ($)† |
|---|---|---|---|---|---|
| No screening | 5712 | 2027 | 22.3929 | 1663 | Base case |
| Uniform 10-yearly colonoscopy | 3026 | 794 | 22.4340 | 2310 | Dominated |
| Uniform 8-yearly colonoscopy | 2901 | 751 | 22.4362 | 2349 | 15,837 |
| Individualized | 2882 | 739 | 22.4363 | 2340 | 15,565 |

*ICER,* Incremental cost-effectiveness ratio.
*Includes procedural deaths from colonoscopy complications.
†3% discounted.

yet least-effective strategy. The uniform 8-yearly colonoscopy and individualized strategies both increased life expectancy by 0.0433 to 0.0435 years per individual at a cost of $15,565 to $15,835 per life-year gained compared with no screening. The uniform 10-yearly colonoscopy strategy was weakly dominated by both the uniform 8-yearly strategy and the individualized strategy.

Life expectancy and costs for the uniform 8-yearly and individualized colonoscopy strategies by population subgroup are shown in Table 4. The increase in screening intensity in blacks with individualization resulted in 0.0080 years longer life expectancy in black men, whereas, in black women, the life expectancy increased by 0.0076 years. The redistribution of resources from lower-risk whites to higher-risk blacks resulted in a higher starting age (2 years later), with individualization for whites and a slightly decreased life expectancy in this group by 0.0006 years for men and 0.0016 years for women.

## Sensitivity and uncertainty analysis

In the 1-way sensitivity analysis, we assessed the influence of model assumptions on the differences between uniform 8-yearly colonoscopy and individualized screening. In all analyses, both strategies were equivalent in costs and effects (Table 5). The difference in costs never exceeded $12, and the maximum difference in life-years gained was 0.0005 years. With a longer duration of the adenoma-carcinoma sequence of 30 years, the uniform 8-yearly strategy became most effective, which nullified the already very small advantage of individualized screening. Other influential model assumptions on effectiveness were the disparity in CRC risk, colonoscopy sensitivity, and reach, and whether disparities in incidence are caused by the difference in adenoma onset versus faster progression. Costs were mostly influenced by colonoscopy costs and the duration of the adenoma-carcinoma sequence.

For the multivariate uncertainty analysis, the results from 1000 simulations that compared the uniform 8-yearly colonoscopy and individualized strategies are shown in Figure 3. In all simulations, the uniform 8-yearly colonoscopy and individualized strategies remained equivalent in costs and effects. The median difference in life-years gained was 0.0002 life-years. The 25% and 75% percentiles of the increase in life-years gained from the individualized strategy compared with the uniform strategy was 0.0001 and 0.0002 life-years, respectively, whereas the 25% and 75% percentiles for the decrease in cost were $7.20 to $11.50. For blacks, the 25% and 75% percentiles of additional life-years gained were 0.0063 and 0.0079 years and of additional costs were $260 to $465. In 83% of the simulations, the individualized strategy was more effective and less costly than the uniform strategy. Uniform screening was more effective in 3% of simulations, at an incremental cost per life-year gained of $50,000 or less, and, in 7%, at costs of $100,000 or less.

## DISCUSSION

The present analysis suggests that 8-yearly uniform and individualized colonoscopy recommendations by sex and race on a total population level are comparable in costs and effects: the overall (total population) benefit of individualization is limited (0.0002 additional life-years gained, $9.09 lower costs per person). This is explained by the fact that the black population constitutes no more than approximately 20% of the population. For blacks, the increase in life-years gained was more substantial (0.0078 life-years, approximately 14% of total life-years saved with screening), which decreased the disparity in incidence and mortality compared with whites. Our results were robust for changes in model assumptions. In 1000 simulations with different model parameter values, the 8-yearly uniform and individualized strategies remained equivalent in costs and effects. We found that, with individualizing screening, blacks are screened with a 1-year shorter interval than whites and start screening 6 years

**TABLE 4. Comparison of 3% discounted costs and life expectancy between the uniform 8-yearly colonoscopy and individualized strategies, by sex and race, and for the total population**

| | Uniform 8-yearly colonoscopy strategy | | | Individualized strategy | | | |
|---|---|---|---|---|---|---|---|
| Population subgroup | Uniform strategy | Costs ($)* | LE-40 | Individualized strategy | Costs ($)* | LE-40 | Difference in life expectancy |
| White men | 4 screenings, every 8 y; age 51-75 y | 2408 | 21.9418 | 4 screenings, every 7 y; age 53-74 y | 2361 | 21.9412 | −0.0006 |
| Black men | 4 screenings, every 8 y; age 51-75 y | 2240 | 19.8791 | 5 screenings, every 7 y; age 47-75 y | 2582 | 19.8871 | +0.0080 |
| White women | 4 screenings, every 8 y; age 51-75 y | 2314 | 23.4309 | 4 screenings, every 8 y; age 53-77 y | 2221 | 23.4293 | −0.0016 |
| Black women | 4 screenings, every 8 y; age 51-75 y | 2299 | 21.9359 | 5 screenings, every 7 y; age 47-75 y | 2671 | 21.9435 | +0.0076 |
| Total population† | | 2349 | 22.4362 | | 2340 | 22.4363 | +0.0002 |

*LE-40,* Life expectancy at age 40 y.
*Lifetime per person cost for CRC screening and treatment after age 40 y.
†Average of results for population subgroups, weighted by size of population subgroup.

earlier, whereas the recommended screening ages and frequency for men and women remain similar.

Our findings support the recommendation of the American College of Gastroenterology to begin screening 5 years earlier for blacks than for whites. Starting screening at an earlier age, without increasing the number of screenings, results in saving 0.0052 additional life-years for blacks (data not shown). Also, increasing the number of screenings, as recommended from our study, significantly further increases the additional life-years gained, to 0.0078. Individualization, therefore, can play a significant role in reducing disparities between blacks and whites. Our results are in line with other studies that showed that the average cost-effectiveness of CRC screening is better in black men than in other population subgroups.[57,58] Based on these results, the investigators advocate earlier screening in blacks. However, basing individualized guidelines on average cost-effectiveness does not necessarily lead to efficient use of resources. In the present analysis, we determined individualized guidelines based on incremental cost-effectiveness and hence ensured efficient use of resources.[30,31]

Besides the current recommendation of 4 screenings every 10 years from age 50 years to age 80 years, we also used another uniform colonoscopy strategy as a comparator to enable a fair comparison between uniform and individualized screening. We could not use the exact recommendation for that purpose, because it was not optimally cost effective, although it was close. The current guidelines were not based on a formal decision analysis but on studies on colonoscopic efficiency[1] and on simplicity and clarity. Individualized guidelines are more complex than uniform ones, and, therefore, one could argue that recommendations should not be individualized unless benefits are substantial. Individualized screening guidelines may confuse providers and consumers to the point of decreasing adherence. A decrease in adherence will easily offset the gains from individualization. Currently, 40% of black men and 32% of black women aged 50 years and older reported having had either a fecal occult blood test (FOBT) within the past year or a colorectal endoscopy within the past 5 years.[59] Based on these figures, much can be gained from increased adherence to screening guidelines. However, individualization of screening guidelines must be considered in the context of a general trend toward personalized medical care.[60,61] As a result, screening adherence might improve, because individuals appreciate that the recommendation is based on their personal risk profile. In any case, in a situation in which individualization of medical care, and especially of screening, becomes the standard, it would be only natural to also account for race and sex differences, given the expected benefit and regardless of its size. To avoid too much complexity, one could recommend not changing the guidelines for whites but changing screening for blacks to every 9 years from age 45 years onward (a similar change as the results of this study). Compared with the current screening guidelines, this recommendation would result in 0.0076 more life-years gained for blacks, comparable with the 0.0078 found in this study.

In this analysis, we assumed that all disparities in cancer incidence are caused by differences in adenoma incidence. This assumption is supported by results from the Clinical Outcomes Research Initiative, which showed a higher percentage of patients with adenoma and with

**TABLE 5. Results of 1-way sensitivity analysis: comparison of 3% discounted costs and life expectancy in the total population with the uniform 8-yearly colonoscopy and individualized strategies for different model assumptions**

| | Differences of the individualized strategy compared with the uniform 8-yearly colonoscopy strategy | | | | | |
|---|---|---|---|---|---|---|
| | Low value | | | High value | | |
| Model parameter | Gain in LE | Costs ($)* | ICER | Gain in LE | Costs ($)* | ICER |
| Base assumptions | +0.0002 | −9.09 | Dominant | +0.0002 | −9.09 | Dominant |
| Fast progression of adenomas† | +0.0001 | −7.89 | Dominant | | | |
| Duration adenoma carcinoma sequence§ | +0.0005 | −10.11 | Dominant | −0.0000 | −6.66 | $546,213‡ |
| Risk blacks§ | +0.0001 | −6.67 | Dominant | +0.0003 | −9.40 | Dominant |
| Reach colonoscopy§ | +0.0003 | −8.01 | Dominant | +0.0002 | −8.09 | Dominant |
| Sensitivity colonoscopy§ | +0.0002 | −8.58 | Dominant | +0.0001 | −7.82 | Dominant |
| Specificity colonoscopy§ | +0.0002 | −8.05 | Dominant | +0.0002 | −7.97 | Dominant |
| Cost colonoscopy§ | +0.0002 | −4.18 | Dominant | +0.0002 | −11.56 | Dominant |
| Cost polypectomy§ | +0.0002 | −8.03 | Dominant | +0.0002 | −7.65 | Dominant |
| Complication rate of colonoscopy§ | +0.0002 | −7.93 | Dominant | +0.0002 | −8.09 | Dominant |
| Cost treatment complications§ | +0.0002 | −7.99 | Dominant | +0.0002 | −8.51 | Dominant |
| Cost treatment§ | +0.0002 | −8.05 | Dominant | +0.0002 | −7.96 | Dominant |

*LE*, Life expectancy; *ICER*, incremental cost-effectiveness ratio; Dominant, the individualized strategy was both more effective and less costly than the uniform strategy.

*Lifetime per person cost for CRC screening and treatment after age 40 y.

