Cost-Effectiveness of Colonoscopy in Screening for Colorectal Cancer
Amnon Sonnenberg, MD, MSc; Fabiola Delco`, MD, MPH; and John M. Inadomi, MD

Background: Fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy are used to screen patients for colorectal cancer.

Objective: To compare the cost-effectiveness of fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy.

Design: The cost-effectiveness of the three screening strategies was compared by using computer models of a Markov process. In the model, a hypothetical population of 100 000 persons 50 years of age undergoes annual fecal occult blood testing, sigmoidoscopy every 5 years, or colonoscopy every 10 years. Positive results on fecal occult blood testing or adenomatous polyps found during sigmoidoscopy are worked up by using colonoscopy. After polypectomy, colonoscopy is repeated every 3 years until no polyps are found.

Data Sources: Transition rates were estimated from U.S. vital statistics and cancer statistics and from published data on the sensitivity, specificity, and efficacy of various screening techniques. Costs of screening and cancer care were estimated from Medicare reimbursement data.

Target Population: Persons 50 years of age in the general population.

Time Horizon: The study population was followed annually until death.

Perspective: Third-party payer.

Outcome Measure: Incremental cost-effectiveness ratio.

Results of Base-Case Analysis: Compared with colonoscopy, annual screening with fecal occult blood testing costs less but saves fewer life-years. A screening strategy based on flexible sigmoidoscopy every 5 or 10 years is less cost-effective than the other two screening methods.

Results of Sensitivity Analysis: Screening with fecal occult blood testing is more sensitive to changes in compliance rates, and it becomes easily dominated by colonoscopy under most conditions assuming less than perfect compliance. Other assumptions about the sensitivity and specificity of fecal occult blood testing, screening frequency, efficacy of colonoscopy in preventing cancer, and polyp incidence have a lesser influence on the differences in cost-effectiveness between colonoscopy and fecal occult blood testing.

Conclusions: Colonoscopy represents a cost-effective means of screening for colorectal cancer because it reduces mortality at relatively low incremental costs. Low compliance rates render colonoscopy every 10 years the most cost-effective primary screening strategy for colorectal cancer.
METHODS

General Assumptions of the Markov Model

The cost-effectiveness of fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy were compared by using computer models based on a Markov process (12). Medical events are modeled as transitions of patients among a predefined set of health states; the occurrence of each transition is governed by a probability value (Appendix Figure). The time frame of the analysis is divided into equal increments of 1 year, during which patients may cycle from one state to another. Only the gray and black ovals of the Appendix Figure show states in the true sense of a Markov process, because patients remain in these states for at least a full 1-year cycle. The white ovals represent the intermediate states of screening procedures. Patients can enter and leave these intermediate states during one cycle before settling in a true Markov state.

In the first model of screening by fecal occult blood testing, the initial population comprises 100 000 patients 50 years of age who are offered the test. Depending on the initial compliance rate and the outcome of the test (positive or negative), patients then undergo colonoscopy or enter the pool of patients waiting for their next fecal occult blood test in 1 year’s time. In the case of normal results on colonoscopy (no adenomatous polyp), annual fecal occult blood testing is resumed 10 years after colonoscopy. If an adenomatous polyp is found, surveillance colonoscopy is repeated every 3 years until adenomatous polyps are no longer found. Patients with a positive result on fecal occult blood testing who decline colonoscopy or those who decline to have repeated fecal occult blood testing after 1 year enter the state of noncompliance.

Patients in any Markov state can develop colorectal cancer; the probability stems from the age-specific incidence rate. The likelihood of developing cancer is reduced in patients after colonoscopy plus polypectomy, depending on the rate of preventive efficacy assigned to the procedure. The length of time for which colonoscopy plus polypectomy protects against colorectal cancer is equal to the screening interval. In addition to the states shown in the Appendix Figure, the population in each state is also subjected to natural attrition by the annual age-specific death rate of the U.S. population (13).

Screening with flexible sigmoidoscopy is modeled similarly to fecal occult blood testing (Appendix Figure). The simulation is started with 100 000 patients being offered screening with flexible sigmoidoscopy. The transitions out of this intermediate state depend on whether a polyp is found during sigmoidoscopy. After normal flexible sigmoidoscopy without adenomatous polyps, patients stay in the pool waiting for the next screening sigmoidoscopy in 5 years. The remainder of the model is similar to that of fecal occult blood testing.

