COST-EFFECTIVENESS OF SCREENING THE AVERAGE-RISK POPULATION FOR COLORECTAL CANCER

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This article examines the cost-effectiveness of screening the average-risk population for colorectal cancer. Before discussing the economics of alternative screening practices, a few definitions are noteworthy. The most formally correct definition of cost-effective is "producing additional benefits that are worth the additional costs." By definition, the practice or program under evaluation must be compared with a relevant alternative. A cost-effective practice produces additional benefits that are worth the additional cost, compared with an alternative practice (e.g., colorectal cancer screening with annual fecal occult blood test [FOBT] is cost-effective compared with no screening if the additional benefit obtained from screening in terms of cancers and cancer deaths avoided is worth the additional cost of screening). This definition evaluates the relative worth of one strategy compared with another. It is possible that the more cost-effective strategy is also more expensive. A cost-effective practice does not necessarily save money. Judgments about the cost-effectiveness of alternative strategies are frequently based on a cost-effectiveness ratio or an incremental cost-effectiveness ratio, which is the criterion or unit of measure for cost-effectiveness analyses. This ratio is calculated as the change in cost divided by the change in life expectancy for one strategy

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compared with another. For example, the incremental cost-effectiveness ratio for screening for colorectal cancer with annual FOBT is:

(the cost of a screening program with annual FOBT − the cost of no screening) ÷ (the life expectancy of screened patients − the life expectancy of unscreened patients).

The results produce a ratio of dollars per life-year (LY) gained. These cost-effectiveness ratios alone, however, cannot identify cost-effective practices. They must be placed in a decision context that is expressed in one of two forms. In the first form, an explicit threshold or maximum amount that a policy maker is willing to spend is stated (e.g., $50,000 per LY gained). In the second form of decision context, a list of medical practices and their associated cost-effectiveness ratios, also known as a *league table*, is used as a basis for comparison with the practice under evaluation (e.g., colorectal cancer screening). Practices with lower cost-effectiveness ratios are considered cost-effective compared with those with higher ratios. The practice with the lowest cost-effectiveness ratio is the most cost-effective practice on the list. The policy maker can use these ratios to set priorities for funding.

A few other definitions are important for the discussion of the cost-effectiveness of colorectal cancer screening. Screening, in which the general public is invited to undergo a variety of tests, may be used to stratify those with higher and lower probabilities of disease. Screening for colorectal cancer is offered to the general public who are without symptoms relative to colorectal cancer; are without a family history of colorectal cancer; and who have no predisposing conditions for colorectal cancer, such as inflammatory bowel disease. Surveillance refers to the ongoing follow-up of those in whom a neoplastic lesion has been identified and removed (e.g., a colonic polyp) or those who are at increased risk for malignancy,[11] such as those with ulcerative colitis.

Finally, before discussing the economic analyses of colorectal cancer screening for average-risk individuals it is worthwhile to provide a framework for interpretation and application. Drummond et al[1] provides a criteria for the critical appraisal of an economic analysis, which can be used as a guide for reading and interpreting the literature on the cost-effectiveness of colorectal cancer screening in the average-risk individual. These criteria are*:

1. Was a well-defined question posed in answerable form?
2. Was a comprehensive description of the competing alternatives given?
3. Was there evidence that the program's effectiveness had been established?
4. Were all the important and relevant costs and consequences for each alternative identified?
5. Were costs and consequences measured accurately in appropriate physical units?
6. Were costs and consequences valued credibly?

From Drummond MF, Stoddart GL, Torrance GW (eds): Critical assessment of economic evaluation. *In* Methods for the Economic Evaluation of Health Care Programs. New York, Oxford University Press, 1987, pp 18–38; with permission.

7. Were costs and consequences adjusted for differential timing?
8. Was an incremental analysis of costs and consequences of alternatives performed?
9. Was a sensitivity analysis performed?
10. Did the presentation and discussion of study results include all issues of concern to users?

The clinician reading the literature on the cost-effectiveness of colorectal cancer screening is interested in knowing if the results of the economic analysis apply to their patients. Several factors are involved in this determination. First, there should be a clear statement of the objective of the analysis, such as a statement of the hypothesis for the analysis or the question that the analyst is asking. A statement of the perspective of the analysis is also necessary (e.g., HMO, third-party payer, or society). Second, the screening strategies that are included in the analysis must be defined, and the evidence that these strategies are effective in reducing colorectal cancer and cancer mortality should be provided. Other important components include information about the relevant costs and outcomes related to screening. These typically include the direct medical costs of the alternative screening practices (e.g., the cost of FOBT, flexible sigmoidoscopy, colonoscopy, and so forth) and any induced costs, such as costs for the evaluation of a positive FOBT, costs for colonoscopy and polypectomy in individuals found to have polyps on barium enema, and costs of surgery, chemotherapy, and radiation in those diagnosed with cancer. A distinction should be made between costs and charges. Costs reflect the resources consumed to provide a medical service, whereas charges may reflect profit or loss to an institution and may be falsely inflated or deflated. Current recommendations suggest that costs be included in economic analyses,[5] although many analyses continue to incorporate charges.

