

Cost-effectiveness of Screening for Colorectal Cancer in the General Population

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COLORECTAL CANCER (CRC) IS the second leading cause of cancer-related mortality in the United States, resulting in approximately 56600 deaths in 1999.¹ Screening for CRC reduces mortality through detection of malignancy at an earlier, more treatable stage as well as by identification and removal of the precursor lesion, the adenomatous polyp. A recent panel recommended that average-risk individuals begin screening at the age of 50 years with one of the following strategies: annual fecal occult blood testing (FOBT), flexible sigmoidoscopy (SIG) every 5 years, annual FOBT plus SIG every 5 years, double-contrast barium enema (DCBE) every 5 to 10 years, or colonoscopy (COL) every 10 years.²

Colorectal cancer screening tests vary considerably in terms of their performance characteristics, complication rates, acceptability, and cost. Moreover, only the effectiveness of FOBT has been established by randomized clinical trial.³ To inform the debate on the health and economic impact of the various CRC screening strategies, we constructed a decision-analytic model to evaluate the cost-effectiveness of CRC screening in average-risk individuals. While 3 prior models have shown CRC screening to be economically attractive,⁴⁻⁶ in our analysis we specifically evaluate those strategies currently condoned by

Context A recent expert panel recommended that persons at average risk of colorectal cancer (CRC) begin screening for CRC at age 50 years using 1 of several strategies. However, many aspects of different CRC screening strategies remain uncertain.

Objective To assess the consequences, costs, and cost-effectiveness of CRC screening in average-risk individuals.

Design Cost-effectiveness analysis from a societal perspective using a Markov model.

Subjects Hypothetical subjects representative of the 50-year-old US population at average risk for CRC.

Setting Simulated clinical practice in the United States.

Main Outcome Measures Discounted lifetime costs, life expectancy, and incremental cost-effectiveness (CE) ratio, compared used 22 different CRC screening strategies, including those recommended by the expert panel.

Results In 1 base-case analysis, compliance was assumed to be 60% with the initial screen and 80% with follow-up or surveillance colonoscopy. The most effective strategy for white men was annual rehydrated fecal occult blood testing (FOBT) plus sigmoidoscopy (followed by colonoscopy if either a low- or high-risk polyp was found) every 5 years from age 50 to 85 years, which resulted in a 60% reduction in cancer incidence and an 80% reduction in CRC mortality compared with no screening, and an incremental CE ratio of \$92900 per year of life gained compared with annual unhydrated FOBT plus sigmoidoscopy every 5 years. In a base-case analysis in which compliance with screening and follow-up is assumed to be 100%, screening more often than every 10 years was prohibitively expensive; annual rehydrated FOBT plus sigmoidoscopy every 5 years had an incremental CE ratio of \$489900 per life-year gained compared with the same strategy every 10 years. Other strategies recommended by the expert panel were either less effective or cost more per year of life gained than the alternatives. Colonoscopy every 10 years was less effective than the combination of annual FOBT plus sigmoidoscopy every 5 years. However, a single colonoscopy at age 55 years achieves nearly half of the reduction in CRC mortality obtainable with colonoscopy every 10 years. Because of increased life expectancy among white women and increased cancer mortality among blacks, CRC screening was even more cost-effective in these groups than in white men.

Conclusions Screening for CRC, even in the setting of imperfect compliance, significantly reduces CRC mortality at costs comparable to other cancer screening procedures. However, compliance rates significantly affect the incremental CE ratios. In this model of CRC, 60% compliance with an every 5-year schedule of screening was roughly equivalent to 100% compliance with an every 10-year schedule. Mathematical modeling used to inform clinical guidelines needs to take into account expected compliance rates.

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expert panels,^{2,7-10} address the ongoing debate about the use of rehydration for FOBT, evaluate the impact of performing a follow-up COL after the detection of a small tubular adenoma by SIG, and consider the impact of imperfect compliance with screening.