Screening with colonoscopy is modeled by using a Markov process similar to that used for the two previous strategies, except that all states associated with a different screening test other than colonoscopy are eliminated (Appendix Figure).

All three models were simulated by using Excel spreadsheets (Microsoft Corp., Redmond, Washington).

Transition Probabilities

The transition probabilities built into the model and the ranges tested in the sensitivity analyses are shown in the Appendix Table. Most large prospective trials of fecal occult blood testing used nonrehydrated slides. The sensitivity and specificity of testing for colorectal cancer varied from 30% to 50% and 90% to 99%, respectively (14, 15, 24–28). Estimates of 40% and 97.5% for the two parameters are supported by data from a recent large prospective trial comprising more than 8000 participants (15). The rate of positive results on fecal occult blood testing was calculated as the sum of true-positive and false-positive results. Screening intervals were chosen to agree with the most recent set of recommendations (7).

Three types of compliance rates are built into the model; screened patients must be compliant with the initial screening procedure, each repeated screening, and colonoscopy after a positive result on fecal occult blood testing or flexible sigmoidoscopy. Under baseline conditions, all compliance rates were assumed to be 100%. In the sensitivity analysis, the rates of initial, repeated, and follow-up compliance were varied according to estimates published for the three screening methods (9, 24, 29–34).

The prevalence of adenoma per 10-year age group was available from autopsy studies (16, 17). An annual incidence of 1% was calculated as the average difference between the prevalence rates of two consecutive age groups. In the sensitivity analysis, the annual incidence of adenomatous polyps was varied from 1% to 6%. The Markov model uses the polyp rate to calculate the number of polypectomies and repeated colonoscopies after polypectomy. The number of cases of cancer prevented was calcu-
lated from the age-specific incidence rates of colorectal cancer. About 45% of all polyps are within the reach of flexible sigmoidoscopy (18, 22, 35). The annual age-specific incidence rate of colorectal cancer is taken from published statistics of the Surveillance, Epidemiology, and End Results Program (36). Depending on the type of historical control group chosen, the National Polyp Study showed an efficacy of colonoscopy in reducing the incidence of colorectal cancer ranging from 76% to 90% (9). Because other studies have suggested an efficacy of only 49% to 59% (8, 10, 11), we chose a median value of 75% as the baseline rate.

Effectiveness and Costs

Effectiveness of screening is measured in terms of life-years saved through prevention of colorectal cancer and improved survival of earlier cancer stages. Without screening, 40% of all colorectal cancers were assumed to result in death within 5 years (36). Because detection of colorectal cancer at earlier stages improves the overall 5-year survival rate, survival after annual screening was adjusted to reduce mortality from colorectal cancer by 18% (37). The life-years lost by the age-dependent proportions of patients dying prematurely of colorectal cancer are accumulated for each cycle during the entire expected lifetime. The number of life-years saved because of screening corresponds to the difference in life-years lost from cancer-related deaths between a Markov model with and one without screening.

Medical, surgical, and diagnostic services were assigned Current Procedural Terminology or diagnosis-related group codes to identify the health care resources utilized for each patient (19, 20). These codes were converted into costs for each health care resource utilization (Table 1). The costs represent the average payments allowed for each coded procedure by the U.S. Health Care Finance Administration during fiscal year 1998. The costs also include the possibility of hospitalization for bleeding or perforation after endoscopy with or without polypectomy (21, 38–43). Published cost estimates for the medical care of patients with colorectal cancer range from $25,000 to $45,000 (4, 7, 23, 44). We used the most recent data available from a study by Lee and colleagues (44). All future costs arising from screening or care of colorectal cancer and all future life-years saved through screening are discounted at an annual rate of 3% (45).

<table>
<thead>
<tr>
<th>Table 1. Costs Based on Medicare Payments in 2000*</th>
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<tbody>
<tr>
<td>CPT Code (DRG Code)</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td>82270</td>
</tr>
<tr>
<td>45330</td>
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</table>

† Sum of all included costs.
‡ Costs include professional fees and facility costs.
§ Facility costs among inpatients are covered by payment for the corresponding DRG code; all other costs arise from professional fees.

Role of the Funding Sources

Dr. Delco’s salary was supported by a grant from the Swiss Foundation for Grants in Medicine and Biology. Drs. Inadomi and Sonnenberg were full-time employees of the Department of Veterans Affairs. The funding sources had no role in the collection, analysis, or interpretation of the data or in the decision to submit the paper for publication.