The outcomes of screening in terms of improved survival caused by cancer prevention, and the consequences of screening (e.g., perforation, surgery, and surgical complications) should also be included. The other critical components of any economic analysis of colorectal cancer screening include aspects of the methodology, such as adjustment for differential timing, performing an incremental analysis, and performing sensitivity analyses. In any screening, program costs and risks of screening procedures occur early on (at the inception of the program and in the ensuing years). The benefits of the program, however, in terms of cancer prevention and prevention of deaths caused by colorectal cancer occur much later (up to 20 years or more). This differential timing of costs and benefits should be considered in any economic analysis of screening whose time frame exceeds 1 year and is achieved through discounting. Discounting considers that a dollar today is worth more than a dollar in the future, and because years of life gained through screening are valued relative to dollars, they must also be discounted. There are standard formulas for discounting that should be applied.[5] Recommended annual discount rates range from 3% to 6% annually with 3% perferred.[5]

An incremental analysis should be performed and the results presented as incremental cost-effectiveness ratios. An incremental analysis considers the additional costs for the additional benefits of performing one screening strategy compared with another. From a clinical perspective, we are interested in knowing what is the additional cost for a more effective, more expensive strategy compared with a less effective, less expensive one (e.g., for adding flexible sigmoidoscopy to annual FOBT) and what is the additional benefit in terms of gains in life expectancy for the combination of annual FOBT and flexible sigmoidoscopy every 5 years compared with only annual FOBT. The incremental cost-effectiveness for the combined strategy compared with FOBT alone provides this information and is calculated as the change in costs divided by the change in life expectancy to perform annual FOBT and flexible sigmoidoscopy every 5 years compared with performing annual FOBT alone:

(cost of annual FOBT and flexible sigmoidoscopy every 5 years − cost of annual FOBT)	÷	(gain in life expectancy of those who undergo annual FOBT and flexible sigmoidoscopy − gain in life expectancy of those who undergo annual FOBT only).

The results are reported as a ratio of dollars to LY gained or saved. The incremental cost-effectiveness ratio provides those who make health policy with information about how to maximize health benefits with a limited budget. Using incremental cost-effectiveness ratios, the policy maker can compare the cost-effectiveness of colorectal cancer screening using annual FOBT and flexible sigmoidoscopy with the cost-effectiveness of other screening modalities, such as screening for hemochromatosis and breast cancer screening.

The final component of an economic analysis that is critical to the generalizability of the analysis is sensitivity analysis. In sensitivity analysis, each parameter is varied over a broad range to determine if the preferred strategy is altered. In the case of colorectal cancer screening, a critical parameter about which there is some uncertainty in the literature is the rate at which adenomatous polyps develop and become cancer. In sensitivity analysis this parameter is varied over a broad range of plausible values to determine the impact on the preferred strategy. Sensitivity analysis provides the opportunity to consider any variation in the literature surrounding the estimates included in the model and the effect of this variation on the results of the analysis. Sensitivity analyses also provide the reader with a method to determine if the results are generalizable to their patients. For example, the test characteristics of certain modalities (e.g., barium enema) may vary based on the setting. If individuals are aware of the accuracy of barium enema in their setting, they can determine if the model considers that level of accuracy and whether or not the results for the barium enema strategy are generalizable to their practice setting. The final step for the reader is to determine if the presentation and discussion of study results have included all of the issues and concerns that are important to them.

ECONOMIC ANALYSES OF COLORECTAL CANCER SCREENING

With these criteria as a reference, selected economic analyses of colorectal cancer screening in the average-risk individual are examined. It should be noted that most of these analyses examine combinations of strategies that were recommended by the Agency for Health Care Policy and Research ([AHCPR] now the Agency for Healthcare Research and Quality) after an extensive systematic literature review.[17] The strategies that were recommended for screening in the average-risk individual include: (1) annual FOBT, (2) flexible sigmoidoscopy every 5 years, (3) annual FOBT and flexible sigmoidoscopy every 5 years, (4) double-contrast barium enema (DCBE) every 5 to 10 years, and (5) screening colonoscopy every 10 years.

One of the first economic models that considered these strategies was developed by Lieberman.[7] The model examines a 10-year time frame and calculates charges and number of cancer cases for 1000 screenees. The outcome measure is cost for preventing one death from colorectal cancer for each strategy, and although the perspective of the analysis is not stated, the institution or payor is implied. The model uses published literature of the efficacy of screening tests and considers the induced costs and consequences of screening including the cost of follow-up for a positive test (e.g., colonoscopy for a positive FOBT); the cost of surveillance colonoscopy in those found to have adenoma; and the cost of treating cancer in those who are diagnosed through screening. The cost and consequences of complications of screening, such as perforation, were also considered. Sensitivity analyses were performed on the cost of colonoscopy, the frequency of surveillance, and the impact of compliance on costs and outcomes. The model calculates cost of colorectal cancer death prevented (undiscounted). Based on these results, the cost per death prevented ranged from $225,000 (for a 10-year period, not discounted) for annual FOBT to $280,000 for barium enema, the most expensive strategy. In sensitivity analysis, the cost of colonoscopy was varied over a broad range. The results suggest that if the cost of colonoscopy falls to $750 or less, then one-time colonoscopy in the 10-year period is less expensive than FOBT alone at equal levels of compliance. The model also suggests that when compliance falls to 50%, the cost per death prevented is similar for FOBT, FOBT and flexible sigmoidoscopy, and colonoscopy and ranges from $331,000 to $337,000. The increased cost at the reduced compliance level is related to the increased cost of cancer treatment, because fewer cancers are prevented by screening.