METHODS

Model Overview

We developed a state-transition Markov model to simulate the evolution from normal colonic epithelium to adenomatous polyp to malignancy. Superimposed on the natural history of colorectal disease was a screening mechanism that allowed for the detection and removal of polyps and the detection and treatment of cancer. Persons representative of the 50-year-old US population, based on sex and race, were placed into health states defined by the presence or absence of a polyp (low risk or high risk, defined as either ≥ 1 cm or containing villous histology) or cancer (localized, regional, or distant) in either the distal or proximal colon. The 2 sides of the colon were modeled separately because SIG can only visualize the distal colon. The population transitioned through the different health states on an annual basis (ie, cycle length) based on transition probabilities estimated from the literature.

The strategies evaluated include the 6 strategies endorsed by the expert panel,² 1-time screens at 55 years of age, use of rehydrated (RFOBT) vs unrehydrated FOBT (UFOBT), and different follow-up regimens for SIG. Persons with a positive FOBT or DCBE test result were referred for follow-up COL. For polyps detected during SIG or COL, a polypectomy was performed during the procedure. The 2 different follow-up procedures after a positive SIG were as follows: (1) only persons found to have a high-risk polyp were referred for follow-up COL (SIG₁) vs (2) persons found to have any adenomatous polyp, regardless of size or histology, were referred for follow-up COL (SIG₂). Individuals diagnosed with a high-risk polyp underwent surveillance COL every 3 years. Screening

and/or surveillance continued until 85 years of age.

Incremental analyses were performed by rank ordering the strategies by increasing effectiveness after eliminating those that were more costly and less effective than an alternative (ie, ruled out by simple dominance). We then calculated the incremental cost-effectiveness (CE) ratio for each strategy (additional cost divided by additional benefit) compared with the next least expensive strategy. Strategies with a lower effectiveness and higher CE ratio than another strategy were ruled out by weak dominance, eliminated from the rank-ordered list, and the incremental CE ratios were then recalculated.¹¹ Sensitivity analyses were performed to assess the stability of the results to plausible ranges of uncertain parameters. Future costs and life-years were discounted at an annual rate of 3%.¹¹ The model was programmed in SMLTREE software (James Hollenberg, MD, Roslyn, NY).

Clinical Data

Natural History of Colorectal Polyps and Cancer. TABLE 1 shows selected parameter estimates.^{2,12-33} We estimated the age- and sex-specific prevalence of adenomatous polyps using a weighted logistic regression analysis of results from 6 autopsy studies.¹²⁻¹⁷ For example, the prevalence of polyps for men aged 50 years was estimated at 21%, of which 98% were low risk and 61% were in the distal portion of the colon.^{12-17,31-33} The subsequent incidence of polyps among those polyp free at 50 years of age was estimated to match the autopsy results for older age groups. We estimated that 28% of persons with proximal CRC would have a "sentinel" polyp in the distal portion of the colon that could trigger further workup after SIG.³⁴

The probability of transformation from low-risk to high-risk polyp was estimated from studies of small polyps left in situ and reexamined annually.¹⁸⁻²⁰ The probability that a high-risk polyp would develop into localized cancer was derived from a study of patients who refused resection of a high-risk polyp.²¹ There are no empirical data with which

to estimate the rates of progression through cancer stages or to determine the likelihood of presentation with symptoms. Thus, we varied the estimates of cancer progression and symptom detection across clinically plausible ranges so that the stage distribution and CRC incidence predicted by our model was similar to those reported by the Surveillance Epidemiology and End Results (SEER) program.²²

Prevalence of CRC and stage distribution at 50 years of age was obtained from SEER data.²² Distal vs proximal site of the cancer was determined as a function of age using published Medicare data.³⁵ SEER estimates of sex-, race-, and stage-specific CRC mortality (L. Ries, MS, written communication, May 17, 1995) were applied uniformly to all malignancies regardless of means of detection (by symptoms or screen) or state of detection (diagnosed vs undiagnosed cancer).

The Effects of Screening. Where data were available, we estimated test sensitivity separately for the detection of low-risk polyps, high-risk polyps, and cancer.^{2,23-29} Mortality caused by the risk of perforation was assigned to the endoscopic procedures (1.4×10^{-6} for SIG and 5.0×10^{-5} for COL).^{36,37}

Recurrence rates after polypectomy were higher for individuals with a history of a high-risk polyp diagnosis (25% in the first year and 7.5% a year thereafter) compared with a prior diagnosis of low-risk polyp (18% in the first year and 6% per year thereafter).³⁸⁻⁴⁴ Only the transition from normal epithelium to low-risk polyp was increased among those with a history of polyp.