†For this assumption, there was no high or low value; it was just varied from the base assumption where differences in CRC risk were caused by differences in adenoma incidence. In this sensitivity analysis, it was assumed that differences were caused by differences in progression rates of adenomas.

‡The incremental cost per life-year gained of the uniform 8-yearly colonoscopy strategy compared with the individualized strategy.

§Duration: low value = 10 y, high value = 30 y

- Risk blacks: low value = 10% lower risk, high value = 10% higher risk than values in Table 1.
- Reach colonoscopy: low value = 80% reach cecum, high value = 99% reach cecum.
- Sensitivity colonoscopy: low and high values set at 95% CIs (see MISCAN-Colon microsimulation model in Materials and Methods section).
- Specificity colonoscopy: low value = 0.78, high value = 1.
- Cost colonoscopy: low value = $285, high value = $1012.
- Cost polypectomy: low value = $159, high value = $507.
- Complication rate of colonoscopy: low value = 1 per 1000, high value = 4 per 1000.
- Cost treatment complications: low value = $4360, high value = $26,000.
- Cost treatment: low and high values set at 95% CIs (see Table 2).

polyps >9 mm in blacks than in whites.[62] Furthermore, observational studies show that CRC risk factors have a similar effect on adenoma prevalence as on CRC incidence.[63-68] Theoretically, a higher CRC incidence could also be caused by more rapid adenoma and cancer progression. In this case, development of adenomas into CRC would have a shorter duration in blacks than in whites. When we assumed a faster progression for blacks, with a strongly reduced average preclinical disease duration, the benefit of individualization was slightly reduced.

We assumed that differences in the observed CRC incidence and stage distribution between blacks and whites reflect true differences in risk and are not because of differences in screening utilization. However, when considering that screening rates are lower for blacks than for whites,[59] the risk difference between blacks and whites may be smaller. The sensitivity analysis shows that, with a lower CRC risk in blacks (ie, smaller difference with whites), the benefit of individualization was reduced. Furthermore, we only considered life-years gained and not quality-adjusted life-years. The reason for this is that the effect of CRC screening on quality of life has hardly been studied. There was 1 study that estimated quality of life 30 days before and after colonoscopy, which found that mental health and vitality domains of quality of life significantly improved after colonoscopy.[69] However, quality of life at the moment of colonoscopy was not assessed. In population screening, large numbers of individuals undergo colonoscopy and even a minor effect of colonoscopy on quality of life will have a large impact on quality-adjusted life-years gained. Our results are only influenced by adjusting for quality of life when this differs between population subgroups. Crimmins and Saito[70] showed that blacks and whites not only differ in life

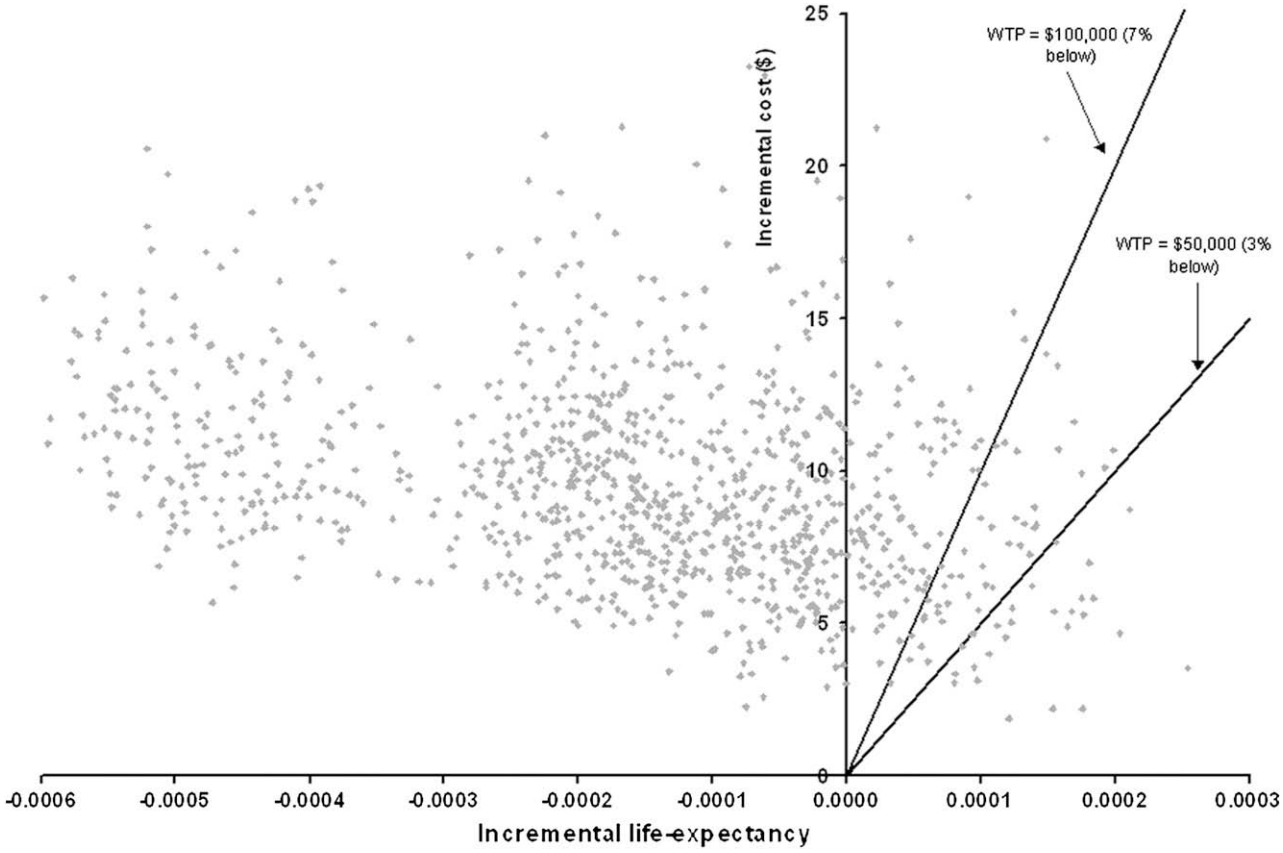


**Figure 3.** Multivariate uncertainty analysis by using 1000 simulations. This analysis simultaneously varies all parameters over the full range of possible values. Each point represents the incremental costs and life-years gained of uniform 8-yearly colonoscopy screening over individualized screening generated in one simulation; 83% of points fall in the upper left corner of the graph, which means that uniform screening is both less effective and more costly than individualized screening. The *solid lines* represent the willingness to pay (*WTP*) thresholds of $50,000 and $100,000. Points to the right and under this line represent simulations in which uniform screening was more effective than individualized screening at incremental costs of $50,000 or less and $100,000 or less, respectively.

expectancy (for which we accounted in the present analysis) but also in the proportion of healthy life-years, because blacks have more comorbidities at older ages. Therefore, intensive colonoscopy screening at older ages may be less feasible in blacks and also less beneficial in terms of quality-adjusted life-years gained, which reduces the potential benefit of individualization.

Age-specific CRC incidence and mortality in men reaches levels of risk comparable with women 4 to 8 years later in life.[71] Also, more women than men need to be screened for the detection of one advanced neoplasia.[19,62,72] Therefore, one may have expected that men need earlier and more intensive screening than women. However, our results show that the cost-effective individualized policies for men and women are comparable. This is because of the longer life expectancy of women. Although women have fewer advanced adenomas than men, more of those adenomas can evolve into CRC during the longer lifetime. This means that the number needed to screen to detect one advanced adenoma in women may be higher than in men but that the number of detected adenomas needed to prevent 1 case of CRC is lower. This makes the number needed to screen to prevent 1 CRC case similar for men and women. Our finding of similar screening strategies is supported by the fact that the absolute number of CRC cases in men and women is comparable.[73]

This study aimed to explore the cost-effectiveness of individualization of screening guidelines. We restricted ourselves to colonoscopy, the preferred method of screening according to the American College of Gastroenterology.[74] Fortunately, the results can be generalized to other screening modalities. The costs per life-year gained will be different for other screening modalities, but the conclusion that individualization is cost effective will remain, as well as the result that it is more cost effective for blacks to be screened over a wider age range and with greater frequency than whites. We focused the analysis on black and white (including Hispanic) population subgroups. In a more extensive study, Hispanics and non-Hispanics could be considered separately, and Asians, Pacific Islanders, American Indians, and Native Alaskans could be included to explore further benefit of

individualization. However, for these groups, incidence and mortality data will be based on small numbers. CRC incidence and mortality tend to be lower in Hispanics, Asians, Pacific Islanders, American Indians, and Native Alaskans than in whites.[75] When these data are confirmed, a less intensive screening schedule for these groups could be considered.

In conclusion, our study suggests that 8-yearly uniform and individualized colonoscopy screening are comparable in costs and effects in the total population. However, individualized guidelines could contribute to decreasing disparities between blacks and whites. The acceptability and feasibility of individualized guidelines, therefore, should be explored.

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**APPENDIX 1. The MISCAN-Colon microsimulation model OUTLINE**



## MODEL OVERVIEW

The MISCAN-Colon model is a semi-Markov microsimulation model. The population is simulated individual by individual, and each person can evolve through discrete disease states. However, instead of modeling yearly transitions with associated transition probabilities, the MISCAN-Colon model generates durations in states. This improves model performance. With the assumption of exponential distribution of the duration in each state, this way of simulating leads to the same results as a Markov model with yearly transition probabilities. The advantage of the MISCAN approach is that durations in a certain state need not necessarily be a discrete value but can be continuous. MISCAN uses the Monte Carlo method to simulate all events in the program. Possible events are birth and death of a person, adenoma incidence and transitions from one state of disease to another.

The basic structure of MISCAN-Colon is illustrated in Figure A1-1. Figure A1-1 clearly demonstrates that MISCAN-Colon consists of three parts:

- demography part
- natural history part
- screening part

These parts are not physically separated in the program, but it is useful to consider them separately.

