

# A DECISION MODEL AND COST-EFFECTIVENESS ANALYSIS OF COLORECTAL CANCER SCREENING AND SURVEILLANCE GUIDELINES FOR AVERAGE-RISK ADULTS

Rezaul K. Khandker

Jane D. Dulski

Jeffrey B. Kilpatrick

Randall P. Ellis

Janet B. Mitchell

*Health Economics Research, Inc.*

William B. Baine

*Agency for Healthcare Research and Quality*

## Abstract

**Objectives:** Guidelines for colorectal cancer screening and surveillance in people at average risk and at increased risk have recently been published by the American Gastroenterological Association. The guidelines for the population at average risk were evaluated using cost-effectiveness analyses.

**Methods:** Since colorectal cancers primarily arise from precancerous adenomas, a state transition model of disease progression from adenomatous polyps was developed. Rather than assuming that polyps turn to cancer after a fixed interval (dwell time), such transitions were modeled to occur as an exponential function of the age of the polyps. Screening strategies included periodic fecal occult blood

The authors gratefully acknowledge the contributions of Francis D. Chesley, MD, in reviewing this study and identifying necessary clinical parameters, James P. Summe in developing the database used, William Yu in commenting upon the model and reviewing the manuscript, and Kathleen A. Weis, DrPH, MSN, RN, ENP-C, PhD, for case definition and review and comment upon the model.

The study was conducted under Contract No. 282-95-2002 from the former Agency for Health Care Policy and Research. An unpublished report from Health Economics Research, Inc., to the Agency for Health Care Policy and Research served as the basis for this paper. This report includes all of the decision trees, a complete list of the ranges of values for sensitivity analyses, and the *Physicians' Current Procedural Terminology* (CPT) and *International Classification of Diseases—9th Edition—Clinical Modification* (ICD-9-CM) codes used in arriving at cost estimates.

Single copies of this report are available upon written request to William B. Baine, MD, Center for Outcomes and Effectiveness Research, Agency for Healthcare Research and Quality, Suite 300, 6010 Executive Boulevard, Rockville, MD 20852-3813, USA. An earlier version of this paper was presented at the Workshop on Cost-Effectiveness in Health and Medicine, William H. Natcher Conference Center, National Institutes of Health, Bethesda, Maryland, November 25–26, 1996.

The statements contained in this paper are solely those of the authors and do not necessarily reflect the views or opinions of the Agency for Healthcare Research and Quality.

test, flexible sigmoidoscopy, double-contrast barium enema, and colonoscopy. Screening costs in 1994 dollars were estimated using Medicare and private claims data, and clinical parameters were based upon published studies.

**Results:** Cost per life-year saved was \$12,636 for flexible sigmoidoscopy every 5 years and \$14,394 for annual fecal occult blood testing. The assumption made for polyp dwell time critically affected the attractiveness of alternative screening strategies.

**Conclusions:** Sigmoidoscopy every 5 years and annual fecal blood testing were the two most cost-effective strategies, but with low compliance, occult blood testing was less cost-effective. Lowering colonoscopy costs greatly improved the cost-effectiveness of colonoscopy every 10 years.

**Keywords:** Colonoscopy, Colorectal neoplasms, Cost-benefit analysis, Mass screening, Occult blood

Colorectal cancer is the second leading cause of cancer death in the United States. Together, colon and rectal cancers were estimated to account for 131,200 new cancer cases and 54,900 deaths in 1997 (2). Although a small portion of the population is at high risk of colorectal cancer because of heritable genetic disorders or as a complication of inflammatory bowel disease, most cases of colorectal cancer develop in members of the general population without clearly recognized predisposing conditions. These sporadic cases are now thought to arise through the accumulation of mutations that lead sequentially to the development of small adenomatous polyps, large adenomas, invasive carcinoma, and, in some persons, metastatic disease (4).

In 1994, the former Agency for Health Care Policy and Research (AHCPR) contracted with the American Gastroenterological Association (AGA) to develop guidelines for screening and surveillance of colorectal cancer. A panel of experts convened by AHCPR and a consortium including AGA, the American Society for Gastrointestinal Endoscopy, the American College of Colon and Rectal Surgery, the American College of Gastroenterology, and the Society of American Gastrointestinal Endoscopic Surgeons developed a set of recommendations that were published under AGA auspices in 1997 (38). These recommendations present a choice of alternative screening strategies. This study examines these recommended colorectal cancer screening and surveillance strategies for average-risk adults by using a decision model and cost-effectiveness framework.