RESULTS

Baseline Assumptions

Table 2 shows the outcomes of modeling four programs to prevent colorectal cancer. Future life-years saved and the costs associated with various items reflect the effect of an annual discount rate of 3%. Without screening, the cohort of 50-year-old persons will experience 5904 cases of colorectal cancer and a loss of 10,602 cancer-related life-years. Screening with fecal occult blood testing prevents 16% of all colorectal cancers compared with prevention rates of 34% or 75% with flexible sigmoidoscopy or
colonoscopy, respectively. Screening with colonoscopy results in more life-years saved; that is, it offers a greater reduction in mortality than the two other screening methods. In screening with fecal occult blood testing, the detection of cancer at earlier stages leads to a reduction in mortality beyond cancer prevention alone (18% vs. 16%). Because flexible sigmoidoscopy and colonoscopy are done less frequently, this added benefit of screening is far less pronounced in these two screening strategies.

Table 2. Outcome of Screening Programs To Prevent Colorectal Cancer*

<table>
<thead>
<tr>
<th>Variable</th>
<th>None</th>
<th>FOBT</th>
<th>Sigmoidoscopy</th>
<th>Colonoscopy</th>
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<td>Cases of CRC prevented, n</td>
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<td>926</td>
<td>2027</td>
<td>4428</td>
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<tr>
<td>Prevented cases of CRC/total cases of CRC, %</td>
<td>0</td>
<td>16</td>
<td>34</td>
<td>75</td>
</tr>
<tr>
<td>Life-years saved</td>
<td>0</td>
<td>1896</td>
<td>3636</td>
<td>7952</td>
</tr>
<tr>
<td>Reduction in mortality, %</td>
<td>0</td>
<td>18</td>
<td>34</td>
<td>75</td>
</tr>
<tr>
<td>Procedures, n</td>
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<td>2,464,606</td>
<td>0</td>
<td>0</td>
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<td>FOBT</td>
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<td>2,464,606</td>
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<tr>
<td>sigmoidoscopies</td>
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<td>69,794</td>
<td>27,319</td>
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</tr>
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<td>Colonoscopies</td>
<td>0</td>
<td>62,815</td>
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<td>Diagnostic (without polypectomy)</td>
<td>0</td>
<td>69,794</td>
<td>14,695</td>
<td>36,546</td>
</tr>
<tr>
<td>Therapeutic (with polypectomy)</td>
<td>0</td>
<td>234</td>
<td>313</td>
<td>1224</td>
</tr>
<tr>
<td>Complications, n</td>
<td>0</td>
<td>234</td>
<td>313</td>
<td>1224</td>
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<tr>
<td>Bleeding events</td>
<td>0</td>
<td>152</td>
<td>81</td>
<td>797</td>
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<tr>
<td>Screening-related perforations</td>
<td>0</td>
<td>7</td>
<td>3</td>
<td>37</td>
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<td>Costs, $</td>
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<td>0</td>
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<td>0</td>
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<tr>
<td>sigmoidoscopy</td>
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<td>–</td>
<td>163,313,218</td>
<td>–</td>
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<td>Colonoscopy</td>
<td>0</td>
<td>33,640,016</td>
<td>16,281,508</td>
<td>189,667,598</td>
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<tr>
<td>Care for CRC</td>
<td>136,452,922</td>
<td>115,715,753</td>
<td>89,619,575</td>
<td>34,113,230</td>
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<tr>
<td>Total</td>
<td>136,452,922</td>
<td>154,853,577</td>
<td>269,214,301</td>
<td>223,780,829</td>
</tr>
<tr>
<td>Total costs per life-years saved†</td>
<td>∞</td>
<td>81,678</td>
<td>74,032</td>
<td>28,143</td>
</tr>
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</table>

* Values pertain to a cohort of 100,000 persons 50 years of age who were followed for an average of 28.5 years until death. Future life-years saved and future costs were discounted by using an annual rate of 3%. CRC = colorectal cancer; FOBT = fecal occult blood testing.
† Average cost-effectiveness ratio.

