

# Initial Evaluation of Rectal Bleeding in Young Persons: A Cost-Effectiveness Analysis

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**Background:** Evaluation of rectal bleeding in young patients is a frequent diagnostic challenge.

**Objective:** To determine the relative cost-effectiveness of alternative diagnostic strategies for young patients with rectal bleeding.

**Design:** Cost-effectiveness analysis using a Markov model.

**Data Sources:** Probability estimates were based on published medical literature. Cost estimates were based on Medicare reimbursement rates and published medical literature.

**Target Population:** Persons 25 to 45 years of age with otherwise asymptomatic rectal bleeding.

**Time Horizon:** The patient's lifetime.

**Perspective:** Modified societal perspective.

**Interventions:** Diagnostic strategies included no evaluation, colonoscopy, flexible sigmoidoscopy, barium enema, anoscopy, or any feasible combination of these procedures.

**Outcome Measures:** Life expectancy and costs.

**Results of Base-Case Analysis:** For 35-year-old patients, the no-evaluation strategy yielded the least life expectancy. The incremental cost-effectiveness of flexible sigmoidoscopy compared

with no evaluation or with any strategy incorporating anoscopy (followed by further evaluation if no anal disease was found on anoscopy) was less than \$5300 per year of life gained. A strategy of flexible sigmoidoscopy plus barium enema yielded the greatest life expectancy, with an incremental cost of \$23 918 per additional life-year gained compared with flexible sigmoidoscopy alone.

**Results of Sensitivity Analysis:** As patient age at presentation of rectal bleeding increased, evaluation of the entire colon became more cost-effective. The incremental cost-effectiveness of flexible sigmoidoscopy plus barium enema compared with colonoscopy was sensitive to estimates of the sensitivity of the tests. In a probabilistic sensitivity analysis comparing flexible sigmoidoscopy with anoscopy followed by flexible sigmoidoscopy if needed, the middle 95th percentile of the distribution of the incremental cost-effectiveness ratios ranged from flexible sigmoidoscopy yielding an increased life expectancy at reduced cost to \$52 158 per year of life gained (mean, \$11 461 per year of life saved).

**Conclusions:** Evaluation of the colon of persons 25 to 45 years of age with otherwise asymptomatic rectal bleeding increases the life expectancy at a cost comparable to that of colon cancer screening.

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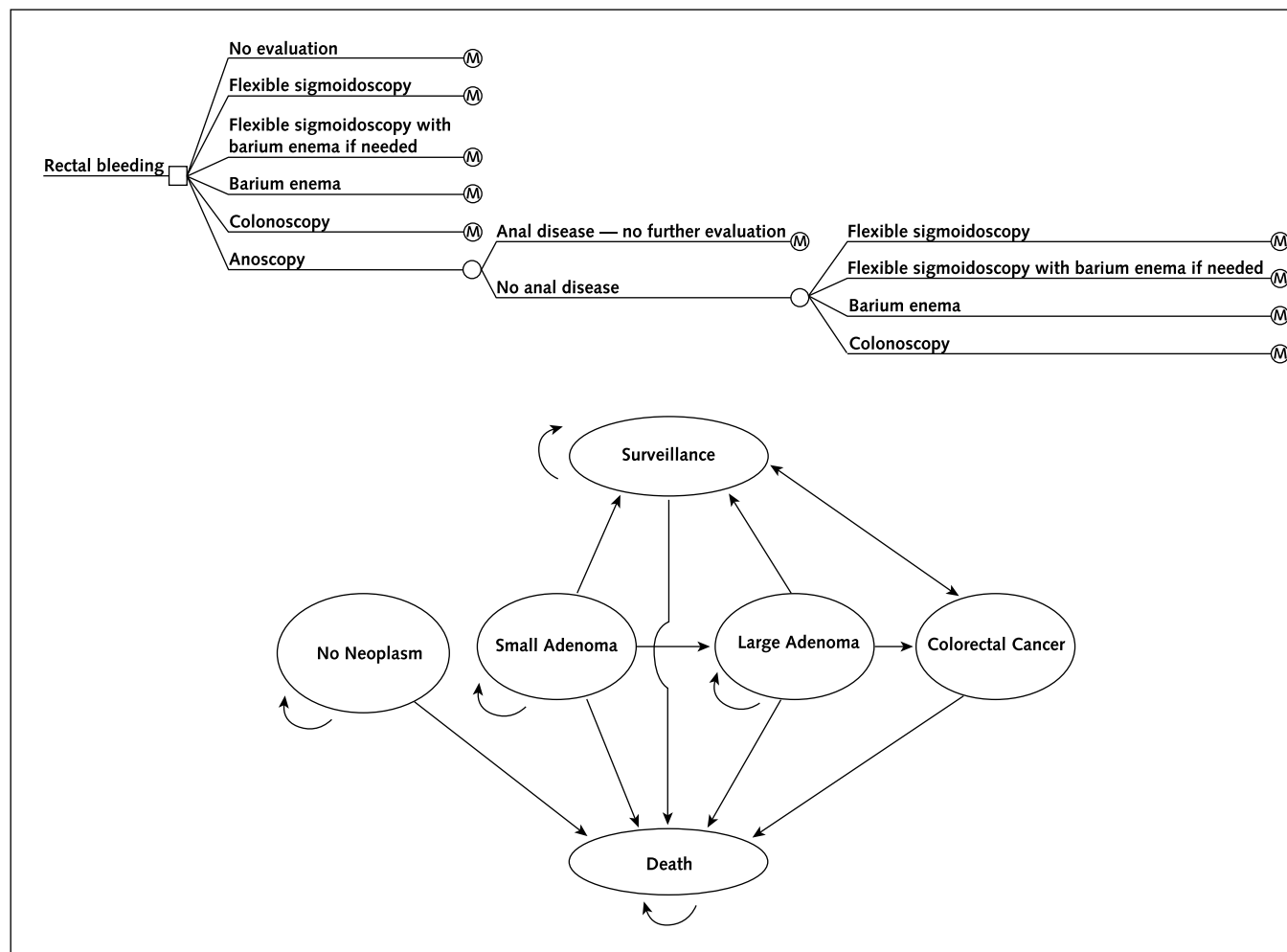
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Colorectal cancer is the third most common cause of cancer-related death in men and women (1). The incidence increases with increasing age, and before 40 years of age, the risk for colorectal cancer is low (2). The disease can be effectively prevented by endoscopic removal of precancerous adenomatous polyps (3). After invasive cancer develops, mortality from colorectal cancer increases with advancing cancer stage at diagnosis (1). Most medical professional societies recommend routine screening with fecal occult blood testing, flexible sigmoidoscopy, colonoscopy, or barium enema beginning at 50 years of age for average-risk patients and 40 years of age for persons at increased risk (1).