This model provided preliminary estimates of the cost for colorectal cancer screening practices and underscored the importance of compliance on the cost. In addition, an important insight was gained into the cost-effectiveness of these alternative practices. The results suggest that if the cost of colonoscopy is reduced to $750 or less, which may be the case in certain managed care situations, then screening colonoscopy becomes less expensive than the less-effective FOBT.[7]

Subsequently, a model by Wagner et al[16] examined the cost-effectiveness of screening with 17 strategies. The model examined annual FOBT. Flexible sigmoidoscopy, DCBE, and colonoscopy every 3, 5, and 10 years were considered as were the combinations of annual FOBT and flexible sigmoidoscopy every 3, 5, or 10 years and annual FOBT and DCBE every 3, 5, and 10 years. In this model, costs for the initial screening tests and induced costs, such as those for the evaluation of positive test, for surveillance colonoscopy in those found to have adenomas, and for complications of procedures, were included. Screening was assumed to cease at age 85. Costs and outcomes were discounted at the 5% rate annually. The model calculates the incremental cost-effectiveness ratio of each strategy compared with no screening. Estimates for the sensitivity and specificity of the screening tests were extrapolated from published literature as were estimates for the polyp prevalence and incidence and the proportion of cancers originating as adenomas. An area of uncertainty related to colorectal cancer screening is the dwelling time for an adenoma (e.g., the time required for an adenoma to become carcinoma). The model by Wagner et al[16] assumed a fixed dwelling time and examined two intervals (5 and 10 years). The model took the perspective of the HMO and used Medicare fees schedules and HMO costs for procedures, and obtained costs for treating colorectal cancer from the Kaiser Foundation Health Plan.[16] Each of the strategies was compared with no screening to calculate an incremental cost-effectiveness ratio. Based on their results, colorectal cancer screening had incremental cost-effectiveness ratios ranging from $9906 per LY gained for annual FOBT (rehydrated) to $14,996 per LY gained for annual FOBT and DCBE every 3 years. Wagner et al[16] provide a context for their results, stating that a benchmark value for preventive technologies is approximately $40,000 per LY gained. Compared with this benchmark, all of the colorectal cancer screening strategies they considered were cost-effective. In sensitivity analysis, they varied the test characteristics (sensitivity and specificity) of flexible sigmoidoscopy and DCBE and found that even at reduced sensitivity, the incremental cost-effectiveness ratios for each of these strategies remained less than $30,000 per LY gained. Changing other assumptions (e.g., using nonrehydrated FOBT) and doubling the costs of procedures and cancer care did not substantially alter the results. The incremental cost-effectiveness ratios for all strategies remained below the benchmark of $40,000 per LY gained. In their explicit statement of the risks and benefits of colorectal cancer screening, the authors affirm the cost-effectiveness of this practice.

The next model for consideration is the MISCAN-COLON Simulation.[8] The MISCAN model was developed as an adaptation of a microsimulation model that was used for the evaluation of breast and cervical cancer screening. The model was constructed based on published literature related to the natural history of colorectal adenomas and cancer and the test characteristics of flexible sigmoidoscopy and colonoscopy. An expert panel was convened to provide estimates when published data were not available. The model considers screening with flexible sigmoidoscopy every 5 years from ages 50 to 75, compared with no screening. Included are the cost for screening, treatment of screen-detected cancers, and of those detected because of symptoms in unscreened patients. Costs of surveillance (for those with adenomas >6 mm) are included (with surveillance colonoscopy performed every 5 years until no adenomas are detected and then the patient reverts back to flexible sigmoidoscopy every 5 years). The screening program is assumed to operate between 1993 and 2023. A broad range of costs and charges are used for procedures and cost of cancer care. Costs and outcomes are discounted at the recommended

3% rate annually.[9] The model calculates costs and savings per person. The results suggest that for this 30-year screening program, approximately $5 per person is saved and life expectancy is increased by approximately 28 years per 1000 screenees (assuming a 20-year dwell time for adenomas). Although there are costs associated with screening sigmoidoscopy, colonoscopy in those found to have a polyp, and subsequent surveillance colonoscopy, costs are actually saved in this program by the removal of adenomas destined to become cancer and the prevention of subsequent cancer (the treatment of which is expensive). The model shows that when the screening program ends in year 30, the breakeven point occurs in year 35 (cumulative undiscounted costs are balanced by savings). The model considers a variety of alternative assumptions about the natural history of polyps including differences in the rate at which polyps become cancer (e.g., a constant versus an exponential progression). In addition, the cost assumptions are varied to consider actual resource costs (e.g., costs in a managed care setting) and charges, which typically are substantially higher. With these various assumptions costs range from a savings of up to $236 per person to an expenditure of $138 per person for this 30-year screening program. This model is unique in that it is one of the few models to consider only flexible sigmoidoscopy every 5 years as a screening strategy and it is one of the very few models to demonstrate a cost savings with screening. The authors provide critical information about the investment required for a colorectal cancer screening program and the potential benefits in terms of cost and lives saved. The breakeven point provides a unique perspective on the value for health care dollars and provides essential information for policy formation.[9]