Table 2 also shows the number of tests done for prevention in each program. The investments in screening with fecal occult blood testing or flexible sigmoidoscopy lead to performance of many fewer colonoscopies in each of the two strategies. Fewer colonoscopies translate into fewer complications. On the basis of the rates shown in the Appendix Table and a mortality rate of 1 per 10,000 colonoscopies (7), one can estimate that in the colonoscopy screening program, an appreciably higher proportion of patients will experience procedure-related bleeding, perforation, or even death compared with those undergoing other screening strategies. Without screening or use of fecal occult blood testing, the largest proportion of costs stems from care of unprevented cancer. In the other two screening programs, endoscopic procedures account for most costs. Although 85% of the total costs in the colonoscopy program arise from the endoscopic procedure itself, colonoscopy contributes 22% and 6% to the total costs of the fecal occult blood testing and sigmoidoscopy screening programs, respectively.

The total costs of managing colorectal cancer increase going from no screening to fecal occult blood testing, colonoscopy, and flexible sigmoidoscopy. At the same time, the effectiveness of screening, as evidenced by the number of life-years saved, increases from no screening to fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy. Table 2 shows the average cost-effectiveness ratios of the screening strategies. Fecal occult blood testing and flexible sigmoidoscopy are relatively expensive strategies compared with colonoscopy. The strategy of no screening results in an infinitely large ratio of costs to life-years saved because costs are positive (from the care of colorectal cancer) but life-years are zero.

The incremental cost-effectiveness ratio shown in Table 3 is more informative than the average cost-effectiveness ratio. It compares each screening strategy with the preceding less effective option, including a strategy of no screening. The incremental cost-effectiveness ratio is calculated as the difference in costs divided by the corre-
Corresponding difference in effectiveness (46, 47). The results of baseline conditions suggest the following interpretation. Fecal occult blood testing represents a cost-effective option compared with no screening. Flexible sigmoidoscopy is an expensive alternative to fecal occult blood testing. Colonoscopy is associated with relatively modest incremental cost-effectiveness compared with fecal occult blood testing and no screening.

Sensitivity Analysis

The base-case analysis indicates that fecal occult blood testing is a cost-effective screening method to prevent colorectal cancer. At a higher total cost of screening, colonoscopy represents a cost-effective alternative because additional life-years are saved to justify additional costs. All measures that make colonoscopy particularly expensive increase its incremental cost-effectiveness ratio compared with fecal occult blood testing.

In the first set of sensitivity analyses, the frequency of colonoscopy is increased to once every 5 years, its efficacy is reduced to 50%, and compliance with repeated colonoscopy is reduced to 80%. Under these conditions, the incremental cost-effectiveness of colonoscopy compared with fecal occult blood testing increases from a baseline value of $11,382 to $27,529, $24,689, and $12,695, respectively. Assuming that all unfavorable conditions apply simultaneously, the incremental cost-effectiveness ratio increases to $54,561. These results suggest that even when some unfavorable assumptions about frequency and compliance are made, colonoscopy remains a relatively cost-effective screening option compared with other health care interventions that are currently standard practice (47).

Variations of Compliance Rates

Under base-case conditions, the incremental cost-effectiveness ratio of colonoscopy compared with no screening is only slightly greater than that of fecal occult blood testing compared with no screening ($10,983 vs. $9705). In subsequent one-way sensitivity analyses, the incremental cost-effectiveness ratios of fecal occult blood testing and colonoscopy (compared with no screening) were assessed by systematically varying all assumptions built into the model. Since flexible sigmoidoscopy is dominated by colonoscopy, only changes in test frequency are considered to reduce its incremental cost-effectiveness ratio.

Because initial compliance determines how many persons enter the screening program, it influences the overall number of cancers prevented and the total costs in a linear fashion. However, the initial compliance rate does not affect the cost-effectiveness of any individual program. A decrease in compliance rate associated with test repetition results in higher costs per life-year saved (Figure 1). Fecal occult blood testing is particularly sensitive to changes in the compliance rate of repeated testing because it is done more frequently than colonoscopy. For instance, a decrease of compliance with annual test repetition to 90% increases the incremental cost-effectiveness ratio of fecal occult blood testing to $14,788. In the case of colonoscopy screening, the same incremental cost-effectiveness ratio is achieved with a decrease in compliance with repeated 10-year colonoscopy to 66% (Figure 1). Similarly, a decrease in compliance with repeated fecal occult blood testing to 80% matches a decrease in compliance with repeated colonoscopy to 37%. Low compliance with colonoscopy after a positive result on fecal occult blood testing also renders the initial screening technique less efficacious and increases its associated costs per saved life-year. If only 75%