Rectal bleeding occurs in approximately 20% of the population annually (4–9) and most commonly results from benign anal disorders (10–14). However, when rectal bleeding is caused by a colorectal neoplasm, expe-

dent evaluation may result in earlier detection of the neoplasm and reduced cancer-related mortality. Most studies examining the risk for colonic neoplasm in patients with rectal bleeding have been conducted predominantly in patients older than 40 years of age (10, 11, 15, 16). The probability that rectal bleeding results from a colorectal neoplasm is much lower in younger patients than in older patients. Many investigators recommend evaluation of the entire colon of older adults with rectal bleeding (10, 11, 15, 16). Rigorous evaluation of the potential risks, benefits, and costs of such a strategy in younger patients has not been reported. Thus, when faced with a young patient with rectal bleeding, clinicians must weigh the potential benefits of identifying and removing relatively rare but potentially fatal colonic neoplasms versus the potential complications and costs associated with diagnostic and therapeutic

Figure 1. Overview of the Markov model.



**Top.** The alternative diagnostic strategies. Patients with rectal bleeding undergo no evaluation, undergo anoscopy, or undergo a diagnostic test. Patients undergoing anoscopy are referred for further diagnostic testing only if no lesions are identified on anoscopy. All patients with colitis eventually undergo colonoscopy. The circled “M” notations represent Markov nodes in the computer program. **Bottom.** The potential consequences of colonoscopy. Patients with detected adenomas or who survive cancer therapy enter surveillance programs. Undetected adenomas may remain as adenomas or may advance to cancer. Adenomas and cancers may also be detected at the time of colorectal cancer screening.

tic tests. We assessed the relative survival and cost-effectiveness of using alternative diagnostic strategies for young persons with otherwise asymptomatic rectal bleeding.

**METHODS**

We developed a Markov analytic decision model (Figure 1) to represent the natural history of patients with rectal bleeding. The base model consisted of a 35-year-old patient presenting with otherwise asymptomatic

rectal bleeding, which we defined as blood in the toilet bowl, on the tissue paper, or mixed with stool. A patient could follow one of nine strategies: no evaluation, flexible sigmoidoscopy, air-contrast barium enema, flexible sigmoidoscopy and air-contrast barium enema, colonoscopy, anoscopy followed by flexible sigmoidoscopy, anoscopy followed by air-contrast barium enema, anoscopy followed by flexible sigmoidoscopy and air-contrast barium enema, or anoscopy followed by colonoscopy. The model assumed that patients who underwent anoscopy were further evaluated by using an-