Costs

The costs of CRC treatment by stage and time period (initial, continuing, and terminal care) were obtained from a cost study from a large health maintenance organization.³⁰ These costs include the actual costs of medical personnel and supplies to provide the service as well as overhead costs, such as administration, charting, and automated information systems. Test costs were obtained from the same health maintenance or-

ganization (S. H. Taplin, Group Health Cooperative, Seattle, Wash, written communication, September 30, 1996). All costs were updated to 1998 dollars using the medical care component of the Consumer Price Index.⁴⁵

Compliance

Compliance rates of 50% to 70% have been obtained in the optimized setting of clinical trials of CRC screening.^{25,46,47} Therefore, we estimated a realistic goal for compliance with CRC

screening to be 60% for initial tests and 80% for follow-up or surveillance COL. At each particular screening event, we assumed that a random 60% of the population underwent the initial screening test, independent of whether they were compliant with past tests. Among persons referred for follow-up COL, we assumed that a random 20% would not undergo this diagnostic test. We also show the results for an initial compliance rate of 100%, which models results of screening based on actual tests received by patients.

Table 1. Base-Case Values and Ranges Used in Sensitivity Analysis*

Variable	Value (Range)	References
Prevalence of polyps at age 50 y, %	21 (11-42)	12-17
Polyps that are distal at age 50 y, %	61 (30-70)	12-17
Polyps that are high risk at age 50 y, %	2 (1-10)	31-33
Annual transition probabilities		
Normal epithelium to low-risk polyp	Age-specific	12-17
Low-risk polyp to high-risk polyp	0.02 (0.01-0.04)	18-20†
High-risk polyp to localized cancer	0.05 (0.02-0.10)	21†
Localized cancer to regional cancer	0.28 (0.10-0.50)	†
Regional cancer to distant cancer	0.63 (0.32-0.80)	†
Probability CRC will be diagnosed due to symptoms, %		
Localized cancer	25 (15-35)	†
Regional cancer	55 (45-65)	
Distant cancer	100 (90-100)	
Annual CRC-specific mortality rate‡		
Localized cancer	0.002	22
Regional cancer	0.032	
Distal cancer	0.566	
Unrehydrated FOBT, %		
Sensitivity for polyps	10 (5-20)	23, 24
Sensitivity for cancer	33 (20-40)	
Specificity	97 (95-99)	
Rehydrated FOBT, %		
Sensitivity for polyps	10 (5-20)	23, 24
Sensitivity for cancer	60 (40-65)	25, 26
Specificity	90 (85-95)	25, 26
Double-contrast barium enema, %		
Sensitivity for low-risk polyps	30 (30-70)	27, 28
Sensitivity for high-risk polyps	50 (50-70)	
Sensitivity for cancer	70 (60-90)	
Specificity	86 (80-98)	
Sigmoidoscopy and colonoscopy, %		
Sensitivity for low-risk polyps	85 (80-85)	2, 29
Sensitivity for high-risk polyps or cancer	95 (85-90)	
Specificity	100	
Costs, 1998 US \$		
Annual FOBT	38 (5-40)	§
Screening sigmoidoscopy	279 (80-300)	§
Sigmoidoscopy and polypectomy	564	§
Double-contrast barium enema	296 (50-300)	§
Screening colonoscopy	1012 (400-1500)	§
Colonoscopy and polypectomy	1519	§
Localized cancer, predicted lifetime costs	22 000	30
Regional cancer, predicted lifetime costs	43 900	30
Distant cancer, predicted lifetime costs	58 300	30

*CRC indicates colorectal cancer; FOBT, fecal occult blood test.

†Estimated by calibration to national data on cancer incidence and stage distribution (Ries et al²³).

‡Mortality rate specific for white men.

§Stephen H. Taplin, MD, MPH, written communication, Group Health Cooperative, Seattle, Wash, September 30, 1996.