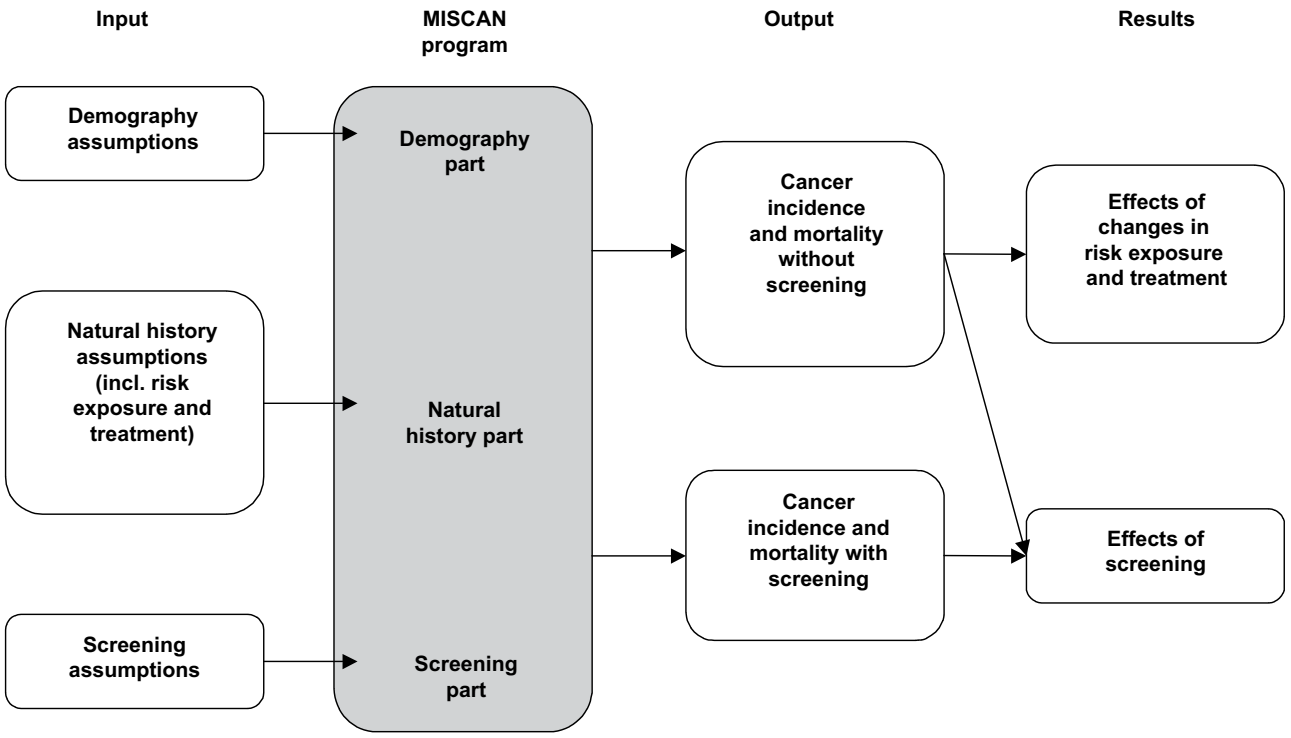


**Figure A1-1.** Structure of MISCAN-Colon.

*DEMOGRAPHY PART*

The demography part of the model simulates individual life histories without colorectal cancer to form a population. For each person, a date of birth and a date of death of other causes than colorectal cancer are simulated. The distribution of births and deaths can be adjusted to represent the population simulated. For example, a population of white women will have higher death ages than a population of black men.

*NATURAL HISTORY PART*

The Natural History part of MISCAN-Colon simulates the development of colorectal cancer in the population. We assume all colorectal cancers develop according to the adenoma-carcinoma sequence of Morson[1] and Vogelstein[2] (Fig. A1-2). For each individual in the simulated population, a personal risk index is generated. Subsequently, adenomas are generated in the population according to this personal risk index and an age specific incidence rate of adenomas. This results in no adenomas for most persons and one or more adenomas for others. The distribution of adenomas over the colorectum is simulated according to the observed distribution of colorectal cancer incidence. Each of the adenomas can independently develop into colorectal cancer. Adenomas can progress in size from small (1-5 mm) to medium (6-9 mm) to large (10+ mm). Most adenomas will never develop into cancer (nonprogressive adenomas), but some (progressive adenomas) may eventually become malignant, transforming to a stage I cancer. The cancer may then progress from stage I to stage IV. In every stage, there is a chance of the cancer being diagnosed because of symptoms. The survival after clinical diagnosis depends on the stage of the cancer.

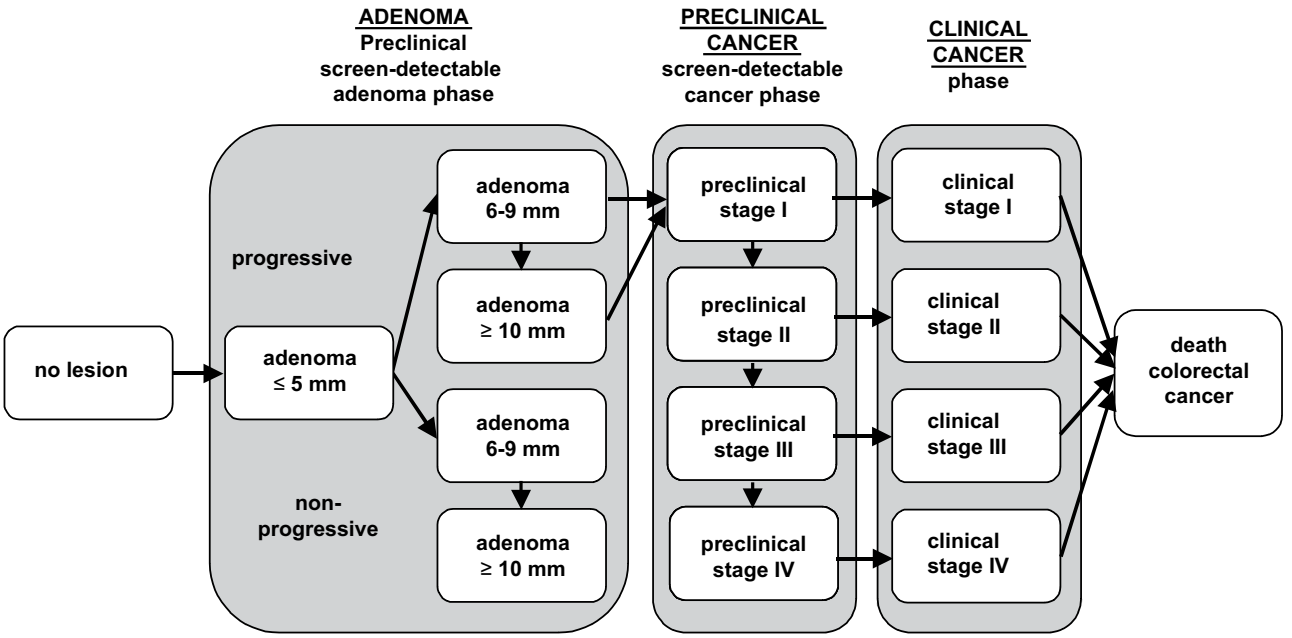


**Figure A1-2.** Adenoma and cancer stages in the MISCAN-Colon model. Cancer stages correspond to the American Joint Committee on Cancer/International Union Against Cancer staging system for colorectal cancer. Adenomas are categorized by size. The size-specific prevalence of adenomas, as well as the proportion of adenomas that ever develop into cancer, is dependent on age.

*SCREENING PART*

Screening interrupts the development of CRC. With screening, adenomas may be detected and removed and cancers may be found, usually in an earlier stage than with clinical diagnosis. In this way screening prevents CRC incidence or CRC death. The life-years gained by screening are calculated by comparing the model-predicted life-years lived in the population with and without screening. The effects of different screening policies can be compared by applying them to identical natural histories.

*INTEGRATION OF THE THREE MODEL COMPONENTS*

For each individual, the demography part of the model simulates a time of birth and a time of death of other causes than colorectal cancer, creating a life history without colorectal cancer (top line in Fig. A1-3a). Subsequently adenomas are simulated for that individual. For most individuals no adenomas are generated, for other multiple. In the example in Figure A1-3, the person gets two adenomas (2nd and 3rd line in Fig. A1-3a). The first adenoma arises at a certain age, grows to 6 to 9 mm, and eventually becomes larger than 10 mm. However, this adenoma does not become cancer before the death of the person. The second adenoma is a progressive adenoma. After having grown to 6 to 9 mm, the adenoma transforms into a malignant carcinoma, causing symptoms and diagnosis and eventually resulting in an earlier death from CRC. The life history without CRC and the development of the two adenomas in Figure A1-3 together lead to the combined life history with CRC depicted in the bottom line. Because this person dies from colorectal cancer before he dies from other causes, his death age is adjusted accordingly.