**Table 1. Probability Estimates Included in the Model**

Variable	Base Estimate (Range)	Reference
5-year relative survival rate		
With local-stage colorectal cancer	0.914*	17
With regional-stage colorectal cancer	0.661*	17
With advanced-stage colorectal cancer	0.085*	17
Annual mortality from other causes	Age-specific	18
Perforation from barium enema	0.00005 (0.00001–0.0001)	1
Perforation from colonoscopy	0.001 (0.0001–0.002)	1
Perforation from flexible sigmoidoscopy	0.00015 (0.0001–0.0002)	1
Hemorrhage after polypectomy	0.006 (0.00001–0.012)	19, 20
Perforation from polypectomy	0.003 (0.001–0.005)	19, 21–25
Die as a result of a perforation	0.015 (0.001–0.03)	1
Prevalence of neoplasm†		
At age 25 y	0.005 (0.001–0.01)	26–29
At age 35 y	0.03 (0.01–0.05)	26–29
At age 45 y	0.15 (0.1–0.2)	26–29
Colonic neoplasm within the reach of flexible sigmoidoscopy	0.80 (0.65–0.90)	1, 30–33
Relative prevalence of isolated nonadenomatous polyps‡	0.73 (0.0001–2.0)	32–34
Proportion of nonadenomatous polyps within reach of flexible sigmoidoscopy	0.70 (0.5–1.0)	35, 36
Increased risk for neoplasms in persons with rectal bleeding	2.0 (1.0–3.0)	30, 31, 37, 38
Proportion of polyps > 9 mm at time of bleeding	0.16 (0.10–0.22)	10, 11, 39–41
Colonic neoplasm contains invasive cancer	0.002 (0.001–0.004)	17
Cancer is local stage at time of bleeding	0.50 (0.3–0.7)	17
Cancer is regional stage at time of bleeding	0.25 (0.15–0.35)	17
Symptoms from undiagnosed local-stage cancer	0.18 (0.10–0.26)	17, 30, 31
Symptoms from undiagnosed regional-stage cancer	0.63 (0.46–0.80)	17, 30, 31
Symptoms from undiagnosed distant-stage cancer	1.00 (1.0–1.0)	17, 30, 31
Small polyp advances to large polyp	0.05 (0.01–0.09)	1, 26, 42
Large polyp advances to local-stage cancer	0.03 (0.01–0.05)	1, 26, 42
Prevalence of anal disease§	0.70 (0.5–0.9)	9, 10, 12, 13, 43–46
Prevalence of colitis	0.05 (0.01–0.09)	10, 11, 13, 43–45
Relative risk for colonic neoplasm in patients with anal disease	0.60 (0.3–0.9)	11, 12, 47
Sensitivity of barium enema for small neoplasms	0.65 (0.50–0.80)	1
Sensitivity of barium enema for large neoplasms	0.80 (0.70–0.90)	1
Specificity of barium enema for neoplasms	0.83 (0.66–1.0)	1
Sensitivity of colonoscopy for small neoplasms	0.78 (0.70–0.85)	1
Sensitivity of colonoscopy for large neoplasms	0.95 (0.90–0.99)	1
Sensitivity of colonoscopy for symptomatic cancer	1.00 (1.0–1.0)	1
Sensitivity of flexible sigmoidoscopy for small neoplasms	0.78 (0.70–0.85)	1
Sensitivity of flexible sigmoidoscopy for large neoplasms	0.95 (0.90–0.99)	1
Sensitivity of colorectal cancer screening for polyps or cancer	0.75 (0.6–0.9)	1, 32, 33
Proportion of patients screened with flexible sigmoidoscopy	0.30 (0.1–0.5)	48
Proportion of screened patients entering colonoscopic surveillance	0.20 (0.1–0.3)	32, 33
Efficacy of cancer surveillance	0.995 (0.99–1.0)	1, 3
Proportion of patients with recurrent polyps identified during surveillance	0.45 (0.3–0.5)	49
New distal adenomas at time of screening in patients with previously isolated proximal neoplasm	0.50 (0.0–0.5)	32, 33

\* Because of the large sample sizes used in the Surveillance, Epidemiology, and End Results (SEER) program calculations, no variability was assumed for relative survival rates.

† Neoplasm includes adenomatous polyps and colorectal cancer.

‡ Prevalence of isolated nonneoplastic polyps such as hyperplastic polyps relative to neoplastic adenomatous polyps.

§ Anal disease includes hemorrhoids and fissures.

|| Assumes that 95% of cancers diagnosed during surveillance are local stage, 4.5% are regional stage, and 0.5% are distant stage.

other test only if anoscopy revealed no apparent source of bleeding (such as hemorrhoids) in the anorectal region. The model similarly assumed that patients underwent barium enema after flexible sigmoidoscopy only if sigmoidoscopy had identified no source of bleeding other than anal disease. All patients with a colonic neoplasm identified by using flexible sigmoidoscopy or bar-

ium enema were assumed to have subsequently undergone colonoscopy.

### Probability Estimates

Table 1 summarizes the source, base-case estimates, and ranges for the probability estimates included in the

**Table 2. Cost Estimates Incorporated in the Model**

Variable	Base Estimate (Range), \$
Flexible sigmoidoscopy without biopsy	174.24 (139.11–223.31)
Flexible sigmoidoscopy with biopsy	205.08 (163.47–263.28)
Colonoscopy	606.55 (484.13–777.58)
Polypectomy	254.04 (203.89–323.66)
Pathology review of biopsy specimens	180.78 (68.74–180.78)
Barium enema	186.92 (145.70–245.69)
Care for early-stage cancer	35 000 (25 000–45 000)
Care for advanced-stage cancer	45 000 (35 000–55 000)
Care for perforation during diagnostic procedure	13 032 (13 032–35 000)
Care for postpolypectomy bleeding	4360 (3000–5000)

model. After reviewing previous autopsy studies, Koretz (26) estimated that the prevalence of colonic neoplasms in persons 30 to 39 years of age was 0.04 for men and 0.02 for women (26). On the basis of studies of rectal bleeding in patients of all ages with colorectal cancer and polyps (30, 31, 37, 38), we estimated for our analyses that patients with rectal bleeding had a twofold increased prevalence of neoplasms. In addition, on the basis of studies of patients of all ages (9, 12, 14, 29), we assumed that patients with rectal bleeding patients and anal disease (hemorrhoids or anal fissures) identified at anoscopy were less likely than patients with rectal bleeding but without anal disease to have neoplastic lesions. In the base-case analysis, we assumed that the prevalence of neoplasms in patients with rectal bleeding and anal disease was 40% lower than that in patients with bleeding and no anal disease. Thus, in our base-case analysis, 70% of the rectal bleeding population was considered to have anal disease, and in this group, the prevalence of colonic neoplasms was estimated to be 0.036 (1.2 times that of the general population); in the 30% of the rectal bleeding population with no anal disease, the prevalence of colonic neoplasms was considered 0.06 (2.0 times that of the general population). The overall prevalence of neoplasms in persons with rectal bleeding was estimated to be 0.0432 (1.44 times that of the general population). This estimate is close to the prevalence of colonic neoplasms (0.043) reported in an endoscopic study of young persons with rectal bleeding (27). The Appendix shows the formula that we used to calculate the prevalence of neoplasms.