RESULTS

Base-Case Analysis at 60% Compliance

The health and economic outcomes of 22 CRC screening strategies for white men at average risk are shown in TABLE 2 and the FIGURE. All screening strategies resulted in reductions in CRC incidence and mortality. The least intensive strategy, screening once at 55 years of age with SIG, reduced CRC incidence by 14% and mortality by 16%, whereas the most intensive strategy, repeated screening from ages 50 to 85 years with RFOBT plus SIG every 5 years, reduced CRC incidence by 60% and mortality by 80%.

Although every CRC screening strategy extended life expectancy, 7 strategies were more effective for a lower cost per life-year saved than the alternatives. Screening once at 55 years of age with SIG or with SIG every 10 years (regardless of follow-up) resulted in incremental CE ratios of less than \$17 000 per life-year saved. Unrehydrated fecal occult blood testing plus SIG₂ every 10 years had a CE ratio of \$21 200 per life-year saved compared with SIG₂ every 10 years, whereas UFOBT plus SIG₂ every 5 years had a CE ratio of \$51 200 per life-year saved compared with UFOBT plus SIG₂ every 10 years. Rehydrated fecal occult blood testing plus SIG₂ every 5 years was the most effective CRC screening strategy, resulting in an incremental CE ratio of \$92 900 per life-year saved compared with UFOBT plus SIG₂ every 5 years. Other strategies recommended by the expert panel were eliminated by either simple or extended dominance. In

the Figure, dominated strategies fall below the lines connecting the nondominated alternatives.

We directly compared UFOBT and RFOBT and found an incremental CE ratio of RFOBT compared with UFOBT

of \$45 000 per life-year saved. Rehydrated fecal occult blood testing resulted in a 65% reduction in cancer mortality, whereas annual UFOBT resulted in only a 55% reduction. However, RFOBT was dominated as a stand-

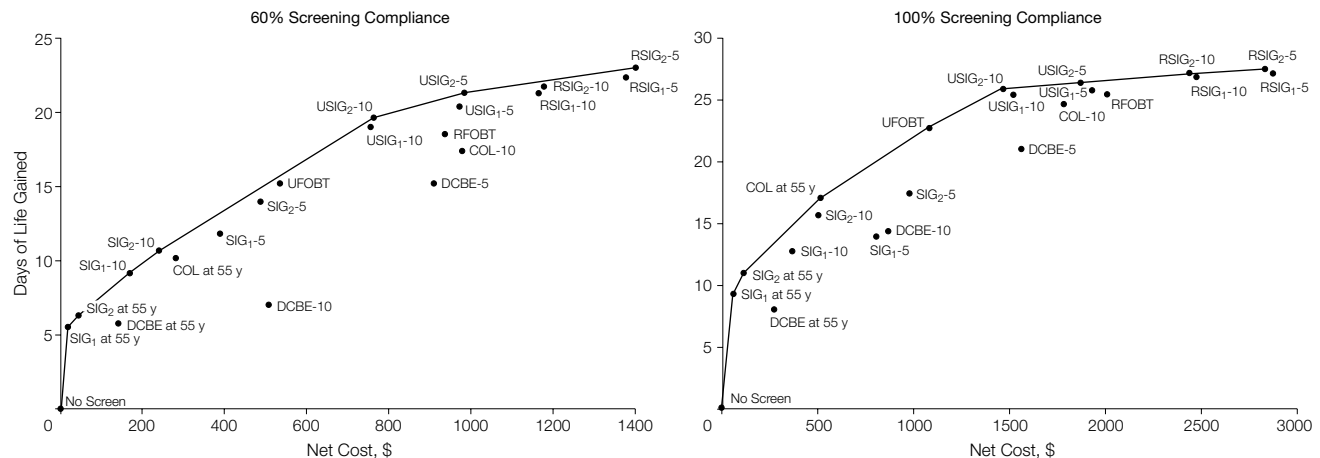
alone test because the combination of UFOBT plus SIG₂ every 10 years was less expensive but more effective. The more aggressive follow-up after a positive sigmoidoscopy (SIG₂) was only modestly more costly than the less ag-

Table 2. Cost-effectiveness (CE) of 22 Strategies of Colorectal Cancer Screening Among White Men, 60% Compliance*