Table 3. Incremental Cost-Effectiveness Ratios*

<table>
<thead>
<tr>
<th></th>
<th>No Screening</th>
<th>Fecal Occult Blood Testing</th>
<th>Sigmoidoscopy</th>
<th>Colonoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No screening</td>
<td>0</td>
<td>9705</td>
<td>36,509</td>
<td>10,983</td>
</tr>
<tr>
<td>Fecal occult blood testing</td>
<td>–</td>
<td>0</td>
<td>65,704</td>
<td>11,382</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td>Dominates†</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0</td>
</tr>
</tbody>
</table>

* The difference between total costs of strategy 2 and strategy 1 was divided by the difference between life-years saved by strategy 2 and strategy 1.
† Strategy 2 is less costly and more effective than strategy 1.
of positive fecal occult blood tests were followed by colonoscopy, the incremental cost-effectiveness ratio of fecal occult blood testing would increase to $10,281.

Because it depends on several types of patient compliance, screening by fecal occult blood testing is generally more sensitive to changes in compliance rates. For instance, 93% compliance with repeated fecal occult blood testing has been reported (29). On the basis of compliance rates reported for repeated sigmoidoscopy and surveillance colonoscopy after polypectomy, an 80% compliance rate appears reasonable to expect for repeated colonoscopy (9, 33). We also estimated compliance rates of 75% for colonoscopy after a positive result on fecal occult blood testing or after sigmoidoscopy that is positive for polyps (34). Under these conditions, the incremental cost-effectiveness ratios of screening with fecal occult blood testing and colonoscopy (compared with no screening) change to $14,071 and $13,081, respectively.

Variation of Test Characteristics

Although the model considers the occurrence of adenomatous polyps and the influence of polypectomy on life-years saved, the sensitivity and specificity of the fecal occult blood test used in the current analysis pertain only to colorectal cancer as the disease of interest. The outcome of the analysis is affected more by assumptions underlying the sensitivity of the fecal occult blood test than by its specificity (Figure 2). Improvement of test sensitivity results in detection of cancers at an earlier stage and reduced mortality from colorectal cancer. The change in test specificity has a two-sided effect. On one hand, improved specificity results in fewer colonoscopies performed after false-positive results on fecal occult blood tests. This effect is responsible for the decrease in the incremental cost-effectiveness ratio as the specificity increases to 70% to 95%. On the other hand, the opportunity to prevent future colorectal cancers is partly forgone as the specificity improves, since fewer positive test results lead to fewer colonoscopies with polypectomies. This effect becomes especially dominant as the specificity increases above 98%. Within the ranges tested in the sensitivity analysis, the overall influence on the incremental cost-effectiveness ratio exerted by the sensitivity or specificity of fecal occult blood testing does not exceed $2000 (Figure 2).

Although screening by colonoscopy is slightly more sensitive than fecal occult blood testing to changes in the incidence of polyps, the increments of costs per life-year saved and the relationship between the two screening procedures remain largely unaffected. Changes in the efficacy of colonoscopy plus polypectomy in preventing colorectal
cancer and their influence on the incremental cost-effectiveness ratio are shown in Figure 3. An increase in preventive efficacy decreases the costs of all screening methods, again with relatively little influence on the relationship between the competing methods.

Variation of Screening Frequency and Costs

In the following analyses, changes in the screening frequency are assumed to occur without influencing the efficacy of colonoscopy plus polypectomy in preventing colorectal cancer. Under baseline conditions, screening by colonoscopy is done every 10 years. Shortening the interval of repeated colonoscopy affects all three screening methods because screening with any method is resumed earlier and all screening strategies become more expensive and less cost-effective. If colonoscopy is scheduled every 5 years, for instance, the incremental cost-effectiveness ratio of fecal occult blood test or colonoscopy compared with no screening increase to $20,746 and $26,385, respectively. Changes in the surveillance interval after polypectomy exert only small influences in all three programs without affecting their relative difference. Scheduling one flexible sigmoidoscopy every 10 years reduces its associated costs per life-year saved but fails to abolish the dominance of colonoscopy over flexible sigmoidoscopy. Finally, reducing the frequency of screening with fecal occult blood testing from once annually to once every 3 years increases its incremental costs per life-year saved from a baseline value of $9705 to $9843, as costs savings become partly negated by fewer life-years saved through early cancer detection.