Several investigators have previously estimated the time required for benign adenomas to become invasive cancer (1, 26, 42). In our model, we divided neoplasms into small adenomas (diameter < 10 mm), large adeno-

mas, and invasive cancer. We assumed a constant annual probability that small adenomas would advance to large adenomas and that large adenomas would advance to cancer. By using the base-case estimates, we determined that approximately 9% of polyps present at the time of bleeding would progress to cancer in 10 years and that approximately 22% would progress in 20 years. Similarly, in the base case, the incidence of cancer diagnosed in the no-evaluation group was 2.1 times the expected rate for the U.S. population at 5 years and subsequently decreased toward normal (17).

### Cost Estimates

The model used a modified societal perspective by including all direct medical costs (Table 2) regardless of who incurred the cost. Indirect costs, such as time lost from work, were not included. For the direct costs of diagnostic procedures, including physician and facility fees, we assumed that procedures were performed in an outpatient setting. We estimated the physician fees on the basis of the median fees for U.S. physicians for 2000. We based the ranges for sensitivity analyses on the maximum and minimum physician fees and based facility fees on the national average allowable charge by Medicare for 1998 (Gant G. Personal communication). In determining the cost of a surveillance colonoscopy, we assumed that 45% of patients would require polypectomy (49). We estimated the cost of caring for patients with colorectal cancer on the basis of a recent National Cancer Institute–sponsored study (50) of the costs of treating patients in the Kaiser Foundation Health Plan. All costs for treating colorectal cancer were assumed to be incurred during the first year after diagnosis. The cost for pathology review of biopsy specimens and the costs for the management of perforations and bleeding after polypectomy were based on a recent cost-effectiveness model that used Medicare reimbursement rates (51). We did not include the cost of office visits for rectal bleeding or for anoscopy because we assumed that these costs would be incurred regardless of treatment strategy (the model begins after the initial office visit). We applied a 3% discount rate to costs and benefits (52).

### Additional Assumptions Included in the Model

In the model, we did not account for the progression of new polyps over time, although we did account for the occurrence of new polyps identified in patients

undergoing cancer screening. On the basis of current understanding of the adenoma–carcinoma sequence, a new polyp probably would not advance to invasive cancer more rapidly than a polyp present at the time of bleeding. Thus, the model depicted the effect of the diagnostic strategies on the natural history of the polyps and cancers present at the time of first bleeding.

The model assumed that all patients with bleeding secondary to colitis would undergo colonoscopy in the first 2 years of symptoms as a result of persistent or worsening symptoms or as follow-up to flexible sigmoidoscopy or barium enema.

The model assumed that without therapy, local-stage cancer would advance to regional-stage cancer within 2 years and that regional-stage cancer would advance to distant-stage cancer within 1 year. The model also assumed that all cases of advanced-stage cancer were diagnosed during the first year as a result of screening or symptoms.

The model assumed that screening with flexible sigmoidoscopy would be offered every 5 years, beginning at age 50 years, but assumed that only some patients would agree to undergo screening. We assumed that surveillance colonoscopy was performed every 5 years after the diagnosis of adenomatous polyps or cancer.

### Quality of Life

We did not assign quality-of-life estimates to the different health states in the primary model because limited data were available. However, in sensitivity analyses, we assumed that during the first 5 years after diagnosis, quality of life would decrease by 5% for patients with local or regional cancer and would decrease by 20% for patients with distant cancer.

### Analysis

We report the results of the cost-effectiveness analyses as incremental cost-effectiveness, which we defined as the increase in cost necessary to yield a 1-year increase in survival compared with the alternative strategy. We performed one-way sensitivity analyses across the range of variables in the model and performed two-way analyses to examine the relationship of test sensitivity on the incremental cost-effectiveness ratio.

We used a Monte Carlo simulation to examine the variability in the incremental cost-effectiveness ratios

while allowing all probability estimates to vary simultaneously. In this analysis, we performed 1000 trials. In each trial, the values for each probability variable were sampled once from across the full range of potential values. The logit normal distribution was assumed for probabilities. An infinite number of persons were then simulated for each trial to obtain the mean cost and effectiveness values for the trial. We then calculated the mean, standard deviation, and range of the middle 95th percentile (from the 2.5th to the 97.5th percentiles) for the distribution of incremental cost-effectiveness ratios. Because costs of procedures tend not to vary within a single location, we used fixed cost estimates in these analyses.