Another recently published article[6] examines the cost-effectiveness of colorectal cancer screening based on the guidelines published by the AHCPR with some additional strategies that increase the frequency of flexible sigmoidoscopy and colonoscopy.[17] The strategies evaluated in this model include (1) annual FOBT, (2) flexible sigmoidoscopy every 3 years, (3) flexible sigmoidoscopy every 5 years, (4) annual FOBT and flexible sigmoidoscopy every 3 years, (5) annual FOBT and flexible sigmoidoscopy every 5 years, (6) DCBE every 5 years, (7) colonoscopy every 5 years, and (8) colonoscopy every 10 years. Screening begins at age 50 in average-risk individuals and ends at age 85. Rather than assuming that polyps become cancer after a fixed interval or fixed dwell time as in other previously described models,[7, 16] polyps were assumed to become cancer exponentially based on the age of the polyp. The model included the costs and risks of screening procedures and the induced costs, risks, and benefits of follow-up for positive screening tests, and surveillance of those found to have polyps. Costs were obtained from insurance claims data for patients under the age of 65 and from Medicare reimbursement rates for those 65 and older. Costs and outcomes (additional years of life gained) were discounted at the 3% rate. The perspective of the analysis is not stated. Incremental cost-effectiveness ratios were calculated comparing each strategy with no screening. Among the eight strategies, flexible sigmoidoscopy every 5 years had the lowest incremental cost-effectiveness ratio ($12,636 per LY gained); annual FOBT had an incremental cost-effectiveness ratio of $14,394 per LY gained; and colonoscopy every 5 years, the most expensive strategy, had an incremental cost-effectiveness ratio of $28,724 per LY gained. Sensitivity analyses were performed on several parameters in the model including the probability of a polyp becoming cancer after it has been present for 10 years. When likelihood of a polyp becoming cancer after 10 years was 100%, the incremental cost-effectiveness ratios were low and ranged from $3504 per LY gained for flexible sigmoidoscopy every 5 years to $7048 per LY gained for colonoscopy every 5 years. When the likelihood of a polyp becoming cancer after 10 years was only 25%, the incremental cost-effectiveness ratios ranged from $18,848 per LY gained for flexible sigmoidoscopy every 5 years to $38,536 per LY gained for colonoscopy every 5 years. This group also examined compliance with recommended screening. When compliance was reduced from 100% to 23%, flexible sigmoidoscopy every 3 and 5 years was the most cost-effective strategy. With reduced compliance, less frequently performed strategies, such as colonoscopy, became more cost-effective, whereas the less effective strategies, such as annual FOBT, became less cost-effective as the advantage conferred by repeated tests disappeared. Other assumptions regarding the costs and effectiveness were also tested. In general, flexible sigmoidoscopy every 5 years and annual FOBT remained the most cost-effective strategies. When the cost of colonoscopy was low (cost not provided), however, screening colonoscopy every 10 years was a more cost-effective strategy.

To summarize, the analysis suggests that compared with no screening, screening with any of the strategies recommended by the AHCPR[17] is effective and has incremental cost-effectiveness ratios that range from $12,636 to $28,724 per LY gained, well below the previously cited benchmark of $40,000 per LY gained[16] for prevention programs. This model, like the MISCAN model,[9] is unique in that it uses an exponential probability distribution for the likelihood that a polyp becomes cancer, one that increases with the length of time that the polyp has been present.[6]

Another economic model, also based on the AHCPR guidelines,[17] compares 22 strategies for colorectal cancer screening, with no screening.[4] The model considers the strategies endorsed by the AHCPR panel[17]: (1) annual FOBT, (2) flexible sigmoidoscopy every 5 years, (3) annual FOBT and flexible sigmoidoscopy every 5 years, (4) DCBE every 10 years, and (5) colonoscopy every 10 years. Also considered were a variety of other strategies, such as one-time screening with flexible sigmoidoscopy at age 55; flexible sigmoidoscopy every 10 years; rehydrated FOBT; flexible sigmoidoscopy with colonoscopy reserved only for those with high-risk adenomas, such as those that are greater than or equal to 1 cm or contain villous histology; or flexible sigmoidoscopy with colonoscopy follow-up for those with any adenoma. Surveillance colonoscopy every 3 years was included for those found to have a high-risk polyp on flexible sigmoidoscopy. Complications of procedures were included as were the induced costs of cancer diagnosis and treatment. The likelihood that a low-risk polyp would progress to high-risk and a high-risk polyp would become cancer was modeled as a constant annual rate, which was obtained from published literature. Costs were obtained from an HMO.

This model is distinct from previously discussed models in that it addresses the ongoing controversy about rehydration of FOBT samples and examines the impact of performing colonoscopy for both low-risk and high-risk polyps independently. The model takes a societal perspective and examines screening with these alternative strategies for average-risk, white men age 50 and older, assuming 60% compliance with recommended screening and 80% compliance with follow-up tests. The authors calculate incremental cost-effectiveness ratios for these strategies by comparing each strategy with the next most effective and expensive one. For example, no screening is the least expensive and least effective strategy, costing $1052 per person screened (lifetime cost) and is associated with an additional 17.3481 years of life for a 50-year-old man. One-time flexible sigmoidoscopy at age 55, followed by colonoscopy only if a high-risk polyp is detected costs $1070 and provides an additional 1.3632 years. The incremental cost-effectiveness ratio for flexible sigmoidoscopy, the change in cost divided by the change in life expectancy to go from no screening to flexible sigmoidoscopy, is $1200 per LY gained. The incremental cost-effectiveness ratio for flexible sigmoidoscopy with colonoscopy for any polyp detected is calculated similarly, comparing flexible sigmoidoscopy with colonoscopy found for any polyp to flexible sigmoidoscopy with colonoscopy for only high-risk polyps.