Approximately 30% of persons develop some type of colonic polyp by age 50 (34). Many such polyps are hyperplastic (generally small and of no clinical importance), but others are adenomatous (premalignant) and can lead to cancer unless detected and removed early in their growth phase. The effectiveness of screening average-risk persons is derived from early detection of cancer and removal of polyps, lowering the incidence of cancer and cancer-related deaths. Early detection of polyps and cancer can also reduce eventual treatment costs. However, screening everyone for colorectal cancer is expensive. Whether to screen all persons after a certain age, what types of screening methods to use, and how frequently to apply the tests are important policy questions. The choice and frequency of tests determine not only how quickly polyps and cancers are detected and treated but also how much it will cost to implement such screening and surveillance programs.

This study developed an elaborate model by which polyps may lead to colorectal cancer, compared alternative screening strategies, and conducted extensive sensitivity analyses. Past studies have concluded that screening after a certain age can be a cost-effective method of reducing morbidity and mortality from colorectal cancer (11;12;22;30;34;35). This study significantly extended earlier work in terms of the assumptions regarding polyp dwell time and post-polypectomy surveillance. While earlier studies provide comparisons of alternative screening tools, no clear consensus has emerged regarding the most appropriate screening strategies. In part, this lack of consensus reflects a lack of understanding of the colorectal

cancer disease process, including the dwell times of polyps at different stages of development. Considerable uncertainty surrounds how polyps progress, and the effectiveness of the various screening options depends critically upon that process. This study particularly addressed this issue, using a disease model that captured the uncertainty associated with polyp dwell time. This model also built an extensive surveillance period during which screening of heightened intensity could be applied upon the basis of guidelines recommended for the surveillance population.

## METHODS

### Screening and Surveillance Strategies

The analyses considered four principal methods of screening for colorectal cancer addressed by the AGA guidelines—fecal occult blood testing (FOBT), flexible sigmoidoscopy, double-contrast barium enema, and colonoscopy (38). FOBT is widely used to screen for colorectal cancer because the method is simple and inexpensive. Polyps and cancers may bleed, and FOBT detects neoplasms by revealing blood in the stool. However, FOBT is least effective at detecting small polyps. Sigmoidoscopy and colonoscopy permit inspection of the colonic lumen, and barium enemas display the contours of the colonic mucosa. Sigmoidoscopy does not permit examination beyond the left (descending) side of the colon, whereas colonoscopy offers the potential of surveying the entire colon. Colonoscopy can be used both as a screening and as a surveillance procedure and is often selected to follow other screening tests when polyps or cancer are suspected. Removal of polyps (polypectomy) can also be carried out in the course of colonoscopy, so this procedure can provide definitive therapy for premalignant polyps as well as diagnostic information.

Only average-risk persons were included in this analysis. This group included those aged 50 and older without predisposing factors, who account for approximately 75% of colorectal cancer incidence (38). Based upon tests and intervals recommended by Winawer et al. (38), the following eight screening strategies were modeled: a) annual FOBT; b) flexible sigmoidoscopy every 3 years; c) flexible sigmoidoscopy every 5 years; d) annual FOBT and flexible sigmoidoscopy every 3 years; e) annual FOBT and flexible sigmoidoscopy every 5 years; f) double-contrast barium enema every 5 years; g) colonoscopy every 5 years; and h) colonoscopy every 10 years. Screening started at age 50 and continued until age 85.

### Decision Model

The disease and screening process was based upon a dynamic state transition model. During each cycle, each person would occupy one of eight primary states (disease-free, hyperplastic polyp, adenomatous polyp, undetected cancer, surveillance, treatment, death due to colorectal cancer or test complications, and death from other causes). The complete model had more than 60 states, depending upon polyp histology (size and stage of development), location of polyp and cancer (distal or proximal), age (5-year intervals), and cancer stage (local, regional, distant, and number of years in each stage). Each state was assigned an initial probability, representing the distribution of a hypothetical cohort. A probabilistic model of transitions determined the state in each subsequent cycle, with the transition probabilities based upon the incidence and progression of polyps and cancer and upon interventions and the outcome of screening tests. During each cycle, the subject in the model accumulated cost and, by living through the cycle, gained life-years. Iterating the model until death yielded the average life expectancy and the total costs of colorectal cancer screening, diagnosis, and treatment.