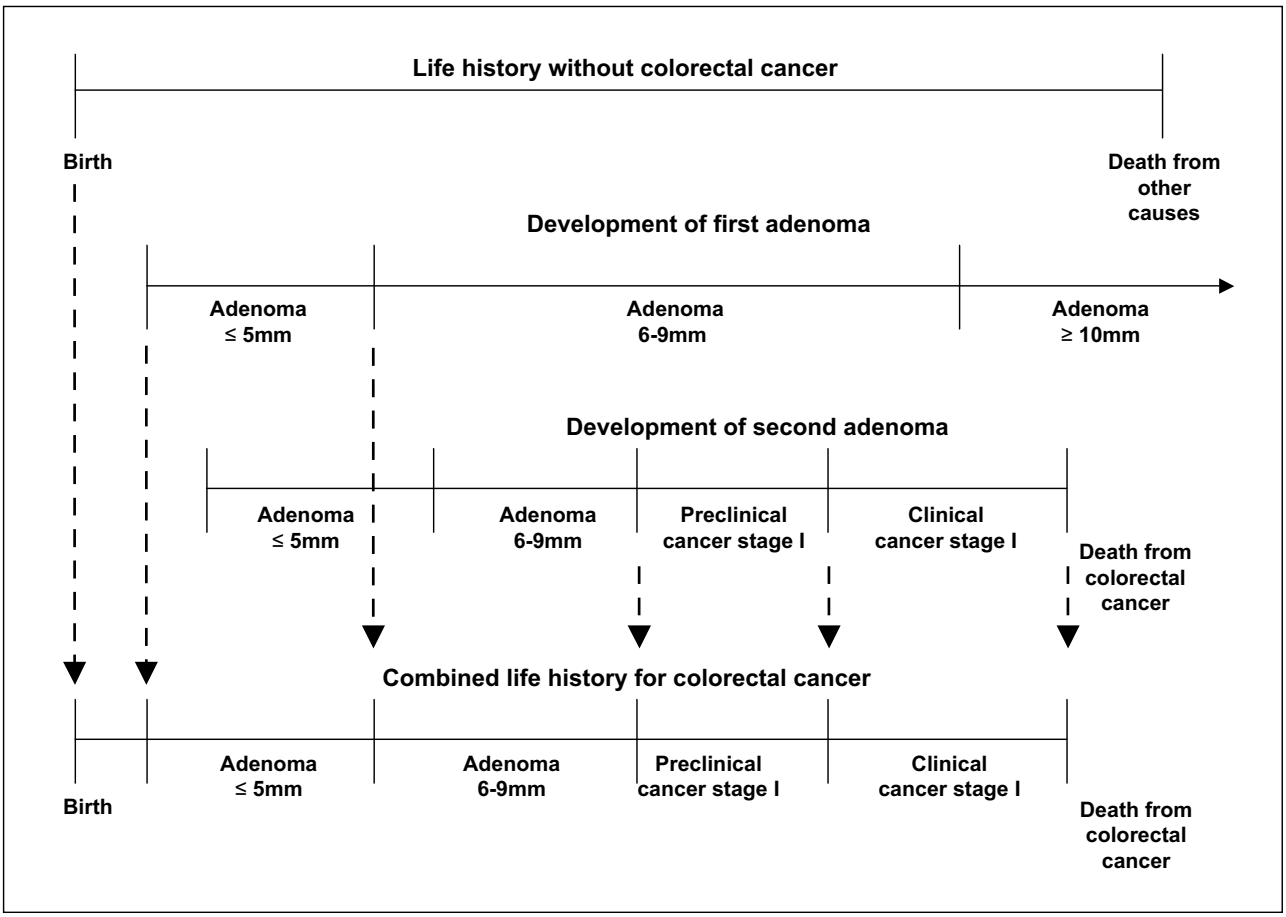


**Figure A1-3a.** Modeling natural history into life history.

After the life history of a person is adjusted for colorectal cancer, the history will now be adjusted for the effects of screening. The effect of screening on life history is explained in Figure A1-3b. The top line in this figure is the combined life history for colorectal cancer from Figure A1-3a. The development of the separate adenomas is repeated in the second and third line. In this picture, there is one screening intervention. During the screening, both prevalent adenomas are detected and removed. This results in a combined life history for colorectal cancer and screening (bottom line). From the moment of screening, the adenomas are removed and this individual becomes adenoma and carcinoma free. He does not develop cancer because the precursor lesion has been removed. Therefore the person dies at the moment of death from other causes and the effect of screening is the difference in life-years in the situation without screening and the situation with screening. Of course, many other possibilities could have occurred: a person could have developed new adenomas after the screening moment or an adenoma could have been missed by the screening test, but, in this case, this individual really benefited from the screening intervention.

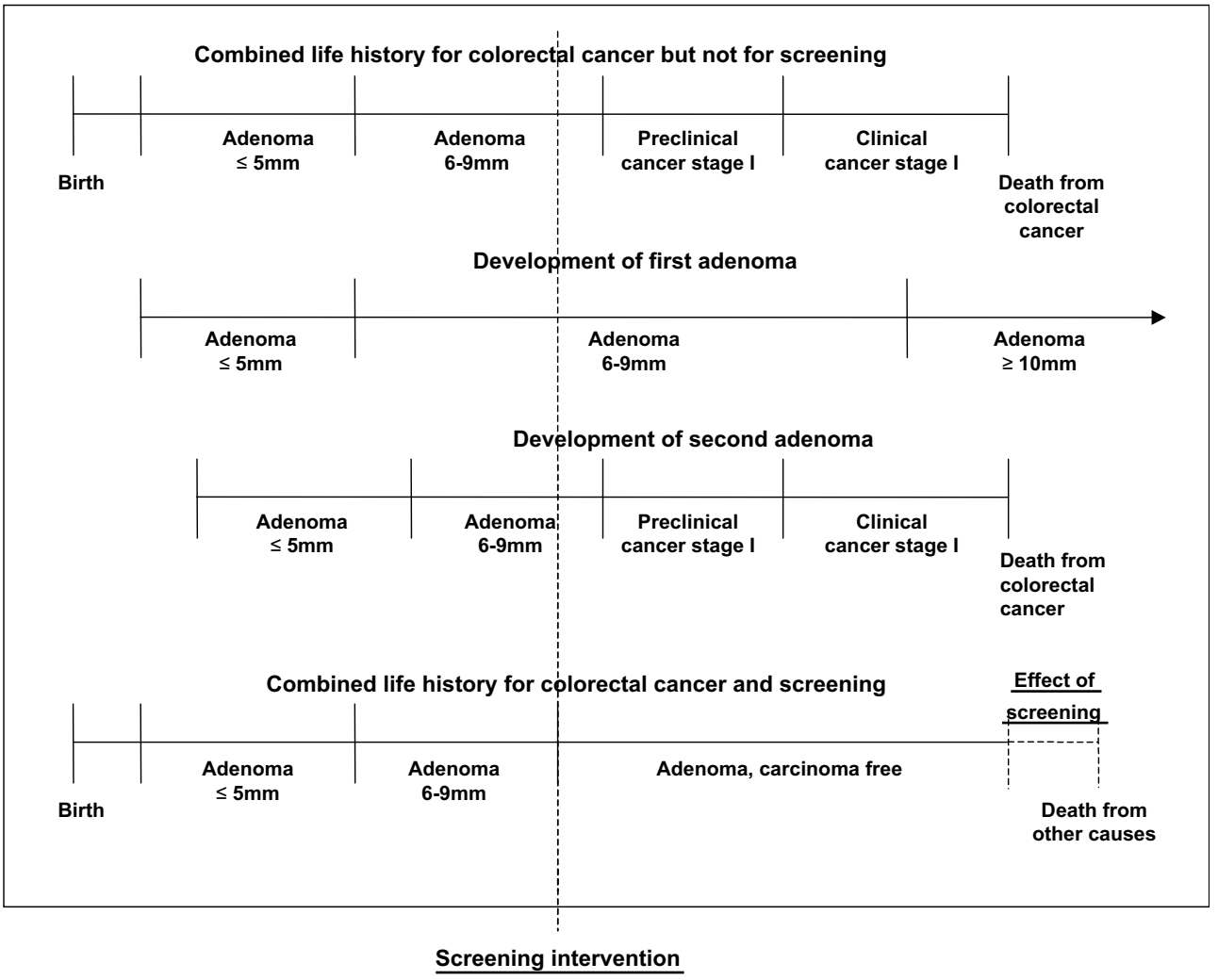


**Figure A1-3b.** Modeling screening into life history.

MODEL QUANTIFICATION

For this analysis we developed four different models, for white men, white women, black men, and black women. For each group we simulated a cohort born in 1967.

*DEMOGRAPHY PARAMETERS*

There are two types of demography parameters: birth tables and life tables. In this case all individuals were born in 1967. The life tables were derived from the 2000 US Life Table published by the National Center for Health Statistics (http://www.cdc.gov/nchs/products/pubs/pubd/lftbls/life/1966.htm). These life tables include colorectal cancer mortality and the demography part simulates mortality from other causes than colorectal cancer. However, we decided not to adjust the life tables because the percentage of colorectal cancer mortality in overall mortality is small and the data on colorectal cancers deaths by age, sex, and race are sparse.

*NATURAL HISTORY PARAMETERS*

The parameters for natural history model that could not be directly estimated from data or fit to reference data were established based on expert opinion. At two expert meetings at the NCI on June 5–7, 1996, and May 12–13, 1997, a model structure was devised in agreement with the currently accepted model of the adenoma–carcinoma sequence. It was assumed that all cancers are preceded by adenomas.

The expert panel agreed on an estimate of the average sojourn time (ie, the duration between onset of a progressive adenoma and the clinical diagnosis of subsequent cancer) of 20 years. However, some adenomas do not make it to cancer in that time period, because people die of other causes before the cancer could actually manifest. These are mainly the slower-developing adenomas with a longer duration than the average. The result is that the average duration of the adenomas that actually make it to diagnosed cancer is shorter, on average 10 years. The average duration of cancer in preclinical stages I–IV was 2 years, 1 year, 1.5 years, and 0.8 year, respectively, which resulted in a total average duration of 3.6 years because not every cancer reaches stage IV before clinical diagnosis. These sojourn times were based on the ratio between the stage-specific detection rate at first screening in fecal occult blood test trials and the background incidence, accounting for a 60% sensitivity of fecal occult blood test for all cancer stages.[3,4] All durations were governed by an exponential probability distribution. Durations in each of the invasive cancer stages, as well as durations in the stages of the noninvasive adenomas, were assumed to be 100% associated with each other, but the durations in invasive stages as a whole were independent of durations in noninvasive adenoma stages that precede cancer. These assumptions resulted in an exponential distribution of the total duration of progressive noninvasive adenomas and of the total duration of preclinical cancer, which has also been used in other cancer screening models.[3,5]

It was assumed that 30% of the cancers arise from adenomas of 6 to 9 mm and that 70% arise from larger adenomas. Initially, the preclinical incidence of progressive adenomas was chosen to reproduce the colorectal cancer incidence by age, stage, and localization in the United States in 1978.[6] During this period, almost no screening was performed. The size distribution of adenomas over all ages was assumed to be 56% for stages less than or equal to 5 mm, 24% for stages 6 to 9 mm, and 20% for stages greater than or equal to 10 mm.[7-11] The preclinical incidence of nonprogressive adenomas that will never grow into cancer was varied until the simulated prevalence of all adenomas was about 15% in age group 50 to 59 years, 27% in age group 60 to 69 years, and 33% in age group 70 or more years, in agreement with data from the Kaiser study in Northern California[12] and with data from autopsy and colonoscopy studies.[7-11]

For this analysis, the 1978 total population model was adjusted to obtain 1997-2001 models for white and black men and women. We assumed that all difference in CRC incidence between the 1978 general population model and the 1997-2001 race- and sex-specific models was caused by differences in adenoma incidence. We, therefore, adjusted the age-specific incidence of both progressive and nonprogressive adenomas so that the colorectal cancer incidence by sex, race, age, stage, and location from 1997 to 2001 was reproduced. The anatomic site distribution of both progressive and nonprogressive adenomas, and thus of preclinical and clinical cancers, is assumed to be equal to the site distribution of colorectal cancers in the United States in 1997 to 2001.[6] The stage-specific survival after the clinical diagnosis of colorectal cancer is taken from the Surveillance, Epidemiology, and End Results registry data from 1987 through 2001.[6]

Table A1-1 contains a summary of the model input values and its data-sources.