The results suggested that all strategies increased life expectancy. Seven strategies, however, were more effective and had a lower cost per LY saved than the alternatives. These included flexible sigmoidoscopy once at age 55 or flexible sigmoidoscopy every 10 years beginning at age 55. For each of these two strategies, both alternative follow-up strategies were considered (e.g., for high- or low-risk polyps). All of these strategies had incremental cost-effectiveness ratios that were less than $17,000 per LY saved. Unrehydrated FOBT plus flexible sigmoidoscopy (with colonoscopy performed for any polyp found) had an incremental cost-effectiveness ratio of $21,200 per LY saved compared with flexible sigmoidoscopy alone every 10 years (with colonoscopy performed for any polyp found). Unrehydrated FOBT plus flexible sigmoidoscopy every 5 years (with colonoscopy performed for any polyp found) had an incremental cost-effectiveness ratio of $51,200 per LY saved compared with unrehydrated FOBT and flexible sigmoidoscopy every 10 years. Rehydrated FOBT plus flexible sigmoidoscopy every 5 years provided the greatest gain in life expectancy and had an incremental cost-effectiveness ratio of $92,900 per LY saved compared with unrehydrated FOBT and flexible sigmoidoscopy every 10 years (with colonoscopy performed for any polyp found). All other strategies either cost more and yielded a lower life expectancy or had higher incremental cost-effectiveness ratios than more effective strategies.

This model took a unique approach to the test characteristics of sigmoidoscopy and colonoscopy. The two sides of the colon (right and left) were modeled separately because sigmoidoscopy can only examine the left colon. This tends to overestimate the sensitivity of sigmoidoscopy, however, because although the sensitivity for flexible sigmoidoscopy may be 90% or more for polyps or cancer in the left colon, it is 0% for right-sided lesions. Failure to consider this overestimates the effectiveness of sigmoidoscopy. This model not only considered reduced compliance but also examined strategies that included rehydrated FOBT, a practice that is typically not performed in clinical practice. The incremental analysis performed by the authors, comparing one strategy with the next most effective and expensive alternative, provides the clinician with important information for decision making: for a modest increase in cost, what is the additional gain in terms of cancers prevented and lives saved to perform this more effective and expensive strategy?[4]

Next, the authors focus on screening colonoscopy and its costs. Sonnenberg et al[13] developed a model to compare the cost-effectiveness of FOBT, flexible sigmoidoscopy, and colonoscopy. They developed a computer simulation of 100,000 hypothetical 50-year-old average-risk individuals. The strategies included annual FOBT, flexible sigmoidoscopy every 5 years, colonoscopy every 10 years, and no screening. The model includes published literature on the effectiveness of the screening modalities and their associated risks, and the prevalence and incidence of polyps and cancer. Medicare reimbursement rates were used for the costs. The induced costs of complications, evaluation of a positive test, and surveillance colonoscopy (every 3 years) in those found to have adenomas are included. Costs and life expectancy were discounted at the 3% rate annually. The authors took the perspective of the third-party payor. The results suggested that compared with no screening, annual FOBT had an incremental cost-effectiveness ratio of $9705 per LY saved. In the incremental analysis, flexible sigmoidoscopy every 5 years had an incremental cost-effectiveness ratio of $65,704 compared with annual FOBT. Colonoscopy was less costly and more effective than flexible sigmoidoscopy, and, thus, it dominated flexible sigmoidoscopy and was the preferred strategy. Screening with colonoscopy remained a cost-effective strategy over a wide range of assumptions including changes in effectiveness and compliance. This model is unique in that it calculated the total costs for implementing a screening program. Using current population estimates for individuals aged 50, a program of annual FOBT costs $1.6 billion. If screening with colonoscopy is implemented, the cost amounts to $7.6 billion annually. The results emphasize the superiority of colonoscopy as a screening method and highlight that when compliance is reduced, less frequent tests are more effective and cost-effective because the benefit of repeat testing (e.g., annual FOBT) diminishes.[13]

The author examined colorectal cancer screening in a managed care setting. Lieberman's model[7] was modified to calculate costs per LY saved and incremental cost-effectiveness ratios for average-risk individuals enrolled in a managed care plan. The following strategies were evaluated: (1) colonoscopy every 10 years, (2) barium enema every 5 years, (3) annual FOBT and flexible sigmoidoscopy every 5 years, (4) annual FOBT, and (5) no screening. Published clinical data[7] on the risks and benefits of screening in a decision model that simulates lifetime events were included. The perspective of the HMO was used, and using a standard discount rate of 3%, direct medical costs for procedures, surgery, radiation, chemotherapy, and postoperative and hospice care from Duke University were used.[14] The model calculates the incremental cost-effectiveness ratios for each strategy for 1000 patients over a 10-year period. Based on the results, screening colonoscopy was the most effective strategy, preventing up to 12 cancers and increasing life expectancy by a total of 82 years (for 1000 patients over a 10-year period). Compared with no screening, it had an incremental cost-effectiveness ratio of $6300 per LY gained. All other strategies were inferior to screening colonoscopy because they had higher incremental cost-effectiveness ratios and were less effective in preventing cancer deaths. Given the benchmark of $40,000 per LY saved for prevention strategies,[16] screening colonoscopy was found to be cost-effective compared with this standard for prevention practices.[10]

Finally, the authors discuss the cost-effectiveness of a new modality, virtual colonoscopy, compared with conventional colonoscopy and with no screening. This model by Sonnenberg et al[12] evaluates these alternative strategies in a hypothetical cohort of 50-year-old, average-risk individuals. Published literature on the efficacy and risks of colonoscopy was included. The efficacy of virtual colonoscopy was calculated as the efficacy of colonoscopy multiplied by the sensitivity of virtual colonoscopy. Complications of colonoscopy were considered and surveillance colonoscopy every 3 years for those diagnosed with adenomas was included. Costs were obtained from Medicare reimbursement schedules. Compliance with initial procedures was varied from 10% to 100% and with follow-up procedures from 50% to 100%. Costs and life expectancy were discounted at the 3% rate annually. The authors took the perspective of the third-party payor.