The first 20 years of dwell time for adenomatous polyps were modeled extensively using 10 states of 2-year duration. Polyps could transform to cancer with a probability that

increased as a function of how long they had dwelled in the colon. This probability distribution was based on an equation derived by Whynes et al. (36) using published data on the radiographic surveillance of adenomas in the period before the availability of colonoscopy. While polyp dwell time is not known with certainty, it holds the key to successful screening. Accordingly, alternative models of dwell time in which polyps turned to cancer after a fixed length of time (34) were explored in sensitivity analysis. Persons who were found to have polyps underwent transition to a surveillance group after polyps were removed. A higher probability of developing polyps was assigned to the surveillance group than to those with no prior polyps (screening). The length of time in surveillance and the frequency of tests depended upon the size and type of polyp (38).

Multiple decision trees were constructed to represent transition into and out of the various primary states. Measures of test sensitivity, which varied by polyp size, and test specificity determined the success or failure of screening tests. Test performance was also a function of the location of the polyp (proximal or distal). When test results were positive, a follow-up colonoscopy was assumed regardless of the polyp size. Implicit in all invasive tests was the risk of complication. Three stages of colorectal cancer, depending on anatomic extent, were modeled—local, regional, and distant, conceptually paralleling carcinoma in situ and Dukes A, Dukes B and C, and Type 4, respectively. Persons with advanced stages of undiagnosed cancer were presumed to have a progressively higher likelihood of seeking medical care, better chances of detection, and higher levels of mortality. In each cancer stage, a patient could stay for as many as 5 years in tunnel states (31). The model also allowed persons with undetected cancer to experience disease progression until screening or symptom-driven visits revealed the disease. The model was evaluated using DecisionMaker 7.0 software (Pratt Medical Group, Boston, MA).

### Parameter Values

Estimates for the model required parameters related to incidence and progression of polyps and colorectal cancer, survival rates, risk factors and complications, compliance, test performance, and costs. For adenomatous and hyperplastic polyps, initial probabilities were estimated to be 25% and 5%, respectively (34;38). Incidence rates for new polyps were estimated as 0.7%, 1%, and 1.5%, respectively, for the three age groups: 50–65, 66–70, and 71–85 years (34;37). The initial probabilities of various cancer stages were based upon Abrams and Reines (1). Rates for large adenomatous polyps' turning to cancer, depending upon polyp dwell time, were based upon Whynes et al. (36). For small polyps, only one-tenth of those probabilities was used (38). A 2-year time period was assumed between the first two cancer stages (11;33). The final stage of cancer developed within 1 year after the second stage. Five-year survival rates based upon Surveillance, Epidemiology, and End Results (SEER) data (26) were used for the yearly probability of dying from colorectal cancer, based upon the stage and number of years with cancer. Age-specific rates of death from other causes were estimated by subtracting the mortality rates for colorectal cancer from those for all causes, as published by the National Center for Health Statistics (23).

The parameter values for screening test performance, shown in Table 1, and for complications were primarily based on Winawer et al. (38). It is important to note that sensitivity and specificity values could vary, depending upon the polyp size, and between polyps and cancer. Very little is known about compliance with colorectal cancer screening; full compliance was assumed for the base model, and a 23% compliance rate was used for sensitivity analyses based upon a study of FOBT compliance (3).

Table 2 reports screening costs for the United States. Costs for the elderly were estimated from procedure claims for the screening tests in a 5% sample of all Medicare beneficiaries from 1992 through 1994. For younger subjects, costs were estimated from claims data for

**Table 1.** Sensitivity and Specificity of Screening Tests

Parameter	Value
<i>Sensitivity of FOBT<sup>a</sup></i>	
Small polyps	0.06
Large polyps	0.10
Cancer	0.60
<i>Specificity of FOBT</i>	0.92
<i>Sensitivity of flexible sigmoidoscopy</i>	
Small distal polyps	0.73
Large distal polyps	0.97
Distal cancer	0.97
<i>Specificity of flexible sigmoidoscopy for distal polyps or cancer</i>	0.92
<i>Sensitivity of double-contrast barium enema</i>	
Small distal polyps	0.67
Large distal polyps	0.82
Distal cancer	0.84
<i>Specificity of double-contrast barium enema for small polyps</i>	0.75
<i>Sensitivity of colonoscopy</i>	
Small distal polyps	0.79
Large distal polyps	0.85
Distal cancer	0.97
<i>Specificity of colonoscopy</i>	1.00

<sup>a</sup> FOBT = fecal occult blood testing.

a large sample of privately insured patients (MEDSTAT Group, Washington, DC). Only outpatient (physician and hospital outpatient department) costs were used, since inpatient procedures were generally confounded with unrelated services. Flexible sigmoidoscopy and colonoscopy costs were separately estimated for simple screening procedures versus those with polypectomy/biopsy and pathology (complex). All cost estimates were adjusted to 1994 dollars using the national medical inflation rate of 4.8% (7). Cancer treatment and lifetime costs were estimated based upon Fireman et al. (14). The cost of complications was based upon Wagner et al. (34).