DISCUSSION

The screening model in our study suggests that colonoscopy once every 10 years is a cost-effective method of screening for colorectal cancer compared with the next best alternative, fecal occult blood testing. Compared with colonoscopy, screening with annual fecal occult blood testing costs less but saves fewer life-years. Annual fecal occult blood testing may be a cost-effective screening method if high patient compliance is maintained over prolonged time periods and if tests can be applied at low costs. A screening strategy based on flexible sigmoidoscopy every 5 or 10 years is less cost-effective than the other two screening methods. Although both fecal occult blood testing and flexible sigmoidoscopy represent less expensive screening programs than does colonoscopy, this seeming cost advantage is offset in part by the subsequent costs of medical care for cancers missed by these two screening methods. The latter two programs also incur additional costs of workup of all positive findings on colonoscopy.

What would it cost to implement a uniform colorectal...
cancer screening program in the United States? As suggested by the estimates in Table 3, for each 100,000 persons turning 50 years of age, it would cost (in current discounted dollars) $39 million for fecal occult blood testing, $180 million for flexible sigmoidoscopy, and $190 million for colonoscopy until that cohort dies out. About 4 million persons annually turn 50 years of age. If everyone were screened with fecal occult blood testing, the expected annual screening cost would amount to $1.6 billion ($39 million \times 40). Using colonoscopy, the annual screening costs would be $7.6 billion. Our calculation suggests a substantial increase in the cost investment for colorectal cancer screening. Some of the investment would be saved by spending less money on medical care for cancer (Table 3). These crude estimates do not consider the fact that many persons already undergo some type of screening. Moreover, only a fraction of the population may actually want to participate in a screening program for colorectal cancer.

Figure 3. Efficacy of colonoscopy in preventing colorectal cancer and its influence on the incremental cost-effectiveness ratio of fecal occult blood testing (dotted line) and colonoscopy (solid line) compared with no screening.

Screening for colorectal cancer with fecal occult blood testing, sigmoidoscopy, or colonoscopy have all been documented to be efficacious in preventing the occurrence of colorectal cancer and reducing its associated mortality (8–11, 24, 29, 49–51). Colonoscopy was shown to be the most efficacious method, and sigmoidoscopy was shown to be more efficacious than fecal occult blood testing. The majority of recommendations for colorectal cancer screening rely on combined use of all three methods. For instance, the recent guidelines of the Health Care Finance Administration allow for reimbursement of annual fecal occult blood testing, flexible sigmoidoscopy, or contrast barium enema once every 4 years and colonoscopy once every 2 years only in high-risk persons (52). The American Cancer Society recommends annual fecal occult blood testing combined with flexible sigmoidoscopy every 5 years, double-contrast barium enema every 5 to 10 years, or colonoscopy every 10 years (1). A position paper by the American Gastroenterological Association includes a screening program comprising annual fecal occult blood testing, flexible sigmoidoscopy every 5 years, and colonoscopy once every 10 years (7).

Three published studies have compared fecal occult blood testing and colonoscopy (2–4). In a cost-effectiveness study by Lieberman (4), colonoscopy was applied only once per lifetime and no repeated colonoscopies were considered in persons without polyps. The outcome, measured as undiscounted costs per prevented deaths from colorectal cancer, showed a moderate advantage of screening with fecal occult blood testing over screening with colonoscopy. By varying the efficacy and cost assumptions in the sensitivity analyses, the difference between the two screening strategies was easily reversed. In a comprehensive analysis of multiple screening strategies, Eddy (2) compared fecal occult blood testing alone with fecal occult blood testing in combination with sigmoidoscopy or colonoscopy every 3 to 5 years. The average cost-effectiveness ratios of the three strategies were $8400, $19,200, and $24,400, respectively. Wagner and coworkers (3, 6, 7), from the Office of Technology Assessment of the U.S. Congress, compared the cost-effectiveness of various screening strategies. Fecal occult blood testing, flexible sigmoidoscopy, and colonoscopy were found to cost on average less than $20,000 per life-year saved, and no screening strategy dominated (in economic terms) the other alternatives. The higher costs per life-year saved compared with those in our analysis stemmed primarily from more frequent screening colonoscopies performed at 5-year intervals. In addition, flexible sigmoidoscopy cost only $80 compared with $382 used in the present analysis.