Strategy (Abbreviation)	Lifetime Cost per Person Screened, 1998 \$	Life Expectancy, y	Incremental Days of Life Gained	Incremental CE Ratio, \$ per Life-Year Gained	Reduction in Colorectal Cancer Incidence, %	Reduction in Colorectal Cancer Mortality, %
No screen	1052	17.3481				
SIG ₁ at age 55 y (Sig ₁ at 55 y)	1070	17.3632	5.5	1200	14	16
SIG ₂ at age 55 y (SIG ₂ at 55 y)	1095	17.3654	0.8	11 000	15	19
DCBE at age 55 y (DCBE at 55 y)	1200	17.3585	8	11
SIG ₁ every 10 y (SIG ₁ -10)	1218	17.3732	2.8	15 800	28	32
SIG ₂ every 10 y (SIG ₂ -10)	1288	17.3775	1.6	16 100	32	38
COL at age 55 y (COL at 55 y)	1312	17.3760	27	31
SIG ₁ every 5 y (SIG ₁ -5)	1438	17.3806	37	40
DCBE every 10 y (DCBE-10)	1514	17.3687	23	28
SIG ₂ every 5 y (SIG ₂ -5)	1536	17.3866	42	50
UFOBT (UFOBT)	1584	17.3901	39	55
UFOBT+ SIG ₁ every 10 y (USIG ₁ -10)	1804	17.4004	54	67
UFOBT+ SIG ₂ every 10 y (USIG ₂ -10)	1810	17.4022	9.0	21 200	55	70
DCBE every 5 y (DCBE-5)	1872	17.3826	38	47
RFOBT (RFOBT)	1986	17.3991	38	65
UFOBT+ SIG ₁ every 5 y (USIG ₁ -5)	2023	17.4041	60	71
COL every 10 y (COL-10)	2028	17.3959	58	64
UFOBT + SIG ₂ every 5 y (USIG ₂ -5)	2034	17.4066	1.6	51 200	61	75
RFOBT + SIG ₁ every 10 y (RSIG ₁ -10)	2214	17.4065	54	74
RFOBT + SIG ₂ every 10 y (RSIG ₂ -10)	2226	17.4078	54	76
RFOBT+ SIG ₁ every 5 y (RSIG ₁ -5)	2428	17.4091	59	77
RFOBT + SIG ₂ every 5 y (RSIG ₂ -5)	2448	17.4110	1.6	92 900	60	80

*SIG₁ indicates sigmoidoscopy followed by colonoscopy if high-risk adenomatous polyp diagnosed; SIG₂, sigmoidoscopy followed by colonoscopy if either low- or high-risk polyp diagnosed at SIG; DCBE, double-contrast barium enema; COL, colonoscopy; UFOBT, unrehydrated fecal occult blood test; and RFOBT, rehydrated fecal occult blood test. Only undominated CE ratios are presented, and costs and life expectancy are discounted at 3% per year. Ellipses indicate no data (incremental days of life gained and incremental CE ratios not calculated for these strategies because they were dominated).

Figure. Cost-effectiveness of Colorectal Screening Strategies Among White Men at Average Risk (60% and 100% Compliance)



For an explanation of the strategies, see Table 2. Dominated strategies fall below the lines connecting the nondominated alternatives.

gressive strategy (SIG₁) with a substantial increase in effectiveness (direct comparisons of SIG₂ vs SIG₁ strategies yielded incremental CE ratios less than \$12 000 per life-year saved).

The estimated health and economic outcomes of CRC screening for white women, black men, and black women are

not shown due to constraints of space. However, the relative ordering of the tests in terms of cost and effectiveness did not change. Because of increased life expectancy (white women) or increased cancer mortality (blacks), CRC screening was even more cost-effective among these groups than for white men.

Base-Case Analysis at 100% Initial Compliance

The relative ordering of the strategies did not substantially change under the assumption of 100% compliance (Figure). However, COL once at 55 years of age replaced SIG every 10 years on the cost-effective frontier (illustrated by the lines in the Figure). Although the DCBE strategies remained dominated, they moved closer to the cost-effective frontier.