## RESULTS

### Base Case

Table 3 shows discounted lifetime measures of cost and effectiveness under eight alternative screening strategies. Each strategy was compared to a baseline of no screening to estimate incremental cost:effectiveness ratios. Without screening, the lifetime cost of colorectal

**Table 2.** Costs of Screening Tests in the United States, 1994 Dollars

Screening test	Patient age	
	Under 65 years <sup>a</sup>	65 years and older <sup>b</sup>
FOBT <sup>c</sup>	\$11	\$7
Double-contrast barium enema	\$176	\$175
Simple flexible sigmoidoscopy	\$176	\$94
Complex flexible sigmoidoscopy	\$299	\$214
Simple colonoscopy	\$670	\$438
Complex colonoscopy	\$981	\$702

<sup>a</sup> MEDSTAT claims data.

<sup>b</sup> Data from Medicare claims, 5% sample.

<sup>c</sup> FOBT = fecal occult blood testing.

**Table 3.** Cost-effectiveness Estimates for Base Case and Fixed-Length Models, 1994 Dollars

	Base case model		Fixed-length (10-year) polyp model	
	Cost (\$ per person)	Effectiveness (life-years)	Incremental cost:effectiveness ratio	Cost:effectiveness ratio (polyp-to-cancer transition probability = 1)  Cost:effectiveness ratio (polyp-to-cancer transition probability = 0.25)
Baseline (no screening)	\$643	18.14	—	—
Annual FOBT <sup>a</sup>	\$2,058	18.24	\$14,394	\$5,586
3-year flexible sigmoidoscopy	\$2,079	18.23	\$16,261	\$3,567
5-year flexible sigmoidoscopy	\$1,713	18.23	\$12,636	\$3,504
Annual FOBT/3-year flexible sigmoidoscopy	\$2,854	18.25	\$20,334	\$5,326
Annual FOBT/5-year flexible sigmoidoscopy	\$2,639	18.25	\$18,204	\$5,070
5-year double-contrast barium enema	\$2,577	18.25	\$17,553	\$4,468
5-year colonoscopy	\$3,906	18.25	\$28,724	\$7,048
10-year colonoscopy	\$2,602	18.25	\$17,696	\$4,657

<sup>a</sup> FOBT = fecal occult blood testing.

**Table 4.** Cumulative Incidence and Death Rates (per 100,000) for Colorectal Cancer

Screening procedure	Cumulative cancer rates			Cumulative cancer deaths		
	Patient age (yr)			Patient age (yr)		
	60	70	85	60	70	85
Baseline (no compliance)	770	2,350	5,550	350	990	2,920
Annual FOBT <sup>a</sup>	630	1,310	2,220	200	340	590
3-year flexible sigmoidoscopy	480	940	1,750	210	390	850
5-year flexible sigmoidoscopy	520	1,030	1,890	220	430	920
Annual FOBT/3-year flexible sigmoidoscopy	450	830	1,130	170	240	360
Annual FOBT/5-year flexible sigmoidoscopy	480	750	1,130	170	240	340
5-year double-contrast barium enema	450	600	770	180	250	310
5-year colonoscopy	350	410	520	150	160	190
10-year colonoscopy	410	560	750	170	230	300

<sup>a</sup> FOBT = fecal occult blood testing.

cancer was \$643 per person due to diagnosis and treatment for those who happened to seek care. Annual FOBT added an additional \$1,415 in lifetime cost, including screening costs for everyone and follow-up diagnostic and other costs for those with a positive FOBT. Absent screening, the model predicted that an average person would live 18.14 years beyond the age of 50 (discounted at 3%). For simplicity, the model did not assign any remaining life beyond age 85 (the end of the screening interval), since the residual life would apply to screening and nonscreening strategies alike. With annual FOBT, persons reaching age 50 were predicted to live 18.24 years, a marginal gain of 0.0983 life-years. Flexible sigmoidoscopy every 5 years had the lowest cost per person (\$1,713) among all screening strategies. Colonoscopy, performed every 5 years, had the highest cost per person. Among the eight strategies, flexible sigmoidoscopy every 5 years ranked lowest in terms of cost per life-year saved (\$12,636). This strategy was closely followed by annual FOBT (\$14,394). Sigmoidoscopy every 3 years cost \$3,625 more than when offered at 5-year intervals. Colonoscopy every 5 years cost the most (\$28,724).