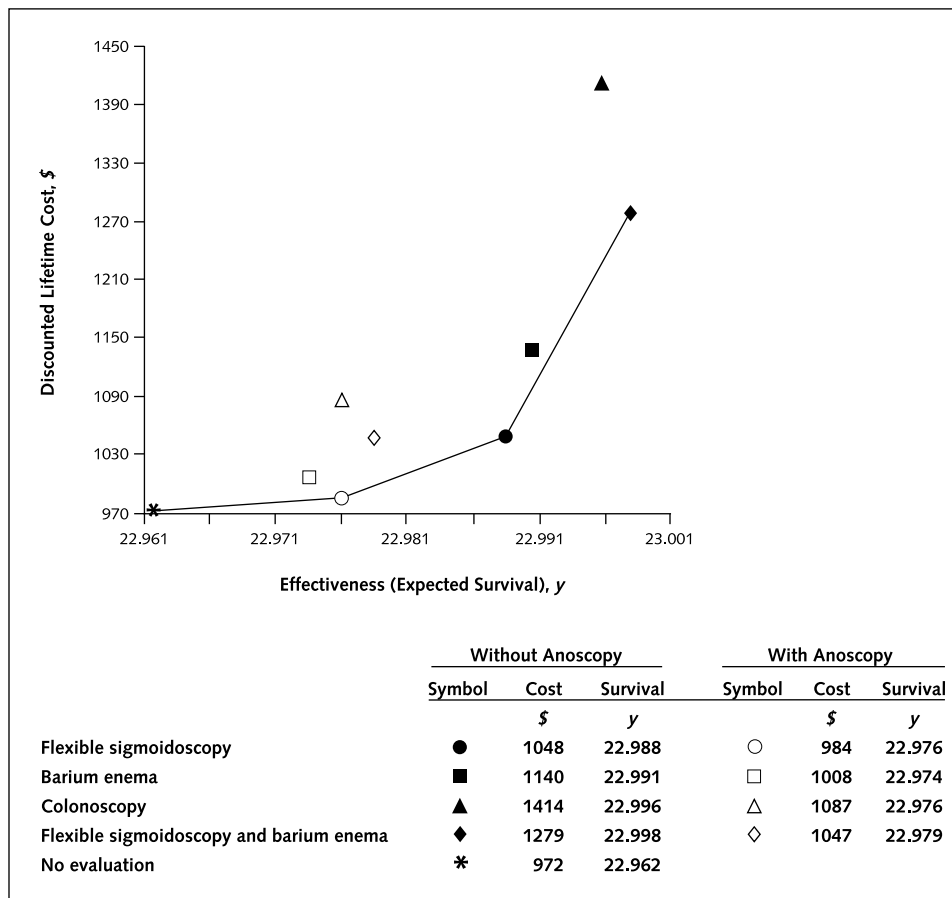
For the analyses, we used the following software: Data 3.5 and Data 4.0 Pro Beta, version 6 (Treeage Software, Inc., Williamstown, Massachusetts); Stata 6.0 (Stata Corp., College Station, Texas); and Microsoft Excel, version 5.0 (Microsoft Corp., Redmond, Washington).

### RESULTS

**Figure 2** shows the results of the base-case analysis. A strategy of no evaluation offered the least life expectancy. The greatest life expectancy was achieved by performing colonoscopy or barium enema plus flexible sigmoidoscopy for all patients. Colonoscopy or barium enema plus flexible sigmoidoscopy yielded an absolute increased life expectancy of 0.089 and 0.095 years, respectively, and 0.034 and 0.036 discounted years, respectively, compared with no evaluation. These strategies also yielded an increased life expectancy of 0.020 and 0.026 years (0.007 and 0.010 discounted years), respectively, compared with flexible sigmoidoscopy. All strategies incorporating anoscopy yielded greater life expectancy than no evaluation but lower life expectancy than strategies that visualized all or part of the colon. Similarly, for the base case, all strategies incorporating diagnostic visualization of the entire colon increased life expectancy compared with diagnostic strategies that visualized only part of the colon.

In one-way sensitivity analyses, the optimal strategy for maximizing life expectancy was relatively insensitive to the variables included in the model. As the probability that a neoplasm was located in the distal colon increased, the effectiveness of flexible sigmoidoscopy also increased; as the probability that a lesion is in the distal

Figure 2. Cost-effectiveness of strategies for the evaluation of rectal bleeding in the base-case analysis.



The figure includes the discounted lifetime cost and expected survival per patient for each of the alternative strategies examined. Incremental cost-effectiveness ratios are equal to the slope of the line between any two points and can be calculated from the data at the bottom of the figure. No evaluation offered the shortest life expectancy, and a strategy of flexible sigmoidoscopy plus barium enema offered the greatest life expectancy. All strategies using anoscopy followed by further evaluation if needed resulted in reduced life expectancy compared with all strategies in which all patients undergo evaluation of the colon with endoscopy or barium enema.

colon approached 83%, the effectiveness of flexible sigmoidoscopy became similar to that of barium enema. Moreover, the effectiveness of barium enema was similar to that of colonoscopy when the sensitivity of barium enema was equal to that of colonoscopy.

As can be computed from data in Figure 2, the incremental cost-effectiveness of flexible sigmoidoscopy compared with no evaluation or with any strategy incorporating anoscopy (followed by further evaluation if no anal disease was found) was less than \$5300 per year of life gained. Compared with flexible sigmoidoscopy, the incremental cost-effectiveness of colonoscopy was \$50 193 per year of life gained. Similarly, compared with flexible sigmoidoscopy, the incremental cost-effec-

tiveness of flexible sigmoidoscopy plus barium enema was \$23 918 per year of life gained.

Because the prevalence of colonic neoplasms increases with age, we examined the incremental cost-effectiveness ratios for persons 25, 35, and 45 years of age. As shown in Table 3, in an incremental cost-effectiveness comparison of each strategy relative to the next most effective strategy, incremental cost-effectiveness decreased with increasing age. For persons 25 years of age, the incremental cost-effectiveness of colonoscopy compared with flexible sigmoidoscopy was nearly \$275 000 per year of life gained. In contrast, for persons 45 years of age, colonoscopy cost only \$9360 per year of life gained compared with flexible sigmoidoscopy.