In our study, screening with fecal occult blood testing, flexible sigmoidoscopy, or colonoscopy was modeled by using a Markov process. Besides preventing colorectal can-
screening procedures were also assumed to detect already existent colorectal cancers at an earlier stage. In designing the model, we tried to reduce the complex natural history of colorectal cancer to few essential states and avoid transition assumptions for which little or no published data existed. For instance, we did not consider potential changes of the sensitivity and specificity in a long series of consecutive fecal occult blood tests. Compliance rates were not modeled as time-dependent variables, and patients who stopped complying with the screening program were assumed to remain noncompliant for the rest of their life. Finally, we omitted the impact of colorectal cancer and screening on indirect costs.

Modeling of colorectal cancer screening is insightful because it helps to quantify the complex interactions among the many variables that affect the model and because it reveals some unexpected and nonlinear behavior of various influences. For instance, the incidence of adenomatous polyps and the efficacy of colonoscopy in cancer prevention affect not only the screening program based on colonoscopy alone but also those based on flexible sigmoidoscopy and fecal occult blood testing. Although a low specificity of fecal occult blood test increases the test’s incremental cost-effectiveness ratio, it also increases the benefit of the test with respect to the number of cancers prevented by leading to more colonoscopies and excisions of adenomatous polyps that would have otherwise progressed to cancer. Rehydration of test slides improves the test characteristics primarily by decreasing the specificity and increasing the rate of positive test results. Compliance rates exert strong nonlinear influences that can markedly alter cost-effectiveness, especially of fecal occult blood testing. A decrease in the compliance rate associated with test repetition results in loss of many patients during the initial years of the program. This exponential decline reduces the overall effectiveness of the program because the incidence of cancer increases with age and the preventive yield of all programs is higher in older age groups.

In conclusion, our findings reveal a potential advantage of one colonoscopy every 10 years as a screening strategy for colorectal cancer. Screening with colonoscopy represents a cost-effective method in addition to initial screening by fecal occult blood testing because it reduces mortality from colorectal cancer at relatively low incremental costs. Our analysis also suggests that low compliance rates are more likely to influence screening with fecal occult blood testing and that under such circumstances, colonoscopy every 10 years may be the most cost-effective primary screening strategy for colorectal cancer.

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Appendix Table. Baseline Assumptions and Ranges Tested in the Sensitivity Analysis*

<table>
<thead>
<tr>
<th>Rate</th>
<th>Baseline Model</th>
<th>Sensitivity Analysis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity of FOBT in detecting colorectal cancer, %</td>
<td>40</td>
<td>20–60</td>
<td>14</td>
</tr>
<tr>
<td>Specificity of FOBT in detecting colorectal cancer, %</td>
<td>97.50</td>
<td>70–99</td>
<td>14</td>
</tr>
<tr>
<td>Screening interval for FOBT, y</td>
<td>1</td>
<td>1–3</td>
<td>15</td>
</tr>
<tr>
<td>Adenomas found by sigmoidoscopy, %</td>
<td>45</td>
<td>–</td>
<td>16–18</td>
</tr>
<tr>
<td>Screening interval for sigmoidoscopy, y</td>
<td>5</td>
<td>3–10</td>
<td>15</td>
</tr>
<tr>
<td>Annual incidence of adenomas, %</td>
<td>1</td>
<td>0–6</td>
<td>25, 26</td>
</tr>
<tr>
<td>Screening interval for colonoscopy, y</td>
<td>10</td>
<td>3–10</td>
<td>15</td>
</tr>
<tr>
<td>Surveillance interval after polypectomy, y</td>
<td>3</td>
<td>1–5</td>
<td>15</td>
</tr>
<tr>
<td>Efficacy of colonoscopy in preventing colorectal cancer, %</td>
<td>75</td>
<td>50–100</td>
<td>6</td>
</tr>
<tr>
<td>Bleeding rate with colonoscopy, %</td>
<td>0.15</td>
<td>–</td>
<td>19</td>
</tr>
<tr>
<td>Bleeding rate with polypectomy, %</td>
<td>2.00</td>
<td>–</td>
<td>20</td>
</tr>
<tr>
<td>Perforation rate with colonoctoscopy, %</td>
<td>0.20</td>
<td>–</td>
<td>19</td>
</tr>
<tr>
<td>Perforation rate with polypectomy, %</td>
<td>0.38</td>
<td>–</td>
<td>20</td>
</tr>
<tr>
<td>Perforation rate with sigmoidoscopy, %</td>
<td>0.011</td>
<td>–</td>
<td>21</td>
</tr>
<tr>
<td>Mortality rate from colorectal cancer, %</td>
<td>40</td>
<td>–</td>
<td>22</td>
</tr>
<tr>
<td>Annual discount rate, %</td>
<td>3</td>
<td>–</td>
<td>23</td>
</tr>
</tbody>
</table>

* FOBT = fecal occult blood test.
Appendix Figure. Markov states in screening for colorectal cancer (CRC) by fecal occult blood test (FOBT) (top), flexible sigmoidoscopy (middle), and colonoscopy (bottom).