Table 4 shows the cumulative numbers of people developing cancer and dying from it at ages 60, 70, and 85. Without cancer screening, 770 persons would develop colorectal cancer by age 60, and 5,550 (approximately 56 per 1,000) would develop colorectal cancer by age 85. Cancer incidence and death rates reduced substantially with screening. Colonoscopy every 5 years led to the lowest cancer rate at each age because of its superior effectiveness (high sensitivity and frequent screening). In contrast, annual FOBT, with its low sensitivity, was associated with the highest cancer rates. Even so, cancer rates were 18% lower by age 60 with annual FOBT relative to no screening. In general, preventive effects of screening increased cumulatively with age for those strategies that involved repeated tests. Without screening, 2,920 people (out of 100,000) would die from colorectal cancer by age 85. Any of the screening strategies lowered death rates considerably. For example, annual FOBT would lead to only 590 deaths by age 85 (80% lower than no screening). Most other strategies, with the exception of flexible sigmoidoscopy, would reduce death rates even further.

### Sensitivity Analysis

Sensitivity analyses focused upon key parameters of the disease process, screening performance, costs, and compliance. Particular attention was directed at polyp dwell time, since much of the preventive effect of screening arose from the time lag inherent in malignant

transformation of adenomatous polyps into cancer. By analogy to Wagner et al. (34), two alternative scenarios were considered at the end of the tenth year with a polyp. In one scenario, precancerous polyps turned to cancer with a probability of 1.0, and in another scenario, with a probability of 0.25. As shown in the last two columns of Table 3, cost-effectiveness estimates were very sensitive to the assumption regarding polyp dwell time. Relative to the base case model with time-dependent polyp-cancer transitions, cost:effectiveness ratios were significantly lower for all screening options (ranging from \$3,504 for 5-year flexible sigmoidoscopy to \$7,048 for 5-year colonoscopy). On the contrary, cost:effectiveness ratios were much higher when polyps had only a 25% chance of turning to cancer at the end of the 10th year. Assuming that malignant transformation occurred abruptly at the end of the 10th year of polyp dwell time, sigmoidoscopy every 5 years was the most cost-effective strategy, followed by sigmoidoscopy every 3 years. Generally, strategies with less frequent screening (i.e., with longer intervals between tests) were dominant over more frequent strategies such as annual FOBT. Wagner et al. (34) generally found strategies with a 10-year screening interval to be most cost-effective given a 10-year dwell time, and 5-year screening strategies to be most cost-effective given a 5-year dwell time.

Sensitivity analysis was performed upon models of flexible sigmoidoscopy with reach-adjusted parameters. Since the flexible sigmoidoscope reaches only a part of the colon, the base case separately modeled proximal and distal parts of the colon and assumed zero sensitivity when polyps were located beyond the reach of the flexible sigmoidoscope. This adjustment was done to avoid overestimating the effectiveness of this test. In sensitivity analysis, an alternative assumption stipulated a sensitivity of 90% for sigmoidoscopy in the distal colon and 0% more proximally. In essence, this model used a 45% reach-adjusted sensitivity parameter if polyps were distributed equally between distal and proximal colons. This approach invariably overestimated the effectiveness of flexible sigmoidoscopy since the calculation ignored the fact that in repeated tests proximal polyps would continue to be undetected. Overestimation of effectiveness in the reach-adjusted model portrayed flexible sigmoidoscopy every 5 and every 3 years as the two most cost-effective strategies.

Sensitivity analysis was also performed at 23% compliance as opposed to 100% as in the base model. Flexible sigmoidoscopy at 3 and 5 years ranked as the two most cost-effective strategies. Annual FOBT became the next to least-preferred alternative, superior only to 5-year colonoscopy, in terms of cost:effectiveness ratio. With imperfect compliance, insensitive strategies such as annual FOBT lost their cost-effectiveness as the advantage conferred by repeated tests was lost.