Our estimates were relatively insensitive to the variables in the model. In one-way sensitivity analyses comparing the strategy of flexible sigmoidoscopy with anoscopy plus flexible sigmoidoscopy (if anal disease was not identified on anoscopy), incremental cost-effectiveness increased by 50% or more only for the discount rate, the annual probabilities of progression of small and large adenomas, the probability that a neoplasm was in the distal colon, and variables that contributed to the estimated prevalence of colonic neoplasms (the prevalence of colonic neoplasms in the general population, the relative risk for neoplasms in persons with anal disease, and the relative risk for neoplasms in the persons with bleeding). In all cases, a comparison of the incremental cost-effectiveness of flexible sigmoidoscopy with that of anoscopy followed by flexible sigmoidoscopy if anal disease was not identified was less than \$30 000 per year of life gained. One-way sensitivity analyses comparing flexible sigmoidoscopy to colonoscopy or to flexible sigmoidoscopy followed by barium enema if needed also demonstrated that the model was most sensitive to variables that predicted the prevalence of colonic neoplasms in persons with rectal bleeding. The highest incremental cost-effectiveness ratios were obtained when we used our lowest estimate for the prevalence of colonic neoplasms in the general population. In this case, the incremental cost-effectiveness ratio in comparisons between flexible sigmoidoscopy and colonoscopy and between flexible sigmoidoscopy and flexible sigmoidoscopy followed by barium enema if needed were \$177 721 and \$83 060 per year of life gained, respectively.

The comparison of a strategy of colonoscopy versus flexible sigmoidoscopy plus barium enema was sensitive to estimates of the sensitivity of these tests. When we used the maximal estimates of sensitivity of colonoscopy and the minimal estimates of sensitivity of barium enema, colonoscopy yielded the greatest life expectancy, at an incremental cost of \$59 391 per year of life gained.

To further examine the variability in the model due to uncertainty surrounding the probability estimates, we performed a probabilistic sensitivity analysis. In comparing the strategy of flexible sigmoidoscopy with anoscopy followed by flexible sigmoidoscopy if needed (Figure 3), the mean incremental cost-effectiveness ( $\pm$ SD) was \$11 461  $\pm$  \$14 773 per year of life saved. The middle 95th percentile of this distribution of the incremental cost-effectiveness ratios ranged from flexible sigmoidoscopy yielding an increased life-expectancy at reduced cost to \$52 158 per year of life gained. In a comparison of flexible sigmoidoscopy with flexible sigmoidoscopy followed by barium enema if needed, the mean incremental cost-effectiveness was \$49 574 per year of life gained. The middle 95th percentile extended from \$1528 per year of life to \$233 667 per year of life gained.

## DISCUSSION

Because of the high frequency of isolated proximal neoplasms, evaluation of the entire colon is recommended for patients older than 50 years of age with rectal bleeding (10, 11, 15, 16). Moreover, there is growing support for routine screening with colonoscopy in average-risk patients beginning at 50 years of age and earlier in patients at increased risk for colorectal cancer (1, 32, 33, 51, 53). Our study supports these recommendations by demonstrating that for patients at least 45 years of age with rectal bleeding, colonoscopy is a very cost-effective diagnostic strategy.

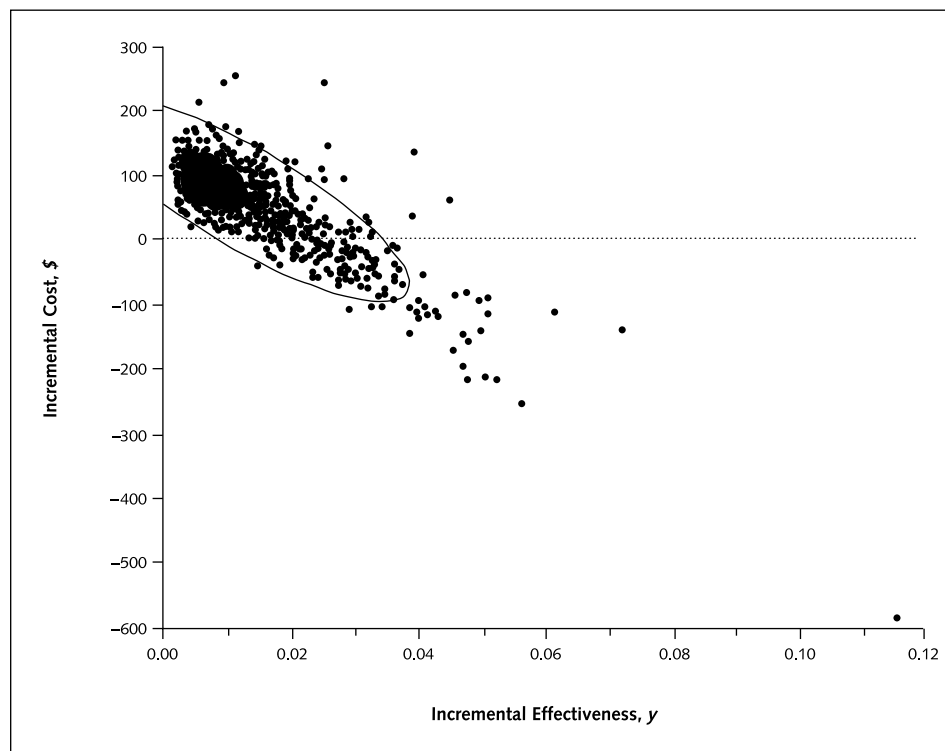
Because most young persons with bleeding do not have colonic neoplasms, physicians may believe that risks, inconvenience, and costs of diagnostic procedures outweigh potential benefits. In addition, physicians may consider an evaluation complete if anal disease is identified on anoscopy. However, the presence of anal disease does not rule out synchronous colorectal neoplasms