The results suggest that compared with no screening, screening colonoscopy has an incremental cost-effectiveness ratio of $10,408 per LY saved, whereas virtual colonoscopy has an incremental cost-effectiveness ratio of $11,484 per LY saved. When comparing virtual colonoscopy with conventional colonoscopy, the authors found that virtual colonoscopy was inferior to conventional colonoscopy because it had a higher incremental cost-effectiveness ratio than conventional colonoscopy, which is a more effective strategy.[12] In sensitivity analysis, several parameters were varied. Both strategies were affected by reduced compliance rate and as compliance with each of them falls, each strategy becomes less expensive. The authors varied the costs of the virtual colonoscopy and found that if the cost of virtual colonoscopy exceeded $336, screening with this procedure spends more money per LY saved and becomes less cost-effective than a screening colonoscopy program.[12] Although there is continued uncertainty about the costs and effectiveness of virtual colonoscopy, this model provides preliminary data on the cost-effectiveness of this practice. Further analyses are warranted.

SUMMARY

This article reviews several of the recent models addressing the cost-effectiveness of colorectal cancer screening in the average-risk individual (Table 1).[4,6,7,10,12,13,16] How can clinicians and policy makers use this

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Table 1. SUMMARY OF ECONOMIC ANALYSES

Study	Design	Outcomes	Results
Lieberman[7]	Study design: Cost-effectiveness analysis Intervention or program under examination: Five colorectal cancer screening strategies compared: (1) annual FOBT (rehydrated); (2) flexible sigmoidoscopy every 5 y; (3) flexible sigmoidoscopy every 5 y and annual FOBT combined; (4) one-time colonoscopy with polypectomy at time of colonoscopy; (5) air-contrast barium enema (every 5 y). Model describes costs and benefits for a hypothetical population of 1000 asymptomatic screenees. Assumes a 10-year screening program beginning at age 55–65. Perspective: Not stated Discount Rate: None	Cost: Costs of screening per 1000 subjects Benefits and Effects: Number of colorectal cancer deaths prevented Cost-effectiveness: Cost per colorectal cancer death prevented Sensitivity analysis: Patient compliance Cost of normal colonoscopy Cost of polypectomy Cost of surveillance colonoscopy Frequency of surveillance colonoscopy Cost of cancer care Cancer detection rate	Costs per deaths prevented ranged from $225,000 (for a 10-year period, not discounted) for annual FOBT to $280,000 for barium enema, the most expensive strategy. Sensitivity analysis examined the cost of colonoscopy. The results suggest that if the cost of colonoscopy falls to $750 or less, then one-time colonoscopy in the 10-year period is less expensive than FOBT alone at equal levels of compliance. When compliance falls to 50%, the cost per death prevented is similar for FOBT, FOBT and flexible sigmoidoscopy, and colonoscopy and ranges from $331,000–$337,000.
Wagner et al[16]	Study design: Cost-effectiveness analysis Intervention or program under examination: Seventeen screening strategies examined based on AHCPR recommendation: Positive screening test to be followed-up with colonoscopy, with polypectomy if polyp detected. Patients undergoing polypectomy underwent surveillance colonoscopy every 4 y thereafter. Model follows hypothetical cohort of 100,000 average-risk 50-year-old Americans. Screening assumed to cease at age 85; surveillance assumed to continue until death in individuals undergoing polypectomy. 5% discount rate. Perspective not stated.	Cost: Cost per 100,000 persons screened Effects and Benefits: Years of life gained per 100,000 persons screened Cost-effectiveness: Cost per year of life gained compared with no screening Sensitivity analysis: Precancerous polyp dwelling time (5 y, 10 y) Effective reach of flexible sigmoidoscopy Sensitivity of double-contrast barium enema Rehydration and unrehydration of FOBT Percentage of cancers arising from adenomas Cost of screening and diagnostic tests Cost of cancer treatment	The incremental cost-effectiveness ratios ranged from $9906 per LY gained for annual FOBT (rehydrated) to $14,996 per LY gained for annual FOBT and DCBE every 3 y.