**TABLE A1-1. Main natural history assumptions in the MISCAN-Colon model**

| Model parameter | Value | Source |
|---|---|---|
| Distribution of risk for adenomas over the general population | Gamma distributed, mean 1, variance 2 | Fit to multiplicity distribution of adenomas in autopsy studies[7-11]: |
| | | Age 60 : |
| | | 1 or more 20% |
| | | 2 or more 6% |
| | | 3 or more 2% |
| | | Age 90 : |
| | | 1 or more 37% |
| | | 2 or more 17% |
| | | 3 or more 9% |
| Adenoma incidence per year | Age, sex, and race dependent | Fit to adenoma prevalence in autopsy and colonoscopy studies of 15% in age group 50–59 to 33% in age group 70+,[7-11] and to cancer incidence per 100,000 in 1997-2001 in SEER registry[6]: |

| | White | | Black | | | White | | Black | |
|---|---|---|---|---|---|---|---|---|---|
| Age: | Men | Women | Men | Women | Age | Men | Women | Men | Women |
| 0-30 years: | 0.0% | 0.0% | 0.0% | 0.0% | 0-20: | 0.1 | 0.1 | 0.1 | 0.0 |
| 30-39 years: | 0.2% | 0.1% | 0.2% | 0.2% | 20-24: | 0.7 | 0.6 | 0.4 | 1.3 |
| 40-44 years: | 0.4% | 0.4% | 1.0% | 0.6% | 25-29: | 1.5 | 1.8 | 2.1 | 1.9 |
| 45-49 years: | 0.9% | 0.6% | 1.3% | 1.2% | 30-34: | 3.6 | 3.5 | 3.1 | 3.8 |
| 50-54 years: | 1.6% | 1.0% | 2.0% | 1.5% | 35-39: | 7.1 | 5.8 | 8.5 | 8.1 |
| 55-59 years: | 2.9% | 1.8% | 3.0% | 2.3% | 40-44: | 12.9 | 11.1 | 17.5 | 14.8 |
| 60-64 years: | 3.2% | 2.2% | 3.3% | 2.4% | 45-49: | 26.3 | 22.2 | 36.9 | 33.1 |
| 65-69 years: | 3.2% | 2.2% | 3.7% | 2.5% | 50-54: | 51.5 | 37.8 | 74.1 | 57.3 |
| 70-74 years: | 3.2% | 2.3% | 4.3% | 2.5% | 55-59: | 91.4 | 60.5 | 111.4 | 97.3 |
| 75-84 years: | 1.8% | 1.2% | 1.3% | 1.0% | 60-64: | 150.0 | 103.5 | 198.4 | 140.1 |
| 85-100 years: | 1.4% | 1.1% | 1.1% | 0.5% | 65-69: | 226.5 | 151.8 | 231.9 | 193.9 |
| | | | | | 70-74: | 302.8 | 212.8 | 315.3 | 237.8 |
| | | | | | 75-79: | 378.1 | 279.9 | 435.7 | 309.0 |
| | | | | | 80-84: | 457.4 | 338.4 | 488.1 | 361.2 |
| | | | | | 85-100: | 500.9 | 391.6 | 469.1 | 335.6 |

| | | |
|---|---|---|
| Probability that a new adenoma is progressive | Dependent on age at onset: | Fit to adenoma prevalence in autopsy studies,[7-11] cancer incidence in SEER registry in 1978.[6] |
| | 0–65 years: 14% | |
| | 65–100 years: linearly increasing from 14% to 96% | |
| Regression of adenomas | No significant regression of adenomas | Expert opinion |
| Mean duration of development of progressive adenomas to clinical cancer | 20 years | Expert opinion* |

(*continued on next page*)

**TABLE A1-1 (*continued*)**

| | | |
|---|---|---|
| Mean duration of preclinical cancer | 3.6 years | Estimated from cancer detection rate at first screening and background cancer incidence in FOBT trials.[3,4] |
| Mean duration of adenoma | 16.4 years | 20 years – 3.6 years |
| Percentage of nonprogressive adenomas that stay 6-9 mm | 50% | Fit to size distribution of adenomas in autopsy studies[7-11]:<br>1-5 mm: 56%<br>6-9 mm: 24%<br>10+ mm: 20% |
| Percentage of nonprogressive adenoma that become 10 mm or larger | 50% | Fit to size distribution of adenomas in autopsy studies[7-11]:<br>1-5 mm: 56%<br>6-9 mm: 24%<br>10+ mm: 20% |
| Percentage of cancers that develops from 6-9 mm adenoma and from 10+ mm adenoma | 30% of cancer develops from 6-9 mm, 70% from 10+ mm | Expert opinion |
| Localization distribution of adenomas and cancer | Dependent on gender and race: | Directly estimated from SEER 1997-2001.[6] |

| | White | | Black | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Rectum: | 22% | 17% | 19% | 15% |
| Rectosigmoid junction: | 9% | 7% | 8% | 8% |
| Sigmoid colon: | 23% | 21% | 20% | 20% |
| Descending colon: | 4% | 4% | 6% | 6% |
| Transverse colon (including flexures): | 14% | 15% | 16% | 16% |
| Ascending colon: | 12% | 14% | 13% | 15% |
| Cecum: | 16% | 21% | 18% | 21% |

| | | |
|---|---|---|
| 10-year survival after clinical diagnosis of CRC | Dependent on stage, sex, and race: | Directly estimated from SEER 1997-2001.[6] |

| | White | | Black | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Stage I: | 95% | 96% | 71% | 89% |
| Stage II: | 76% | 80% | 73% | 68% |
| Stage III: | 58% | 52% | 40% | 43% |
| Stage IV: | 7% | 4% | 5% | 3% |

*To be estimated from randomized controlled endoscopy trials, data not yet available.

*SCREEN PARAMETERS*

Table A1-2 shows the screening test characteristics assumed in the MISCAN-Colon model. We assumed a cecal intubation rate of 95%.[13-15] The sensitivity of colonoscopy for each lesion within realized reach was based on back-to-back colonoscopy studies: 75% in adenomas smaller than or equal to 5 mm, 85% in adenomas 6 to 9 mm, and 95% in adenomas larger than or equal to 10 mm and cancers.[16] At detection, lesions are removed immediately. The percentage of the population without adenomas or cancer but with hyperplastic polyps, lipomas, or other lesions that lead to polypectomy and pathology after colonoscopy has been estimated from Kaiser data[17]: 10%. This percentage was assumed to be independent of the screening round.

The stage-specific survival of patients with screen-detected cancer is assumed to be the same as the survival of patients with cancers clinically diagnosed in the same stage.[18] Removal of an adenoma always prevents development of any subsequent cancer that may have arisen from this adenoma. Risks of complications reported in organized screening programs[19-21] are lower than those reported for general practice colonoscopies.[22,23] The major complications of colonoscopy are perforations (which can occur with or without polypectomy), serosal burns, bleeds requiring transfusion, and bleeds not requiring transfusion.[19-23] We estimated a rate of death among persons of 0.1 per 1000 colonoscopies.[24]

**TABLE A1-2. Screening test characteristic assumptions in the MISCAN-Colon model**

| Parameter | Value | Source |
|---|---|---|
| Sensitivity colonoscopy | Dependent on stage of disease | Back-to-back colonoscopy studies[16] |
| | Adenoma 1-5 mm: 75% | |
| | Adenoma 6-9 mm: 85% | |
| | Adenoma 10+ mm: 95% | |
| | Preclinical cancer: 95% | |
| Cecal intubation rate | 95% | General practice[13,14] and guidelines[15] |
| Complication rate with colonoscopy | 2.4 per 1000 colonoscopies | Organized screening programs[19-21] and general practice[22,23] |
| Perforation | 0.7 per 1000 | |
| Serosal burn | 0.3 per 1000 | |
| Bleed with transfusion | 0.4 per 1000 | |
| Bleed without transfusion | 1.1 per 1000 | |
| Fatal complication rate with colonoscopy | 0.1 per 1000 colonoscopies | Prospective endoscopy study[24] |
| Probability to develop cancer from removed adenoma | 0% | Expert opinion |
| Survival after screen detection of cancer | As after clinical diagnosis in the same stage | FOBT trial[18] |

Model outputs

The model generates the following output, both undiscounted and discounted:

*Demography*

1. Life-years lived in the population by calendar year and age
2. Deaths from other causes than colorectal cancer by calendar year and age

*Natural history*

1. Colorectal cancer cases by calendar year, stage, and age
2. Colorectal cancer deaths by calendar year and age
3. Life-years lived with colorectal cancer by calendar year, stage, and age
4. Total number of life-years with surveillance for adenoma patients
5. Total number of life-years with initial therapy after screen-detected or clinical invasive cancer by stage
6. Total number of life-years with continuing therapy after screen-detected or clinical invasive cancer by stage
7. Total number of life-years with terminal care before death from other causes by stage
8. Total number of life-years with terminal care before death from colorectal cancer by stage

*Screening*

1. Number of invitations for screen tests, screen tests, diagnostic tests, surveillance, and opportunistic screen tests by calendar year
2. Number of positive and negative test results per preclinical state and per year
3. Total number of life years lived, life years lost because of cancer, number of specific deaths, and nonspecific deaths
4. Number of screenings that prevented cancer by year of screening
5. Number of screenings that detected cancer early by year of screening
6. Number of surveillance tests that prevented cancer by year of surveillance
7. Number of surveillance tests that detected cancer early by year of surveillance
8. Number of life-years gained because of screening by year of screening