At 100% compliance, screening more frequently than every 10 years became prohibitively expensive (RFOBT plus SIG₂ every 5 years cost an additional \$489 900 per life-year saved compared with RFOBT plus SIG₂ every 10 years.) However, the results of the model at 60% compliance vs 100% compliance are less disparate than appears at first glance. Sixty percent compliance with an every 5-year strategy translates into an actual interval between screens of almost 10 years. Interestingly, therefore, 60% compliance with an every 5-year strategy is equivalent to 100% compliance with an every 10-year strategy.

Table 3. Sensitivity Analyses*

Variable	Base-Case Values	Sensitivity Analysis	
		Sensitivity Analysis Values	Incremental CE Ratio of RFOBT + Sigmoidoscopy Every 5 y, \$ per Life-Year Saved†
Base case			92 900
Compliance with follow-up colonoscopy	80%		
		70%	81 500
		90%	105 800
Specificity of UFOBT	97%		
		95%	69 100
		99%	122 700
Sensitivity of UFOBT for cancer	33%		
		20%	69 100
		40%	134 500
Sensitivity of UFOBT and RFOBT for polyps	10%		
		5%	69 100
		20%	Dominated‡
Prevalence of polyps at age 50 y	21%		
		10%	156 100
		31%	63 000
Incidence of polyps after age 50 y among those polyp free at baseline	1.0		
		0.5 × baseline	116 000
		1.5 × baseline	77 000
Rate of progression from normal epithelium to recurrent polyp after polypectomy	1.0		
		0.5 × baseline	101 000
		1.5 × baseline	86 000
Annual transition probability from high-risk polyp to cancer	0.05		
		0.02	202 200
		0.10	48 300
Probability that polyp at age 50 y is in distal colon	61%		
		45%	81 300
		70%	102 500
Cost of colonoscopy	\$1012		
		\$500	65 700
		\$1500	143 000
Mortality from colonoscopy	5 × 10 ⁻⁵		
		5 × 10 ⁻⁴	248 000
		5 × 10 ⁻⁶	87 400
Discount rate	3%		
		1%	69 500
		5%	123 900

*CE indicates cost-effectiveness; RFOBT, rehydrated fecal occult blood test; and UFOBT, unrehydrated fecal occult blood test.

†Compared with UFOBT plus sigmoidoscopy every 5 years.

‡RFOBT plus SIG₂-5 is dominated by UFOBT plus SIG₂-5 (see Table 2 for an explanation of SIG₂-5).

Sensitivity Analysis

TABLE 3 shows the variables that caused the incremental CE ratio of RFOBT plus SIG₂ every 5 years to shift by more than 10%. The cost-effectiveness of RFOBT plus SIG₂ every 5 years was most influenced by compliance with follow-up COL, test performance of UFOBT, mortality and cost associated with COL, prevalence and recurrence rate of polyps, and progression from polyp to cancer.

Slight changes in the assumptions about UFOBT (ie, increase in specificity of UFOBT from 97% to 99%; increase in sensitivity of UFOBT for cancer from 33% to 39%; decrease in cost of UFOBT from \$38 to \$32) caused it to become an undominated strategy with a CE ratio less than \$20 000 per life-year saved. Rehydrated fecal occult blood testing strategies dominated all UFOBT strategies when the specificity of RFOBT was greater than 93% (base-case estimate was 90%).

Double-contrast barium enema remained a dominated strategy over a wide range of values for both sensitivity and specificity. Even if the cost of DCBE was less than \$100 (base-case cost was \$296), DCBE every 5 years remains a dominated strategy. If the cost of COL was lowered by 18%, then screening once at 55 years of age with COL was no longer dominated.

Colonoscopy is the most sensitive test, but also the most expensive. If compliance with COL every 10 years was substantially greater than with the other tests (70% vs 40%), then COL every 10 years was the most effective strategy with an incremental CE ratio of \$92 000 per life-year saved compared with RFOBT plus SIG₂ every 5 years. Colonoscopy every 5 years is more effective than RFOBT plus SIG₂ every 5 years, but the costs are prohibitive. If the cost of COL was reduced by 23%, then COL every 10 years became a viable strategy as well.