Loeve et al[9]	Study design: Cost-effectiveness Intervention or program under examination: Two colorectal cancer screening strategies compared: (1) no screening; (2) flexible sigmoidoscopy every 5 y. Positive sigmoidoscopy followed-up by colonoscopy, with removal of all adenomas ≥6 mm. Patients undergoing polypectomy invited for surveillance colonoscopy every 5 y until no lesions are found. Perspective: Not stated. Simulation model used to estimate costs and savings of screening program in a simulated dynamic US population. Patients screened every 5 y from age 50 through 75. Screening program assumed to run from 1993 to 2023. Previously used for the evaluation of breast and cervical cancer screening. Annual discount rate of 3% applied.	Economic analysis: Total costs per person Total induced savings per person Net costs per person Benefits: LY gained per 1000 persons Sensitivity analysis: Adenoma dwelling time probability distribution type (exponential or constant) Mean dwelling time between onset and clinical diagnosis of cancer (20 y, 10 y) Percentage of cancers preceded by an adenoma (100%, 70%) Unit cost of sigmoidoscopy ($50, $100, $200) Unit cost of colonoscopy without polypectomy ($150, $300, $600) Unit cost of colonoscopy with polypectomy ($200, $400, $800) Discount rate (0%, 3%, 5%)	$5 per person is saved and life expectancy is increased by approximately 28 y per 1000 screenees. When the screening program ends in year 30, the breakeven point occurs in year 35 (cumulative undiscounted costs are balanced by savings).
Khandker et al[6]	Study design: Cost-effectiveness analysis Intervention or program under examination: Nine colorectal cancer screening strategies compared. Perspective: Not stated Dynamic state transition model used to estimate costs of screening a hypothetical population of 100,000 average-risk subjects undergoing screening from age 50 to 85. 3% annual discount rate	Cost: Total cost per person Benefits and Effects: LY saved Cost-effectiveness: Cost per LY saved Incremental cost-effectiveness: Each strategy compared with no screening. Sensitivity analysis: Probability of polyp turning into cancer at end of 10th y (1 and 0.25) Sensitivity of sigmoidoscopy in distal colon and more proximally Compliance with initial procedures (23% and 100%) Sensitivity of FOBT Sensitivity of double-contrast barium enema Specificity of colonoscopy Cost of colonoscopy	Flexible sigmoidoscopy every 5 y had the lowest incremental cost-effectiveness ratio ($12,636 per LY gained). Annual FOBT had an incremental cost-effectiveness ratio of $14,394 per LY gained. Colonoscopy every 5 y, the most expensive strategy, had an incremental cost-effectiveness ratio of $28,724 per LY gained.

Table continued on following page

Table 1. SUMMARY OF ECONOMIC ANALYSES (*Continued*)

Study	Design	Outcomes	Results
Frazier et al[4]	Study design: Cost-effectiveness analysis Intervention or program under examination: Twenty-two screening strategies compared. Markov model used to estimate costs of screening a hypothetical population representative of the 50-years-old US population at average risk for colorectal cancer. Screening or surveillance continued until age 85. Computer cohort simulation.	Cost: Lifetime cost per person screened Benefits and Effects: Days of life gained Reduction in colorectal cancer incidence Reduction in colorectal cancer mortality Cost-effectiveness: Cost per LY saved Incremental cost-effectiveness: Incremental cost per LY saved–comparing each strategy with the next most effective and expensive strategy. Sensitivity analysis: Compliance with initial screening test (60% and 100%) Compliance with follow-up colonoscopy Specificity of unrehydrated FOBT Sensitivity of unrehydrated FOBT for cancer Sensitivity of unrehydrated and rehydrated FOBT for polyps Prevalence of polyps at age 50 Incidence of polyps after age 50 among those polyp-free at baseline Rate of progression from normal epithelium to recurrent polyp after polypectomy Annual transition probability from high-risk polyp to cancer Probability that polyp at age 50 is in distal colon Cost of colonoscopy Mortality from colonoscopy Discount rate	Seven strategies preferred: 1 and 2, flexible sigmoidoscopy once at age 55 (two follow-up strategies considered) 3 and 4, flexible sigmoidoscopy every 10 y beginning at age 55 (two follow-up strategies considered) Incremental CE ratios were < $17,000 per LY saved (strategies 1–4). 5, Unrehydrated FOBT plus flexible sigmoidoscopy—incremental CE ratio $21,200 per LY saved compared with flexible sigmoidoscopy alone every 10 y. 6, Unrehydrated FOBT plus flexible sigmoidoscopy—incremental CE ratio $51,200 per LY saved compared with unrehydrated FOBT and flexible sigmoidoscopy every 10 y. 7, Rehydrated FOBT plus flexible sigmoidoscopy every 5 y provided the greatest gain in life expectancy and had an incremental CE ratio of $92,900 per LY saved compared with unrehydrated FOBT and flexible sigmoidoscopy every 10 y.
Sonnenberg et al[13]	Study design: Cost-effectiveness analysis Intervention or program under examination: Four colorectal cancer screening strategies compared: (1) FOBT every y; (2) flexible sigmoidoscopy every 5 y; (3) colonoscopy every 10 y; (4) no screening. Positive findings on FOBT or sigmoidoscopy evaluated by colonoscopy. Polyps removed at time of colonoscopy.	Cost: Total costs per 100,000 subjects Benefits and Effects: LY saved Cost-effectiveness: Cost per LY saved Incremental cost-effectiveness: Incremental cost per LY saved Sensitivity analysis: Compliance with initial procedures Compliance with repeat procedures Compliance with colonoscopy after positive FOBT or sigmoidoscopy Sensitivity of FOBT	Compared with no screening, annual FOBT has an incremental CE ratio of $9705 per LY saved. Flexible sigmoidoscopy every 5 y has an incremental CE ratio of $65,704 compared with annual FOBT. Colonoscopy is less costly and more effective than flexible sigmoidoscopy. A program of annual FOBT costs $1.6 billion. A screening colonoscopy program amounts to $7.6 billion annually.