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## APPENDIX 2. DETAILED OVERVIEW OF EFFICIENT SCREENING POLICIES FOR THE TOTAL POPULATION AND EACH POPULATION SUBGROUP

**TABLE A2-1. Total population (uniform).** Efficient screening policies characterized by age range, screening interval, and number of scheduled examinations, and expressed as the 3% discounted lifetime costs and life expectancy of the policy

| Policy | | | Resources and benefits | |
|---|---|---|---|---|
| No. of scheduled exams | Interval between exams (years) | Age range | Costs ($)*,† | Life expectancy at age 40* |
| 1 | n.a. | 70-70 | 1701 | 22.4063 |
| 1 | n.a. | 65-65 | 1720 | 22.4120 |
| 1 | n.a. | 64-64 | 1725 | 22.4131 |
| 1 | n.a. | 63-63 | 1731 | 22.4142 |
| 1 | n.a. | 62-62 | 1737 | 22.4151 |
| 1 | n.a. | 61-61 | 1747 | 22.4158 |
| 2 | 14 | 60-74 | 1827 | 22.4213 |
| 2 | 14 | 59-73 | 1845 | 22.4223 |
| 2 | 14 | 58-72 | 1866 | 22.4233 |
| 3 | 9 | 57-75 | 2010 | 22.4282 |
| 3 | 10 | 53-73 | 2125 | 22.4315 |
| 3 | 9 | 53-71 | 2151 | 22.4322 |
| 4 | 8 | 52-76 | 2301 | 22.4353 |
| 4 | 8 | 51-75 | 2349 | 22.4362 |
| 5 | 6 | 51-75 | 2563 | 22.4390 |
| 5 | 7 | 47-75 | 2733 | 22.4407 |
| 6 | 6 | 47-77 | 2923 | 22.4426 |
| 7 | 5 | 48-78 | 3077 | 22.4436 |
| 7 | 5 | 47-77 | 3170 | 22.4441 |
| 8 | 5 | 47-82 | 3223 | 22.4443 |
| 8 | 5 | 46-81 | 3329 | 22.4448 |
| 8 | 5 | 43-78 | 3659 | 22.4462 |
| 9 | 5 | 43-83 | 3707 | 22.4464 |
| 10 | 5 | 43-88 | 3732 | 22.4465 |
| 10 | 5 | 42-87 | 3860 | 22.4466 |

*Average of results for population subgroups, weighted by size of population subgroup.
†Lifetime per person cost for CRC screening and treatment after age 40 y.

**TABLE A2-2. White Men.** Efficient screening policies characterized by age range, screening interval and number of scheduled examinations and expressed as the 3% discounted lifetime costs and life expectancy of the policy

| Policy | | | Resources and benefits | |
|---|---|---|---|---|
| **No. of scheduled exams** | **Interval between exams (years)** | **Age range** | **Costs ($)*** | **Life expectancy at age 40** |
| 1 | n.a. | 70-70 | 1824 | 21.9125 |
| 1 | n.a. | 65-65 | 1831 | 21.9186 |
| 1 | n.a. | 63-63 | 1836 | 21.9211 |
| 1 | n.a. | 62-62 | 1840 | 21.9221 |
| 1 | n.a. | 61-61 | 1848 | 21.9229 |
| 2 | 14 | 60-74 | 1916 | 21.9276 |
| 2 | 14 | 59-73 | 1933 | 21.9288 |
| 2 | 14 | 58-72 | 1953 | 21.9297 |
| 3 | 9 | 57-75 | 2082 | 21.9343 |
| 3 | 8 | 57-73 | 2104 | 21.9350 |
| 3 | 8 | 56-72 | 2141 | 21.9360 |
| 3 | 9 | 53-71 | 2220 | 21.9383 |
| 4 | 7 | 53-74 | 2361 | 21.9412 |
| 4 | 7 | 52-73 | 2413 | 21.9421 |
| 5 | 6 | 51-75 | 2609 | 21.9445 |
| 6 | 6 | 47-77 | 2962 | 21.9478 |
| 7 | 5 | 48-78 | 3103 | 21.9488 |
| 8 | 5 | 47-82 | 3241 | 21.9493 |
| 8 | 5 | 43-78 | 3684 | 21.9511 |
| 9 | 5 | 43-83 | 3723 | 21.9512 |
| 10 | 5 | 43-88 | 3742 | 21.9513 |
| 10 | 5 | 42-87 | 3871 | 21.9513 |

*Lifetime per person cost for CRC screening and treatment after age 40 y.

**TABLE A2-3. Black Men.** Efficient screening policies characterized by age range, screening interval, and number of scheduled examinations, and expressed as the 3% discounted lifetime costs and life expectancy of the policy

| Policy | | | Resources and benefits | |
|---|---|---|---|---|
| **No. of scheduled exams** | **Interval between exams (years)** | **Age range** | **Costs ($)*** | **Life expectancy at age 40** |
| 1 | n.a. | 64-64 | 1746 | 19.8487 |
| 1 | n.a. | 63-63 | 1750 | 19.8503 |
| 1 | n.a. | 62-62 | 1754 | 19.8519 |
| 1 | n.a. | 61-61 | 1760 | 19.8533 |
| 1 | n.a. | 60-60 | 1767 | 19.8546 |
| 1 | n.a. | 59-59 | 1777 | 19.8558 |
| 2 | 15 | 58-73 | 1840 | 19.8612 |
| 2 | 14 | 58-72 | 1846 | 19.8616 |
| 2 | 14 | 57-71 | 1866 | 19.8629 |
| 3 | 11 | 53-75 | 2035 | 19.8721 |
| 3 | 10 | 53-73 | 2056 | 19.8731 |
| 3 | 10 | 52-72 | 2090 | 19.8745 |
| 3 | 9 | 52-70 | 2116 | 19.8754 |
| 4 | 9 | 48-75 | 2342 | 19.8822 |
| 4 | 8 | 48-72 | 2401 | 19.8834 |
| 5 | 7 | 47-75 | 2582 | 19.8871 |
| 5 | 7 | 46-74 | 2652 | 19.8882 |
| 6 | 6 | 47-77 | 2735 | 19.8894 |
| 6 | 6 | 46-76 | 2817 | 19.8904 |
| 6 | 6 | 45-75 | 2906 | 19.8913 |
| 7 | 5 | 44-74 | 3249 | 19.8945 |
| 8 | 5 | 43-78 | 3402 | 19.8956 |
| 8 | 5 | 42-77 | 3527 | 19.8961 |
| 9 | 5 | 42-82 | 3556 | 19.8962 |
| 10 | 5 | 42-87 | 3570 | 19.8962 |

*Lifetime per person cost for CRC screening and treatment after age 40 y.

**TABLE A2-4. White Women.** Efficient screening policies characterized by age range, screening interval, and number of scheduled examinations, and expressed as the 3% discounted lifetime costs and life expectancy of the policy

| Policy | | | Resources and benefits | |
|---|---|---|---|---|
| **No. of scheduled exams** | **Interval between exams (years)** | **Age range** | **Costs ($)*** | **Life expectancy at age 40** |
| 1 | n.a. | 72-72 | 1563 | 23.4026 |
| 1 | n.a. | 71-71 | 1567 | 23.4035 |
| 1 | n.a. | 70-70 | 1573 | 23.4045 |
| 1 | n.a. | 65-65 | 1606 | 23.4091 |
| 1 | n.a. | 64-64 | 1614 | 23.4099 |
| 1 | n.a. | 63-63 | 1624 | 23.4106 |
| 2 | 14 | 61-75 | 1721 | 23.4167 |
| 2 | 14 | 60-74 | 1742 | 23.4177 |
| 2 | 14 | 59-73 | 1762 | 23.4185 |
| 2 | 14 | 58-72 | 1785 | 23.4192 |
| 3 | 9 | 57-75 | 1950 | 23.4242 |
| 3 | 10 | 53-73 | 2069 | 23.4265 |
| 4 | 8 | 53-77 | 2221 | 23.4293 |
| 4 | 8 | 52-76 | 2267 | 23.4301 |
| 4 | 8 | 51-75 | 2314 | 23.4309 |
| 5 | 7 | 51-79 | 2458 | 23.4326 |
| 5 | 6 | 51-75 | 2551 | 23.4336 |
| 6 | 6 | 47-77 | 2925 | 23.4365 |
| 7 | 6 | 46-82 | 3074 | 23.4374 |
| 8 | 5 | 46-81 | 3363 | 23.4387 |
| 9 | 5 | 44-84 | 3634 | 23.4396 |
| 9 | 5 | 43-83 | 3750 | 23.4399 |
| 10 | 5 | 43-88 | 3785 | 23.4399 |
| 10 | 5 | 42-87 | 3911 | 23.4400 |

*Lifetime per person cost for CRC screening and treatment after age 40 y.

**TABLE A2-5. Black Women.** Efficient screening policies characterized by age range, screening interval, and number of scheduled examinations, and expressed as the 3% discounted lifetime costs and life expectancy of the policy

| Policy | | | Resources and benefits | |
|---|---|---|---|---|
| **No. of scheduled exams** | **Interval between exams (years)** | **Age range** | **Costs ($)*** | **Life expectancy at age 40** |
| 1 | n.a. | 63-63 | 1716 | 21.9029 |
| 1 | n.a. | 62-62 | 1721 | 21.9045 |
| 1 | n.a. | 61-61 | 1729 | 21.9059 |
| 1 | n.a. | 60-60 | 1736 | 21.9071 |
| 1 | n.a. | 59-59 | 1748 | 21.9081 |
| 2 | 15 | 59-74 | 1819 | 21.9139 |
| 2 | 14 | 58-72 | 1842 | 21.9157 |
| 2 | 15 | 57-72 | 1857 | 21.9167 |
| 2 | 14 | 57-71 | 1865 | 21.9171 |
| 3 | 11 | 53-75 | 2060 | 21.9277 |
| 3 | 10 | 52-72 | 2117 | 21.9307 |
| 4 | 8 | 51-75 | 2299 | 21.9359 |
| 4 | 8 | 49-73 | 2403 | 21.9385 |
| 5 | 7 | 47-75 | 2671 | 21.9435 |
| 6 | 6 | 47-77 | 2851 | 21.9464 |
| 6 | 6 | 46-76 | 2934 | 21.9475 |
| 8 | 5 | 43-78 | 3567 | 21.9525 |
| 9 | 5 | 43-83 | 3613 | 21.9527 |
| 9 | 5 | 42-82 | 3737 | 21.9530 |
| 10 | 5 | 42-87 | 3765 | 21.9530 |

*Lifetime per person cost for CRC screening and treatment after age 40 y.