Under certain scenarios, it was less costly to screen than it was not to screen (ie, the costs of screening were less than the costs of averted cancer treatment). If the cost of SIG was reduced by 15% (\$240) or the cost of cancer treatment was increased by 20%, then screening was cost saving. If the incidence of polyps at 50 years of age was 20% higher than estimated at baseline or the rate of progression from high-risk polyp to cancer was 20% faster than at baseline, then screening was cost saving.

COMMENT

We compared 22 strategies for CRC screening persons at average risk, including all strategies currently recommended by expert panels.^{2,7-10} Seven strategies were not ruled out by either simple or extended dominance. The incremental CE ratios for these strategies ranged from \$1200 per life-year saved (SIG once at 55 years of age) to \$92 900 per life-year saved (RFOBT plus SIG every 5 years). However, factors such as local expertise, availability of providers, and patient preferences should also be

incorporated into the choice of screening strategy in addition to estimates of cost-effectiveness.

The cost-effectiveness of CRC screening compares favorably with the cost-effectiveness of other cancer screening strategies such as annual Papanicolaou testing beginning at 20 years of age (\$99 000 per life-year saved, updated to 1998 dollars) and annual mammography for women ages 55 to 64 years (\$132 000 per life-year saved, updated to 1998 dollars).⁴⁸ Rarely did the cost of CRC screening exceed what we, as a society, are willing to pay for other cancer screening tests, even under the most extreme assumptions in the sensitivity analyses. Conversely, relatively minor changes in baseline assumptions actually made certain less-intensive forms of screening cost saving.

Compliance with screening for CRC is currently quite low in the United States. According to the 1997 Behavioral Risk Factor Surveillance System, only 20% of respondents reported having had FOBT during the preceding year, and only 30% reported having had a proctoscopy or SIG in the preceding 5 years.⁴⁹ Given the low proportion of Americans who currently comply with the recommended screening schedule, advising all Americans to be screened at least once may be a reasonable starting point for national policy. Among the 1-time screening alternatives, COL was the most effective option with a lifetime reduction in CRC mortality of 31% and an incremental CE ratio of \$22 400 per life-year saved compared with 1-time SIG, assuming 60% compliance. A strategy of once-only SIG or COL at 60 years of age has been evaluated for the Netherlands.⁵⁰ Those authors concluded that 40% to 70% of CRC could be prevented at costs comparable to the existent breast cancer screening program.

At 60% compliance, the CE ratio for RFOBT plus SIG every 5 years falls within the parameters of what is paid for other preventive services, but at 100% compliance, the cost is prohibitive. The reason for this difference is that at only 60% compliance, total

screening costs for the strategy are markedly reduced. For instance, over a 10-year period, only 21% of the population will actually have completed screening at baseline, 5 years, and 10 years, and 6% of the population will not have complied with any screening test at all. Should guidelines be based on the assumption of perfect or imperfect compliance? The gold standard for the establishment of clinical guidelines is the results of a clinical trial. However, in a clinical trial, compliance is never 100%. Therefore, we advocate that when using modeling to replicate a clinical situation, compliance rates should be used that mirror the clinical experience.

Colonoscopic follow-up for everyone found to have an adenomatous polyp at SIG, regardless of size or histology, typically dominated the more restricted follow-up strategy. Two retrospective analyses have suggested that subsequent risk of malignancy in patients with adenomas less than 1 cm is minimal.^{21,51} However, 2 recent reports^{52,53} have shown an elevated risk of advanced proximal neoplasia among patients with distal polyps that are either small (<10 cm) or of tubular histology. Furthermore, those 2 studies reported that approximately 50% of patients found to have advanced proximal neoplasia had no distal pathology. The accompanying editorial advocated the use of COL rather than SIG as a screening test for CRC.⁵⁴ In our model, COL every 10 years was more effective than SIG every 5 years; however, it was slightly less effective than the combination of annual FOBT plus SIG every 5 years. The addition of annual FOBT allows for the detection of polyps that would develop in the 10-year interval between COL screens.