Table 5 illustrates the impact of high and low values of selected other parameters upon cost:effectiveness ratios. Strategies are ranked from the most cost-effective (ranked 1) to the least cost-effective (ranked 8). Using low values for sensitivity of FOBT dropped annual FOBT from second to penultimate preferred status. At high values of FOBT sensitivity, annual FOBT ranked as the most cost-effective strategy, followed by sigmoidoscopy every 5 years. In general, flexible sigmoidoscopy at 5-year intervals and annual FOBT continued to be the two most cost-effective strategies under a broad range of assumptions. However, poor compliance made annual FOBT less cost-effective, and low colonoscopy cost made that test more cost-effective when performed every 10 years.

## DISCUSSION

The study provides an economic evaluation of the colorectal cancer screening options recommended by the AGA. Under a realistic assumption of polyp-cancer transitions as demonstrated by the base case model, most of the screening options had a cost-effectiveness ratio less than \$20,000 per life-year saved in 1994 dollars. Although the definition of what



**Table 5.** Ranking of Screening Strategies Under Selected Alternatives<sup>a</sup>

Assumptions	Annual FOBT	5-year DCBE	5-year FSIG	3-year FSIG	Annual FOBT/ 5-year FSIG	Annual FOBT/ 3-year FSIG	10-year colonoscopy	5-year colonoscopy
<i>Baseline values</i>	2	4	1	3	6	7	5	8
<i>50% below baseline value</i>								
FOBT sensitivity	7	3	1	2	5	6	4	8
DCBE sensitivity	2	7	1	3	5	6	4	8
Colonoscopy sensitivity	3	6	1	2	4	5	7	8
Colonoscopy cost	1	4	3	5	6	7	2	8
<i>50% above baseline value</i>								
FOBT sensitivity	1	4	2	3	6	7	5	8
DCBE sensitivity	2	4	1	3	6	7	5	8
Colonoscopy sensitivity	2	4	1	3	7	6	5	8
Colonoscopy cost	3	4	1	2	5	6	7	8

<sup>a</sup> 1 = lowest cost:effectiveness ratio; 8 = highest cost:effectiveness ratio.

Abbreviations: FOBT = fecal occult blood testing; DCBE = double-contrast barium enema; FSIG = flexible sigmoidoscopy.

is an acceptable cost:effectiveness ratio remains arbitrary, the median cost per life-year saved reported for 310 healthcare interventions was \$19,000 using 1993 dollars (32). Thus, other than that for 5-year colonoscopy, cost:effectiveness ratios for all screening options considered in this study can be considered at or below the median. The ratios reported here also compared favorably with other mass screening or prevention alternatives. For example, mammography screening for women between the ages of 50 and 69 years had a cost:effectiveness ratio of \$21,400 in 1995 dollars (29). Biennial and triennial Pap smear (with AutoPap-assisted rescreen) for women aged 20 to 65 years yielded \$42,666 and \$16,259, respectively, using 1996 dollars (6). Over a broad range of inputs, cost:effectiveness ratios reported for primary prevention of cardiovascular disease with pravastatin remained below \$25,000 per life-year gained (9).

Both flexible sigmoidoscopy every 5 years and annual FOBT were cost-effective under a broad range of assumptions. FOBT reduces colorectal cancer mortality (19;21) at acceptable cost (18;28;35), and annual FOBT is claimed by some researchers to be most cost-effective (11;22;30). Flexible sigmoidoscopy and barium enema were found to be more cost-effective than some of the other screening tools by other researchers (5;15;34). Due to methodologic differences, these results often are not comparable. For example, Wagner et al. (34) assumed that polyps turn to cancer at fixed intervals, while the current study introduced time dependence by allowing polyps to transform to cancer with higher probability as they dwell longer. A shortcoming of models that assume a constant dwell time, as in the study by Wagner et al., is that they do not explain the empirical observation that the incidence of cancer in general and of colorectal cancer in particular increases exponentially with increasing age (10;20).

The results obtained here should be useful to clinicians, policy makers, and payers in choosing among screening methods and in considering payment for colorectal cancer screening in view of the cost and effectiveness associated with each alternative strategy. However, many key assumptions represent a best guess based upon the available literature. This is partly because of the lack of definitive clinical studies of the kinetics of malignant transformation of adenomatous polyps and the growth and spread of colorectal cancer as well as of the effectiveness of various tests (24). As demonstrated by sensitivity analyses, the dynamics of polyp-cancer transition have significant effect upon the magnitude of the cost:effectiveness ratios. A clearer understanding of the development of colorectal cancer, including the dwell time of polyps and the progress of cancers through different stages of development, is central to understanding the effectiveness of various diagnostic tests.