	Surveillance colonoscopy repeated every 3 y after polypectomy until no polyps found. Perspective: Third-party payer. Markov model used to estimate costs of screening a hypothetical population of 100,000 subjects undergoing screening from age 50 until death.	Specificity of FOBT Efficacy of screening colonoscopy in preventing colorectal cancer Incidence of polyps Screening interval Surveillance interval after polypectomy	
Provenzale et al[10]	Study design: Cost-effectiveness analysis. Intervention or program: Five colorectal cancer screening strategies compared: (1) colonoscopy every 10 y; (2) barium enema every 5 y; (3) annual fecal occult blood testing and flexible sigmoidoscopy every 5 y; (4) annual fecal occult blood testing; (5) no screening Perspective HMO 3% annual discount rate model describes costs and benefits for a hypothetical population of 1000 screenees over a 10-y period in a managed care plan.	Cost: Cost of screening and follow-up of 1000 subjects Benefits and Effects: LY saved Cost-effectiveness: Incremental cost-effectiveness ratios comparing each strategy with the next more effective and expensive strategy	Screening colonoscopy was the most effective strategy, preventing up to 12 cancers and increasing life expectancy by a total of 82 y (for 1000 patients over a 10-y period) compared with no screening. The incremental cost-effectiveness ratio was $6300 per LY gained. All other strategies were inferior to screening colonoscopy (they had higher incremental cost-effectiveness ratios and were less effective in preventing cancer deaths).
Sonnenberg et al[12]	Study design: Cost-effectiveness analysis Intervention or program under examination: Three colorectal cancer screening strategies compared: (1) CT colonography (virtual colonoscopy); (2) conventional colonoscopy; (3) no screening. Suspicious findings on CT colonography evaluated by colonoscopy. Polyps removed at time of colonoscopy. Surveillance colonoscopy repeated every 3 y after polypectomy until no adenomatous polyps found. Perspective: Third-party payer. Markov model used to estimate costs of screening a hypothetical population of 100,000 subjects undergoing screening every 10 y from age 50 until death. Annual discount rate of 3% applied.	Cost: Total costs per 100,000 subjects Benefits and Effects: LY saved Cost-effectiveness: Cost per LY saved Incremental cost-effectiveness: Incremental cost per LY saved Sensitivity analysis: Cost of CT colonography Compliance with initial screening procedure Compliance with repeat procedures Compliance with colonoscopy after positive CT colonography Sensitivity of CT colonography Specificity of CT colonography Screening interval	Compared to no screening, screening colonoscopy has an incremental cost-effectiveness ratio of $10,408 per LY saved and virtual colonoscopy has an incremental cost-effectiveness ratio of $11,484 per LY saved. Comparing virtual colonoscopy with conventional colonoscopy, virtual colonoscopy was inferior to conventional colonoscopy because it had a higher incremental cost-effectiveness ratio than conventional colonoscopy, which is a more effective strategy.

FOBT = Fecal occult blood test; LY = life year; DCBE = double-contrast barium enema; CE = cost-effectiveness.

information for decision making regarding colorectal cancer screening? The cost-effectiveness ratios reported by themselves do not identify cost-effective practices. They must be placed in a decision context that is expressed in one of two forms. In the first form, an explicit threshold or maximum amount that a policy maker is willing to spend is stated (e.g., $40,000 per LY gained, as has been quoted as an acceptable amount for a prevention program).[16] In the second form of decision context, a list of medical practices and their associated cost-effectiveness ratios, also known as a *league table* (Table 2) is used as a basis for comparison with the practice under evaluation (e.g., colorectal cancer screening). The practice with the lowest cost-effectiveness ratio is the most cost-effective practice on the list. Practices with lower cost-effectiveness ratios are considered cost-effective compared with those with higher ratios. Table 2 lists incremental cost-effectiveness ratios for common medical practices. The models discussed in this article suggested that colorectal cancer screening using annual FOBT, flexible sigmoidoscopy at 3 or 5 years, the combination of FOBT and flexible sigmoidoscopy, barium enema, colonoscopy, and even virtual colonoscopy had incremental cost-effectiveness ratios ranging from $6300 to $92,900 per LY saved with most of the cost-effectiveness ratio ranging from $10,000 to $40,000 per LY saved. These ratios are similar to the cost of another widely accepted practice, breast cancer screening with annual mammography in women age 50 and older ($22,000 per LY gained).[15] Colorectal cancer screening with any of the modalities discussed is considered less cost-effective than screening for hemochromatosis, which has an incremental cost-effectiveness ratio of $3665 per LY saved.[3] Based on these ratios, however, screening for colorectal cancer is considered cost-effective compared with cervical cancer screening in women age 20 and older with pap smear every 3 years, which has an incremental cost-effectiveness ratio of $250,000 per LY gained.[2] The clinician can use these incremental cost-effectiveness ratios to evaluate the risks and benefits of alternative practices for the individual, and the policy maker with a limited health care budget can use these ratios to set priorities for funding based on the costs and the expected gains in life expectancy for colorectal cancer screening and for alternative health care programs.

Table 2. INCREMENTAL COST-EFFECTIVENESS RATIOS

	$/Life-Year Gained
Screening for hemochromatosis*	3665 (16)
Breast cancer screening†‡ (mammography every y versus every 1.3 y)	22,000 (18)
Cervical cancer screening with pap smear every 3 y‡§	250,000 (17)

* 3% discount rate.
† Women age 50–70.
‡ 5% discount rate.
§ Women age 20–75.

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