**APPENDIX 3. Derivation of costs**



GENERAL

Screening costs were based on information provided by CMS on Medicare payments of 2007 for procedures and tests associated with CRC screening and complications of screening.[1] Net costs of the management of invasive CRC treatment were obtained from an analysis of SEER-Medicare data.[2] Only direct medical costs were considered, including the co-pays from the beneficiaries.

SCREENING COSTS

Costs for colonoscopy were based on the set of CPT (costs for procedure and treatment) codes relevant to CRC screening in conjunction with the points of service for the procedure. The CPT codes for screening are those stated by the National Coverage Decision (http://www.medicare.gov/health/coloncancer.asp) for the CRC screening benefit, as well as those for associated colonic biopsy or polypectomy (personal communication, John Allen, MD, and Joel Brill, MD). We used the national unadjusted payment amounts under the physician fee schedule for these analyses. Using the national unadjusted payment means that the costs do not adjust for payment for the geographic location.

Points of service considered for screening were the outpatient prospective payment system (OPPS) and the ambulatory surgery center payment system (ASC) with the associated facility charge, and the physician fee schedule (PFS) office system. We did not include any CPT codes of screening associated with in-patient procedures as registered in the inpatient prospective payment system (IPPS). Complication costs were based primarily on inpatient DRG level reimbursement costs.

Screening procedure costs were based on a weighted average of procedures per setting. The cost values per setting and CPT code are given in Tables A3-1 to A3-3. The costs for the ASC setting include the ASC payment rates and the PFS facility charge (Table A3-1). The costs for the OPPS setting included the OPPS payment rates and the PFS facility charge (Table A3-2). For the PFS office setting, we used the office payment rates (Table A3-3). The costs for colonoscopy without polypectomy were based on CPT codes 45378 (diagnostic colonoscopy), G0105 (colon screen in high-risk individuals) and G0121 (colon cancer screening for non-high-risk individual). Costs for colonoscopy with polypectomy or biopsy were composed of codes 45380 (colonoscopy and biopsy), 45381 (colonoscopy, submucous injection), 45382 (colonoscopy/control bleeding), 45383 (lesion removal colonoscopy – fulguration), 45384 (lesion removal colonoscopy-hot biopsy), and 45385 (lesion removal colonoscopy-snare polypectomy).

**TABLE A3-1. Ambulatory surgery center (ASC) payment rates**

| | ASC Payment, $ | | | PFS*- Facility, $ | | | Total ASC (ASC payment + PFS), $ | | |
|---|---|---|---|---|---|---|---|---|---|
| CPT Code | Medicare (M) | Beneficiary (B) | Total (M+B) | Medicare (M) | Beneficiary (B) | Total (M+B) | Beneficiary (B) | Medicare (M) | Total (M+B) |
| Colonoscopy without polypectomy | | | | | | | | | |
| 45378 | 357 | 89 | 446 | 158 | 39 | 197 | 129 | 514 | 643 |
| G0105 | 335 | 111 | 446 | 158 | 39 | 197 | 151 | 492 | 643 |
| G0121 | 335 | 111 | 446 | 158 | 39 | 197 | 151 | 492 | 643 |
| Colonoscopy with polypectomy | | | | | | | | | |
| 45380 | 357 | 89 | 446 | 188 | 47 | 235 | 136 | 545 | 681 |
| 45381 | 357 | 89 | 446 | 178 | 44 | 222 | 134 | 534 | 668 |
| 45382 | 357 | 89 | 446 | 239 | 60 | 299 | 149 | 596 | 745 |
| 45383 | 357 | 89 | 446 | 246 | 61 | 307 | 151 | 602 | 753 |
| 45384 | 357 | 89 | 446 | 198 | 49 | 247 | 139 | 554 | 693 |
| 45385 | 357 | 89 | 446 | 223 | 56 | 279 | 145 | 580 | 725 |
| Pathology | | | | | | | | | |
| 88305 | NA | NA | NA | NA | NA | NA | NA | NA | NA |

*Physician fee schedule.

**TABLE A3-2. Outpatient prospective payment system (OPPS) payment rates**

| | OPPS Payment, $ | | | PFS- Facility, $ | | | Total OPPS (OPPS payment + PFS), $ | | |
|---|---|---|---|---|---|---|---|---|---|
| CPT Code | Medicare (M) | Beneficiary (B) | Total (M+B) | Medicare (M) | Beneficiary (B) | Total (M+B) | Beneficiary (B) | Medicare (M) | Total Cost (M+B) |
| Colonoscopy without polypectomy | | | | | | | | | |
| 45378 | 353 | 186 | 539 | 158 | 39 | 197 | 225 | 511 | 736 |
| G0105 | 335 | 111 | 446 | 158 | 39 | 197 | 151 | 492 | 643 |
| G0121 | 335 | 111 | 446 | 158 | 39 | 197 | 151 | 492 | 643 |
| Colonoscopy with polypectomy | | | | | | | | | |
| 45380 | 353 | 186 | 539 | 188 | 47 | 235 | 233 | 541 | 774 |
| 45381 | 353 | 186 | 539 | 178 | 44 | 222 | 230 | 531 | 761 |
| 45382 | 353 | 186 | 539 | 239 | 60 | 299 | 246 | 592 | 838 |
| 45383 | 353 | 186 | 539 | 246 | 61 | 307 | 247 | 599 | 846 |
| 45384 | 353 | 186 | 539 | 198 | 49 | 247 | 235 | 551 | 786 |
| 45385 | 353 | 186 | 539 | 223 | 56 | 279 | 242 | 576 | 818 |
| Pathology | | | | | | | | | |
| 88305 | 21 | 11 | 32 | 30 | 8 | 38 | 18 | 52 | 70 |

**TABLE A3-3. Office payment rates**

| CPT code | PFS—Office Medicare (M), $ | PFS—Office Beneficiary (B), $ | PFS—Office Total (M+B), $ |
|---|---|---|---|
| Colonoscopy without polypectomy | | | |
| 45378 | 298 | 74 | 372 |
| G0105 | 298 | 74 | 372 |
| G0121 | 298 | 74 | 372 |
| Colonoscopy with polypectomy | | | |
| 45380 | 354 | 88 | 442 |
| 45381 | 343 | 86 | 429 |
| 45382 | 472 | 118 | 590 |
| 45383 | 419 | 105 | 524 |
| 45384 | 349 | 87 | 436 |
| 45385 | 398 | 100 | 498 |
| Pathology | | | |
| 88305 | 82 | 21 | 103 |

*Polyp removal and pathology review*

For the procedures with polypectomy or biopsy we included a pathology charge (CPT code 88305). The Medicare payment rates per jar were $82.40 for the PFS office and ASC setting, and $51.59 for the OPPS setting. All biopsy specimens or polyps are reviewed by pathology. We assumed that a separate jar is submitted to pathology for each of 4 colon segments. The intention of a separate jar for separate segments is that the resection area could be identified should the patient require surgery. We used the simplified assumption of four segments; right side of the colon (cecum and ascending), transverse (hepatic flexure and transverse colon), left side of the colon (splenic flexure, descending colon, and sigmoid), and rectum. Data from the National Colonoscopy Study with screening colonoscopy for individuals aged 40 to 69 years were used to provide the estimate of 1.38 as the average number of jars per patient with polyps (hyperplastic, other polyps, and adenomas), where there is one jar for polyps in each of the four sections (personal communication, Ann Zauber, PhD). Consequently, we used the pathology fee times 1.38 as the pathology cost associated with colonoscopy with polypectomy. Total costs per setting and CPT code are given with and without pathology charge (Table A3-4).

**TABLE A3-4. ASC, OPPS, and office payment rates with the addition of pathology costs (when applicable)**

| | Total ASC | | | | Total OPPS | | | | Total PFS | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CPT code | Beneficiary | Medicare | Beneficiary with pathology review† | Medicare with pathology review† | Beneficiary | Medicare | Beneficiary with pathology review | Medicare with pathology review | Beneficiary | Medicare | Beneficiary with pathology review | Medicare with pathology review |
| Colonoscopy without polypectomy | | | | | | | | | | | | |
| 45378 | 129 | 514 | 129 | 514 | 226 | 511 | 226 | 511 | 74 | 298 | 74 | 298 |
| G0105 | 151 | 492 | 151 | 492 | 151 | 492 | 151 | 492 | 74 | 298 | 74 | 298 |
| G0121 | 151 | 492 | 151 | 492 | 151 | 492 | 151 | 492 | 74 | 298 | 74 | 298 |
| Colonoscopy with polypectomy | | | | | | | | | | | | |
| 45380 | 136 | 545 | 165 | 659 | 233 | 541 | 259 | 612 | 88 | 354 | 117 | 467 |
| 45381 | 134 | 534 | 162 | 648 | 230 | 531 | 256 | 602 | 86 | 343 | 114 | 457 |
| 45382 | 149 | 596 | 177 | 710 | 246 | 592 | 271 | 663 | 118 | 472 | 146 | 586 |
| 45383 | 151 | 602 | 179 | 716 | 247 | 599 | 273 | 670 | 105 | 419 | 133 | 533 |
| 45384 | 139 | 554 | 167 | 668 | 235 | 551 | 261 | 622 | 87 | 349 | 116 | 463 |
| 45385 | 145 | 580 | 173 | 694 | 242 | 576 | 267 | 647 | 100 | 398 | 128 | 512 |

*All values shown in 2007 dollars.
†In the ASC setting pathology review is farmed out to external laboratories, for which PFS Office rates apply.