The mortality reduction of annual FOBT estimated by our model exceeds the mortality reduction reported in the Minnesota Colon Cancer Control Study.²⁵ The difference is due to the fact that in the clinical trial, population ages ranged from 50 to 80 years and follow-up was for 10 to 15 years, whereas in the model, screening began for everyone at 50 years of

Table 4. Comparison of Model Results to Previously Published Models*

Strategy	Model		
	Eddy ⁴	Wagner et al ⁶	Current Study
Annual FOBT compared with no screening			
Incremental cost, \$	328	769	973
Life expectancy gain, y	0.0241	0.0515	0.0375
Cost-effectiveness ratio, \$ per y	14 000	15 000	26 000
FOBT + sigmoidoscopy every 5 y compared with no screening			
Incremental cost, \$	921	941	1651
Life expectancy gain, y	0.0296	0.0628	0.0441
Cost-effectiveness ratio, \$ per y	31 000	15 000	37 000
FOBT + sigmoidoscopy every 5 y compared with annual FOBT			
Incremental cost, \$	593	172	678
Life expectancy gain, y	0.0055	0.0113	0.0066
Cost-effectiveness ratio, \$ per y	108 000	15 000	103 000

*FOBT indicates fecal occult blood test. Costs are updated to 1998 dollars in prior analyses. Costs and life expectancy in the current model are discounted at 5% per year and assume 100% compliance.

age, continued for 35 years, and persons were followed up for their lifetime. When we configured our model to simulate the parameters of the clinical trial, we obtained a 31% reduction in CRC mortality and a 7% reduction in cancer incidence, similar to the results of the trial.²⁵

Our analysis has several limitations, principally reflecting the uncertainty about the natural history of colorectal disease. We assumed that all cancers arose from polyps; we did not allow polyp progression to depend on time; and we modeled the progression of polyps in the distal vs proximal colon as independent events, although they are likely correlated. However, our model was calibrated with the incidence and stage distribution of CRC based on SEER data.²²

Another limitation of our model is that we assumed that the sensitivity of FOBT was the same for initial and repeated tests. Although we were able to simulate the results of the Minnesota trial, the longer-term effects of this assumption could bias our results toward strategies with FOBT. We also assumed that polypectomy would be performed at the time of an initial SIG if a polyp were found, which is not universal practice in the United States. Our model suggests, as do the results of 2 clinical trials,^{52,53} that the finding of a distal polyp warrants a follow-up COL,

regardless of the size or histology of the polyp. The advantage of removing the polyp at the time of SIG is that the effectiveness of the SIG is not dependent on compliance with the follow-up test. However, immediate polypectomy is not always possible because of either the training of the practitioner or the preparation of the patient. Under the assumption that all polypectomies are performed at COL, we found that SIG every 5 to 10 years was dominated and COL once at 55 years of age and annual UFOBT became reasonable strategies. However, the incremental CE ratios of the strategies with FOBT plus SIG every 5 years did not change significantly.

We compared our results with those from 2 other mathematical models designed to evaluate the cost-effectiveness of CRC screening in average-risk individuals.^{4,6} Specifically, we calculated incremental lifetime costs, life expectancy, and CE ratios for UFOBT and UFOBT plus SIG every 5 years (TABLE 4). To make the results more comparable, we assumed 100% compliance and a 5% annual discount rate in our model and updated the costs of the previously published models to 1998 dollars. The life expectancy gains predicted by our model were intermediate to those published previously, and our costs were consistently higher. In a recent report, the MISCAN-COLON

model predicted that screening every 5 years with SIG compared with no screening would be cost saving.⁵ With minor changes in our assumptions, the results of our model concur that CRC screening could be cost saving.

In summary, screening for CRC is as cost-effective as other forms of cancer screening. Among the screening strategies that we considered, RFOBT plus SIG every 5 years was the most effective strategy, with an 80% reduction in CRC mortality and an incremental CE ratio of \$92 900 per life-year saved compared with UFOBT plus SIG every 5 years. Although all other strategies recommended by the expert panel (annual FOBT, SIG every 5 years, DCBE every 5 to 10 years, or COL every 10 years) were dominated, the choice of screening strategy in clinical practice should be determined not just by cost-effectiveness but also by provider competence and patient preferences. A 1-time screen at 55 years of age with COL can achieve a 30% to 50% reduction in CRC mortality, depending on the level of compliance. Although further reductions in mortality can be accomplished with repeated screening, significant progress in reducing CRC mortality can be achieved with a single screen.

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