The black and gray ovals represent Markov states in which patients remain for at least a full 1-year cycle. The white ovals represent intermediate states of screening procedures, which patients may enter and leave during one cycle. The arrows represent transitions between various states.
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References
can Cancer Society; 1998.
2. Eddy DM. Screening for colorectal cancer. Ann Intern Med. 1990;113:373-
84.
4. Lieberman DA. Cost-effectiveness model for colon cancer screening. Gastro-
Screening for colorectal cancer in a high-risk population. Results of a mathemat-
1996;321-56.
Colonoscopy screening: clinical guidelines and rationale. Gastroenterology.
1997;112:594-642.
8. Selby JV, Friedman GD, Quesenberry CP Jr, Weiss NS. A case-control study of
et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National
10. Miller AD, Sonnenberg A. Protection by endoscopy against death from
11. Miller AD, Sonnenberg A. Prevention of colorectal cancer by flexible endo-
904-10.
12. Sonnenberg FA, Beck JR. Markov models in medical decision making: a
Department of Health and Human Services, Centers for Disease Control and
Prevention, National Center for Health Statistics; 1997. DHHS Publication No.
PHS-98-1150-1.
15. Allison JE, Tekawa IS, Ransom L, Adrain AL. A comparison of fecal
155-9.
16. Williams AR, Balasooriya BA, Day DW. Polyps and cancer of the large
17. Vatn MH, Stalsberg H. The prevalence of polyps of the large intestine in
18. Shinya Y, Wolf WI. Morphology, anatomic distribution and cancer poten-
1999.
Lake City: Medicode; 1997.
22. Vukasin AP, Ballantyne GH, Flannery JT, Lerner E, Modlin IM. Increasing
incidence of rectal and sigmoid carcinoma. Data from the Connecticut Tumor
23. Provenzale D, Wong JB, Onken JE, Lipscomb J. Performing a cost-effect-
tiveness analysis: surveillance of patients with ulcerative colitis. Am J Gastro-
24. Hardcastle JD, Chamberlain JO, Robinson MH, Moss SM, Amar SS,
Balfour TW, et al. Randomised controlled trial of faecal-occult-blood screening
25. Ahlquist DA, Wiecek HS, Moertel CG, McGill DB, Loprini CL, O’Connell MJ,
et al. Accuracy of fecal occult blood screening for colorectal neoplasia. A pro-
26. Allison JE, Feldman R, Tekawa IS. Hemoccult screening in detecting colo-
rectal neoplasms: sensitivity, specificity, and predictive value. Long-term follow-up
and rescreening for colorectal cancer. A controlled trial of fecal occult blood
28. Ransohoff DF, Lang CA. Screening for colorectal cancer with the fecal occult
ing for colorectal cancer with fecal occult blood test. A prospective randomized
program of colorectal screening in an asymptomatic population: evaluation of
32. Brevinge H, Lindholm E, Bunten S, Kewenter J. Screening for colorectal
neoplasia with faecal occult blood testing compared with flexible sigmoidoscopy
33. Riff ER, Dehaan K, Garewal GS. The role of sigmoidoscopy for asymptom-
atic patients. Results of three annual screening sigmoidoscopies, polypectomy,
and subsequent surveillance colorectaloscopy in a primary-care setting. Cleve Clin
34. Wallace MB, Kemp JA, Trimble Y, Donovan JM, Farraye FA. Is colonos-
copy indicated for small adenomas found by screening flexible sigmoidoscopy?
He was pacing up and down the room as he was talking. Now he walked up to Anna Ivanovna’s bed and putting his hand on her forehead said, “Go to sleep.” After a few moments she began to fall asleep.

Yura quietly left the room and told Egorovna to send in the nurse. “What’s come over me?” he thought. “I’m becoming a regular quack—muttering incantations, laying on the hands. . . .” Next day Anna Ivanovna was better.

Boris Pasternak

Doctor Zhivago

New York: Pantheon Books; 1997:68-79

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