**Table 3. Incremental Cost-Effectiveness as a Function of Patient Age\***

Incremental Cost-Effectiveness Comparison	Cost-Effectiveness according to Patient Age		
	25 y	35 y	45 y
Anoscopy followed by flexible sigmoidoscopy if needed vs. no evaluation	12 018	832	Dominant
Flexible sigmoidoscopy vs. anoscopy followed by flexible sigmoidoscopy if needed	35 187	5226	Dominant
Flexible sigmoidoscopy followed by barium enema if needed vs. flexible sigmoidoscopy	116 195	23 918	3858
Colonoscopy vs. flexible sigmoidoscopy	272 877	50 193	9360

\* Dominant means that a strategy costs less and yields greater survival.

**Figure 3.** Multiway probabilistic sensitivity analysis comparing flexible sigmoidoscopy in all patients with a strategy of anoscopy followed by flexible sigmoidoscopy if anal disease is not identified on anoscopy.



The multiway analysis allowed all probability variables to vary simultaneously across the full range of values examined. The plotted values represent the incremental cost-effectiveness ratio from 1000 trials. The ellipse shows the middle 95th percentile of this distribution (from the 2.5th to the 97.5th percentiles). The mean incremental cost-effectiveness ratio ( $\pm$ SD) was \$11 461  $\pm$  \$14 773 per year of life saved. Only 2.5% of the values exceeded \$52 158 per year of life gained.

(11, 28, 29). Furthermore, studies demonstrate poor ability of physicians to distinguish which patients with rectal bleeding have colonic neoplasms and which have only benign anal diseases on the basis of patient history and physical examination alone (10–12). We feel that our model includes all viable diagnostic options after routine history and physical examination, including the intermediate option of performing anoscopy as part of a routine office visit for rectal bleeding. Our model demonstrates that under almost all reasonable conditions, evaluation of the colon in young patients with rectal bleeding, regardless of the findings on anoscopy, will increase life expectancy.

Few studies have specifically addressed the cost-effectiveness of evaluating rectal bleeding. In a predominantly older population, Fine and colleagues (28) estimated that for use as an initial test, colonoscopy cost less and was safer than flexible sigmoidoscopy. In our model,

the cost-effectiveness of evaluating the entire colon improved with increasing age. For patients 35 years of age or older, the cost-effectiveness of evaluation of the entire colon compared with evaluation by using flexible sigmoidoscopy was comparable to that of repeated screenings for colorectal cancer (1, 51, 54, 55). However, for 25-year-old patients, our model estimated that colonoscopy cost more than \$270 000 per year of life gained compared with flexible sigmoidoscopy. Thus, in the setting of limited health care resources, some people may perceive that the incremental cost-effectiveness of evaluating the entire colon is justified only for patients 35 years of age or older.

In our model, the absolute increase in life expectancy for the entire cohort was small, measured in terms of days and weeks. As is typical of cost-effectiveness analyses (56), this seemingly small benefit reflects a large benefit in small numbers of patients who avoid dying of

cancer and no measurable benefit in a large number of patients. For example, our model estimates that the prevalence of undiagnosed colorectal cancer at the time of presentation was only 1 in 11 574 patients. Despite this low prevalence of cancer at the time of bleeding, in our base-case model, a strategy of flexible sigmoidoscopy in all patients would have prevented 7.6 cases of colorectal cancer per 1000 patients over the patients' lifetime as a result of detection and removal of precancerous adenomatous polyps.

An important aspect of cost-effectiveness models is the identification of variables for which more precise estimates are needed. Our model was most sensitive to estimates of the prevalence of colonic neoplasms in patients with rectal bleeding and the rate of adenoma progression. We estimated a baseline prevalence of colonic neoplasms of 0.0432 in persons with rectal bleeding. A review of autopsy studies suggested that the prevalence of colonic neoplasms in persons 30 to 39 years of age was approximately 0.03 (26). Endoscopic studies also support our estimate (27–29). For example, Acosta and coworkers (27) found adenomatous neoplasms in 4.3% (12 of 280) of patients younger than 40 years of age with rectal bleeding or occult gastrointestinal bleeding (27). In contrast, Fine and colleagues (28) found adenomatous polyps or cancer in 19% (11 of 58) of patients younger than 40 years of age with rectal bleeding. Our assumed prevalence is therefore relatively conservative. If we have slightly overestimated the prevalence of colonic neoplasms, the magnitude of this error remains small. For example, if the true prevalence of neoplasms in the general population at 35 years of age is 0.02 instead of our estimate of 0.03, the incremental cost-effectiveness ratio comparing flexible sigmoidoscopy with no evaluation would only increase from \$2864 to \$6144 per year of life gained. Similarly, when comparing a strategy of flexible sigmoidoscopy plus barium enema to flexible sigmoidoscopy alone, the incremental cost-effectiveness ratio would only increase from \$23 918 to \$38 574 per year of life gained.

Modeling of strategies to prevent colorectal cancer requires an estimation of the natural history of benign polyps. We have assumed constant annual probabilities of transition from small to large polyps and from large polyps to locally invasive cancer. Our estimates are, again, relatively conservative compared with other models (1, 42). Our base-case model predicts that 9% and

22% of the polyps initially present will progress to invasive cancer by 10 years and 20 years, respectively. Thus, while our model appears to be sensitive to this estimate, a true transition probability lower than our base case is unlikely. Regardless, further research defining the prevalence and natural history of colonic neoplasms in this population is warranted because selection of the most cost-effective diagnostic strategy depends on these measures.