Future studies should also consider patient quality of life and societal impacts arising from adenomatous polyps, colorectal cancer, and screening interventions (16).

## POLICY IMPLICATIONS

The cost of screening is an important issue in the development of public policy. Inherent in a successful colorectal cancer program is the role of population screening. Spurred by mounting evidence that the detection and treatment of early-stage colorectal cancers and adenomatous polyps can reduce mortality, Medicare and some other payers recently authorized reimbursement for colorectal cancer screening in persons at average risk. Medicare beneficiaries may now receive coverage for annual FOBT and for flexible sigmoidoscopy every 4 years, with double-contrast barium enema considered as an alternative. Although private insurers can be expected to provide such coverage, payers carefully weigh the relative risks, costs, and effectiveness of the various test strategies. Some payers may prefer FOBT and sigmoidoscopy because these procedures have the lowest initial costs and meet the standard of care. Other payers with a stable patient base and secure long-term financial future may choose colonoscopy, provided they can negotiate the charge down to an acceptable level (25). However, as this study illustrates, colonoscopy as an alternative is sensitive to its high cost, and its administration every 10 years can be further associated with problems of recall and compliance.

This study, particularly the cost analysis, is oriented to the United States. The economics of colorectal cancer screening are expected to be different across healthcare systems and across countries. Although colorectal cancer meets the World Health Organization's suitability criteria for mass population screening (35), Canada, Australia, and most European countries are still debating adoption of the measure (17;27). Given favorable results based upon randomized studies, the Department of Health in the United Kingdom is considering FOBT for national implementation (27). Data for mammography screening for breast cancer seem no more convincing than that for colorectal cancer screening, yet the United Kingdom adopted national screening programs for the former in the 1980s. A European group of experts has recently published their strong recommendation to implement FOBT associated with follow-up colonoscopy as appropriate (13). Those authors agreed that, due to diverse health systems and resource constraints, a uniform approach to screening across all European countries was not possible.

Policy uncertainties arise from the high cost of national screening programs. The annual cost of FOBT for 52 million persons older than 50 years of age in the United States has been estimated to exceed \$1 billion (8). Rising costs for medical care will only increase the need for economic evaluations of large-scale healthcare interventions. Significant resource utilization issues are involved in procurement and administration, infrastructure and training, education and awareness, and ensuring patient and physician compliance. Without an overall effort, the success of mass screening will not achieve optimal results. In the final analysis, the choice among alternatives is most often based upon societal resource constraints and value judgments.

## REFERENCES

1. Abrams JS, Reines HD. Increasing incidence of right-sided lesions in colorectal cancer. *Am J Surg.* 1979;137:522-526.
2. American Cancer Society. *Cancer facts and figures—1997*. Atlanta: American Cancer Society; 1997.
3. Anderson LM, May DS. Has the use of cervical, breast, and colorectal cancer screening increased in the United States? *Am J Public Health.* 1995;85:840-842.
4. Banerjee AK. DCC expression and prognosis in colorectal cancer. *Lancet.* 1997;349:968.