Multiple polyps requiring the same type of polypectomy removal within a single colonoscopy do not add an incremental charge to the procedure. However, if different types of polypectomy are required in removing multiple polyps then CMS reimburses 100% for the most expensive procedure and 50% of the facility cost for the second procedure. As a simplifying assumption, we use the weights of procedures by CPT type and do not consider different fees for different combinations of endoscopy CPT codes for polyp removal.

The total costs per CPT code were calculated based on the frequencies for points of service as weights for the costs (Table A3-5). The total costs per screening procedure are based on the total costs per CPT code that are part of the procedure. The costs were weighted by the frequencies of the CPT codes (Table A3-6).

**TABLE A3-5. Percentage of procedures by place of service (PoS), weights per place of service, and cost of individual procedures weighted by place of service**

| CPT Code | % of procedures ASC (a) | % of procedures OPPS (b) | % of procedures Office (c) | Total % (d=a+b+c) | ASC Weight* (a/d) | OPPS Weight* (b/d) | Office Weight* (c/d) | Beneficiary Weighted Cost by PoS** (B) | Medicare Weighted Cost by PoS** (M) | Total Weighted Cost by PoS (B+M) |
|---|---|---|---|---|---|---|---|---|---|---|
| Colonoscopy without polypectomy | | | | | | | | | | |
| 45378 | 42.8 | 40.3 | 4.2 | 87.2 | 0.49 | 0.46 | 0.05 | 171 | 502 | 673 |
| G0105 | 53.1 | 43.3 | 2.8 | 99.3 | 0.54 | 0.44 | 0.03 | 149 | 487 | 635 |
| G0121 | 51.0 | 44.5 | 3.2 | 98.7 | 0.52 | 0.45 | 0.03 | 148 | 486 | 634 |
| Colonoscopy with polypectomy | | | | | | | | | | |
| 45380 | 47.3 | 38.1 | 3.3 | 88.7 | 0.53 | 0.43 | 0.04 | 192 | 631 | 824 |
| 45381 | 46.0 | 40.8 | 2.3 | 89.1 | 0.52 | 0.46 | 0.03 | 192 | 622 | 814 |
| 45382 | 20.4 | 29.8 | 1.8 | 52.0 | 0.39 | 0.57 | 0.03 | 216 | 679 | 894 |
| 45383 | 42.3 | 46.9 | 4.5 | 93.6 | 0.45 | 0.50 | 0.05 | 211 | 684 | 895 |
| 45384 | 47.8 | 44.6 | 3.0 | 95.4 | 0.50 | 0.47 | 0.03 | 197 | 640 | 837 |
| 45385 | 48.5 | 41.5 | 3.8 | 93.7 | 0.52 | 0.44 | 0.04 | 202 | 666 | 868 |

*Out of ASC, OPPS, and office.
**Weighted average of costs from Table A3-4 including pathology (if applicable) by PoS.

**TABLE A3-6. Costs of colonoscopy with and without polyps**

| CPT code | Beneficiary Weighted Cost by PoS (B) | Medicare Weighted Cost by PoS (M) | Total Weighted Cost by PoS (B+M) | Total number of procedures per CPT code | Weights by CPT code (w) | Weighted Beneficiary Costs by PoS and CPT code (w*B) | Weighted Medicare Costs by PoS and CPT code (w*M) | Total Weighted Costs by PoS and CPT code (w*(B+M)) |
|---|---|---|---|---|---|---|---|---|
| Colonoscopy without polypectomy | | | | | | | | |
| 45378 | 171 | 502 | 673 | 1,270,881 | 0.71 | 122 | 358 | 480 |
| G0105 | 149 | 487 | 635 | 208,073 | 0.12 | 17 | 57 | 74 |
| G0121 | 148 | 486 | 634 | 302,860 | 0.17 | 25 | 83 | 108 |
| Total | | | | | | **164** | **498** | **662** |
| Colonoscopy with polypectomy | | | | | | | | |
| 45380 | 192 | 631 | 824 | 879,279 | 0.38 | 74 | 242 | 316 |
| 45381 | 192 | 622 | 814 | 33,907 | 0.01 | 3 | 9 | 12 |
| 45382 | 216 | 679 | 894 | 12,530 | 0.01 | 1 | 4 | 5 |
| 45383 | 211 | 684 | 895 | 89,884 | 0.04 | 8 | 27 | 35 |
| 45384 | 197 | 640 | 837 | 381,305 | 0.17 | 33 | 106 | 139 |
| 45385 | 202 | 666 | 868 | 896,966 | 0.39 | 79 | 260 | 339 |
| Total | | | | | | **198** | **649** | **846** |

*COSTS OF TREATING COMPLICATIONS OF COLONOSCOPY*

The costs of complications with colonoscopy were based on DRG codes of similar procedures. We assumed that all perforations and bleeds with transfusion would entail a hospitalization. We assumed that bleeds without transfusion would be handled by an emergency department visit ($320). The cost of perforation was based on DRG 442 for other OR procedures for injuries with complications ($12,446); bleeding with transfusion (all of whom are considered to require hospitalization) was based on DRG 452 for complications of treatment with complications or comorbidities ($5208); and serosal burn generally requires a two-day hospitalization, which was assumed to be the same cost as that as for the bleed with transfusion.

*COSTS FOR COLORECTAL CANCER TREATMENT*

The cost of CRC treatment was derived from comparison of costs for CRC cases relative to those of matched controls in the SEER-Medicare files.[26] Cost data were reported in 2004 dollars and subsequently updated to 2007 dollars by using the medical care component of the Consumer Price Index.

Patients with a diagnosis of invasive CRC between 1973 and 2002 and aged 65 or above at some time between 1998 and 2003 were selected from SEER-Medicare (N = 124,793). Cancer patients with a prior cancer diagnosis (N = 20,277) or who were identified as having cancer through a death certificate or autopsy were excluded (N = 623). An additional 24,920 patients were excluded because they were enrolled in managed care throughout the observation period or did not have both Medicare part A and part B at any point during the observation period. The remaining 76,722 CRC patients were included.

Potential controls were individuals without any cancer diagnoses recorded by SEER and aged 65 or above during the observation period, 1998-2003. A total of 170,491 controls were selected from a 5% random sample of Medicare enrollees and frequency matched to cases by sex, 5-year age strata (65-69, 70-74, 75-79, 80+), and SEER registry areas.

*Phase of care definitions.* Phase of care definitions were based on prior studies of direct medical costs. For cancer patients, months of observation and cost of care between 1998 and 2003 were divided into three clinically relevant phases of care: initial, last year of life, and continuing care based on the month of service on the Medicare claim. Date of death (or its absence) in the Medicare enrollment file through 2004 was used to determine vital status. Cause of death (cancer, noncancer) was identified from SEER. The initial phase was defined as the first 12 months after diagnosis, the last year of life phase was defined as the final 12 months of life, and the continuing phase was defined as all months between the initial and last year of life phases of care. Not all cancer patients contributed to all phases of care, however. For patients surviving less than 24 months after diagnosis, the final 12 months of observation and costs of care were then allocated first to the last year of life phase, because the content of care for patients with short survival is more similar to the last year of life phase than the initial phase. The remainder of months of observation and costs were allocated to the initial phase, with no contribution to the continuing phase. Patients diagnosed before 1997 who survived beyond 2003 contributed months and costs of care only to the continuing phase. Within each tumor site and phase of care, average monthly estimates of cost of care were calculated.

Because control subjects did not have a date of cancer diagnosis, they were randomly assigned a ''pseudo-diagnosis date'' that corresponded to the date of diagnosis of one of the pool of cancer cases. Months of observation and costs of care were assigned to phases of care in the same manner used with cases. In addition to frequency matching by sex, 5-year age group, and SEER area strata, controls were also matched to cases by phase of care in up to a 1:5 case: control ratio based on the number of controls available for each stratum. To reflect costs associated with cancer care in the last year of life, cancer patients who died of cancer were matched to continuing controls, and cancer patients who died of other causes were matched to last year of life controls. As with cancer patients, average monthly estimates of cost of care were calculated for each phase of care for each of group of controls.

For months in which patients received coverage through managed care or were without both Medicare part A and part B, costs and months of observation time were excluded, because these data would not completely capture the care received during this period.

*Cost estimates.* Cancer-related medical costs were estimated as differences in costs for cases and controls by phase of care. The analysis used Medicare payments to reflect costs of care, rather than billed charges. Payments for Medicare Part A (inpatient services) and Part B (outpatient services) were calculated separately. The Hospital Wage Index and the Medicare Economic Index were used to adjust for inflation in Medicare Parts A and B estimates, respectively, during 1998 to 2003. We also adjusted for geographic variability in costs of care across SEER sites. New treatments, including biologicals, such as Avastin (Genentech Inc, San Francisco, Calif) and Erbitux (ImClone Systems Incorporated,

New York, NY),[3] have come into use in the past 3 years; these new drugs are markedly more expensive than the previous drugs. However, the cost of these new drugs would not be captured by the 2004 reimbursement base available for this case–control study. Estimated patient deductibles and coinsurance expenses were added by adjusting Part A and Part B payments with Medicare reimbursement ratios provided by CMS's Office of the Actuary. Over the time period studied, these averaged about 8% for Part A and about 30% for Part B (Table A3-7).

**TABLE A3-7. Net payments for CRC care during 1998-2003 (in $2007)***

| | | | Last Year of Life | |
|---|---|---|---|---|
| AJCC Stage | Initial Phase | Continuing Phase | Died of Cancer | Died of Other Causes |
| Direct Medical Costs | | | | |
| I | 28,668 | 2395 | 51,935 | 12,703 |
| II | 39,700 | 2237 | 51,712 | 11,035 |
| III | 48,951 | 3249 | 54,776 | 14,708 |
| IV | 64,801 | 10,419 | 73,522 | 39,679 |

*The initial phase of care is the first 12 months after diagnosis, the last year of life phase is the final 12 months of life, and the continuing phase is all the months between the initial and last year of life phases. Cancer-related costs in the continuing phase of care are an annual estimate.

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