The diagnostic strategies evaluated in our model exhibit good levels of diagnostic sensitivity (1). Endoscopic tests are more sensitive at detecting small lesions than barium enema (1, 57). Most studies find barium enema or barium enema plus flexible sigmoidoscopy adequate to detect large adenomas (1, 58–60). More recently, the National Polyp Study (57) reported poor sensitivity of air-contrast barium enema, even for large polyps. The authors of that study noted that barium enema was less sensitive for adenomas in the left than in the right colon, further emphasizing the additive benefit of flexible sigmoidoscopy to barium enema. Thus, in choosing a diagnostic strategy for persons with rectal bleeding, physicians should consider the operating characteristics of the diagnostic tests as performed at a specific institution.

Our cost estimates are based on Medicare reimbursement rates and include facility fees. If procedures such as flexible sigmoidoscopy are performed without an associated facility fee, the incremental cost per year of life gained with more expensive strategies would be even greater. Similarly, in health care systems that require gastroenterology consultation before colonoscopy, flexible sigmoidoscopy or barium enema would be more cost-effective. In contrast, in health care systems that have costs lower than our estimates, the incremental cost per year of life gained would be even lower than we have calculated. We did not include the cost of initial primary care office visits because these occur before the decision model begins. However, if evaluation of the colon results in reduced rates of subsequent visits for continued bleeding, these strategies will be even more cost-effective.

Our cost estimates were somewhat lower than those used in recent cost-effectiveness models (51, 54). Use of much higher costs for sigmoidoscopy and colonoscopy, similar to those used by Frazier and coworkers (54), did not appreciably change our conclusions for persons 35

or 45 years of age. However, when costs are high, the optimal strategy for persons 25 years of age may be anoscopy followed by flexible sigmoidoscopy only if anal disease is not identified on anoscopy. Using costs similar to those used by Frazier and coworkers, we found that the incremental cost-effectiveness of anoscopy followed by flexible sigmoidoscopy (if needed) compared with no evaluation was \$21 303 per year of life gained. Performing flexible sigmoidoscopy in all 25-year-old patients instead of only patients in this age group without evidence of anal disease on anoscopy cost an additional \$59 206 per year of life gained. Thus, the most cost-effective strategy depends on patient age, the cost of the procedures, the specialist involved, and the perspective of the decision maker.

In designing the cost-effectiveness model, we elected to focus on the risk for colorectal cancer, since of the potential causes for rectal bleeding, this is the diagnosis with the greatest risk for death. We did not incorporate into our primary model all potential benefits of establishing the cause of rectal bleeding or the effect of colorectal cancer on quality of life. The quality of life of patients with colorectal cancer is generally worse than that of patients without colorectal cancer. Incorporating quality-of-life estimates would make strategies that minimize the risk for colorectal cancer appear more cost-effective. For example, in our sensitivity analyses that assumed a reduced quality of life with cancer, the incremental cost-effectiveness of evaluation with flexible sigmoidoscopy relative to no evaluation in a 35-year-old patient decreased from \$2864 to \$2734 per year of life gained. As with quality of life with colorectal cancer, had we incorporated the utility of other diagnoses (for example, colitis), evaluation of the colon would appear even more cost-effective.

Our model supports previous recommendations that persons older than 50 years of age with rectal bleeding undergo evaluation of the entire colon (10, 11, 15, 16, 28). Evaluation of younger patients with rectal bleeding can be expected to increase the average life expectancy in a cost-effective manner as well. For patients in their mid-30s and older, evaluation of the entire colon appears to yield the greatest life expectancy at an incremental cost comparable to that of other widely used screening strategies. For patients in their mid-20s and younger, flexible sigmoidoscopy alone or anoscopy followed by flexible sigmoidoscopy only in those pa-

tients without anal disease identified at anoscopy may be more cost-effective than evaluation of the entire colon. Selection of the most cost-effective diagnostic approach also depends on the sensitivity of each of the diagnostic procedures and the prevalence, distribution, and natural history of colonic neoplasms in persons with bleeding. Future research should precisely quantify the distribution and prevalence of colonic neoplasms in young patients with rectal bleeding and should evaluate the natural history of adenomatous polyps.

## APPENDIX

The prevalence of colonic neoplasms in our model was calculated as follows:

$$\begin{aligned} \text{Prevalence of neoplasms} \\ = (P_N \times (1 - P_A)) + ((RR_A \times P_N) \times P_A) \end{aligned}$$

$P_A$  = Prevalence of anal disease;  $P_N$  = Prevalence of neoplasms in persons without anal disease;  $RR_A$  = relative risk for colonic neoplasms in patients with rectal bleeding and anal disease compared with patients with rectal bleeding and no anal disease;  $RR_A \times P_N$  = prevalence of neoplasms in patients with anal disease.

The number of cancers prevented over the lifetime of a patient cohort was estimated from the Markov model. For each cycle of the model, we determined the probability that cancer would be diagnosed in a patient. These probabilities were then summed to determine the cumulative probability of newly diagnosed cancer over an average patient's lifetime. This probability was then converted to the cumulative incidence for a cohort of 1000 patients by multiplying the probability estimate by 1000. The difference in the cumulative incidences for patients in the flexible sigmoidoscopy group and the no evaluation group represents the number of cancers prevented over the lifetime of 1000 patients by using the strategy of flexible sigmoidoscopy.

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