5. Bolin TD. Cost benefit of early diagnosis of colorectal cancer. *Scand J Gastroenterol Suppl.* 1996;220:142-146.
6. Brown AD. Cost-effectiveness of three methods to enhance the sensitivity of Papanicolaou testing. *JAMA.* 1999;281:347-353.
7. Bureau of the Census (US). *Statistical abstract of the United States: 1994*, 114th ed. Washington, DC: Bureau of the Census; 1994.
8. Byers T, Gorsky R. Estimates of costs and effects of screening for colorectal cancer in the United States. *Cancer.* 1992;70:1288-1295.
9. Caro J, Klittich W, McGuire A, et al. International economic analysis of primary prevention of cardiovascular disease with pravastatin in WOSCOPS. *Eur Heart J.* 1999;20:263-268.
10. Cohen HJ. Oncology and aging: General principles of cancer in the elderly. In: Hazzard WR, Bierman EL, Blass JP, Ettinger WH Jr, Halter JB, eds. *Principles of geriatric medicine and gerontology*, 3rd ed. New York: McGraw-Hill; 1994:77-89.
11. Eddy DM. Screening for colorectal cancer. *Ann Intern Med.* 1990;113:373-384.
12. England WL, Halls JJ, Hunt VB. Strategies for screening for colorectal carcinoma. *Med Decis Making.* 1989;9:3-13.
13. European Group for Colorectal Cancer Screening. Recommendation to include colorectal cancer screening in public health policy. *J Med Screen.* 1999;6:80-81.
14. Fireman B, Quesenberry C, Somkin C, et al. Cost of care for cancer in a health maintenance organization. *Health Care Financing Review.* 1997;18:51-76.
15. Gelfand DW. Colorectal cancer: Screening strategies. *Radiol Clin North Am.* 1997;35:431-438.
16. Gold MR, Siegel JE, Russell LB, Weinstein MC, eds. *Cost-effectiveness in health and medicine.* New York: Oxford University Press; 1996.
17. Gow J. Costs of screening for colorectal cancer: An Australian programme. *Health Econ.* 1999;8:531-540.
18. Gyrd-Hansen D, Søgaaard J, Kronborg O. Colorectal cancer screening: Efficiency and effectiveness. *Health Econ.* 1998;7:9-20.
19. Hardcastle JD, Chamberlain JO, Robinson MHE, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet.* 1996;348:1472-1477.
20. Kosary CL, Ries LAG, Miller AB, et al., eds. *SEER cancer statistics review, 1973-1992. Tables and graphs.* NIH publication no. 96-2789. Bethesda: National Cancer Institute, National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services; 1995:154.
21. Kronborg O, Fenger C, Olsen J, Jørgensen D, Søndergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. *Lancet.* 1996;348:1467-1471.
22. Lieberman DA. Cost-effectiveness model for colon cancer screening. *Gastroenterology.* 1995;109:1781-1790.
23. National Center for Health Statistics. *Vital statistics of the United States, 1992, vol. II: Mortality, parts A and B.* Washington, DC: Government Printing Office; 1993.
24. Ransohoff DF, Lang CA. Screening for colorectal cancer with the fecal occult blood test: A background paper. *Ann Intern Med.* 1997;126:811-822.
25. Rex DK. Colorectal cancer screening: A guide to the guidelines. *Can J Gastroenterol.* 1999;13:397-402.
26. Ries LAG, Miller BA, Hankey BF, et al., eds. *SEER cancer statistics review, 1973-1991. Tables and graphs.* NIH publication no. 94-2789. Bethesda: National Cancer Institute, National Institutes of Health, Public Health Service, U.S. Department of Health and Human Services; 1994.
27. Robinson MHE, Hardcastle JD. Should we be screening for colorectal cancer? *Br Med Bull.* 1998;54:807-821.
28. Salkeld G, Young G, Irwig L, Haas M, Glasziou P. Cost-effectiveness analysis of screening by faecal occult blood testing for colorectal cancer in Australia. *Aust N Z J Public Health.* 1996;20:138-143.
29. Salzmann P, Kerlikowske K, Phillips K. Cost-effectiveness of extending screening mammography guidelines to include women 40 to 49 years of age. *Ann Intern Med.* 1997;127:955-965.
30. Shimbo T, Glick HA, Eisenberg JM. Cost-effectiveness analysis of strategies for colorectal cancer screening in Japan. *Int J Technol Assess Health Care.* 1994;10:359-375.

Khandker et al.

31. Sonnenberg FA, Beck JR. Markov models in medical decision making: A practical guide. *Med Decis Making*. 1993;13:322-338.
32. Tengs TO, Adams ME, Pliskin JS, et al. Five hundred life-saving interventions and their cost-effectiveness. *Risk Anal*. 1995;15:369-390.
33. Wagner JL, Herdman RC, Wadhwa S. Cost effectiveness of colorectal cancer screening in the elderly. *Ann Intern Med*. 1991;115:807-817.
34. Wagner JL, Tunis S, Brown M, Ching A, Almeida R. The cost effectiveness of colorectal cancer screening in average-risk adults. In: Young GP, Rozen P, Levin B, eds. *Prevention and early detection of colorectal cancer*. Philadelphia: WB Saunders; 1996:321-356.
35. Whynes DK, Neilson AR, Walker AR, Hardcastle JD. Faecal occult blood screening for colorectal cancer: Is it cost-effective? *Health Econ*. 1998;7:21-29.
36. Whynes DK, Walker AR, Hardcastle JD. Cost savings in mass population screening for colorectal cancer resulting from the early detection and excision of adenomas. *Health Econ*. 1992;1:53-60.
37. Williams AR, Balasooriya BAW, Day DW. Polyps and cancer of the large bowel: A necropsy study in Liverpool. *Gut*. 1982;23:835-842.
38. Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: Clinical guidelines and rationale. *Gastroenterology*. 1997;112:594-642.