REVIEW

The Evaluation of Rectal Bleeding in Adults

A Cost-effectiveness Analysis Comparing Four Diagnostic Strategies

Elizabeth Allen, MD,[1] Christina Nicolaidis, MD, MPH,[2] Mark Helfand, MD, MPH[1]

[1]Portland Veterans Affairs Medical Center, Portland, OR, USA; [2]Oregon Health & Science University, Portland, OR, USA.

BACKGROUND: Though primary care patients commonly present with rectal bleeding, the optimal evaluation strategy remains unknown.

OBJECTIVE: To compare the cost-effectiveness of four diagnostic strategies in the evaluation of rectal bleeding.

DESIGN: Cost-effectiveness analysis using a Markov decision model.

DATA SOURCES: Systematic review of the literature, Medicare reimbursement data, Surveillance, Epidemiology, and End Results (SEER) Cancer Registry.

TARGET POPULATION: Patients over age 40 with otherwise asymptomatic rectal bleeding.

TIME HORIZON: The patient's lifetime.

PERSPECTIVE: Modified societal perspective.

INTERVENTIONS: Watchful waiting, flexible sigmoidoscopy, flexible sigmoidoscopy followed by air contrast barium enema (FS+ACBE), and colonoscopy.

OUTCOME MEASURES: Incremental cost-effectiveness ratio.

RESULTS OF BASE-CASE ANALYSIS: The incremental cost-effectiveness ratio for colonoscopy compared with flexible sigmoidoscopy was $5,480 per quality-adjusted year of life saved (QALY). Watchful waiting and FS+ACBE were more expensive and less effective than colonoscopy.

RESULTS OF SENSITIVITY ANALYSES: The cost of colonoscopy was reduced to $1,686 per QALY when age at entry was changed to 45. Watchful waiting became the least expensive strategy when community procedure charges replaced Medicare costs, when age at entry was maximized to 80, or when the prevalence of polyps was lowered to 7%, but the remaining strategies provided greater life expectancy at relatively low cost. The strategy of FS+ACBE remained more expensive and less effective in all analyses. In the remaining sensitivity analyses, the incremental cost-effectiveness of colonoscopy compared with flexible sigmoidoscopy never rose above $34,000.

CONCLUSIONS: Colonoscopy is a cost-effective method to evaluate otherwise asymptomatic rectal bleeding, with a low cost per QALY compared to other strategies.

KEY WORDS: rectal bleeding; hematochezia; cost-effectiveness analysis; diagnosis; colorectal cancer.
DOI: 10.1111/j.1525-1497.2005.40077.x
J GEN INTERN MED 2005; 20:81–90.

Rectal bleeding is a common symptom, with a prevalence of 14% to 19% in adults.[1–4] Most patients bleed from benign sources such as hemorrhoids and diverticula, but others have serious colorectal disease including colon cancer, adenomatous polyps, and inflammatory bowel disease (IBD).

Accepted for publication July 1, 2004

The authors have no conflicts of interest.

Address correspondence and requests for reprints to Dr. Allen: Portland VA Medical Center, P3-Med, P.O. Box 1034, Portland, OR 97207 (e-mail: allenel@ohsu.edu).

Colon cancer is the third leading cause of cancer-related death in this country.[5] The majority of medical societies recommend some form of colon cancer screening for asymptomatic adult patients over age 50. The evaluation of rectal bleeding is different from screening because the risk of serious disease is higher and it is unclear whether early diagnosis and treatment of serious disease results in improved mortality once gross bleeding has occurred.

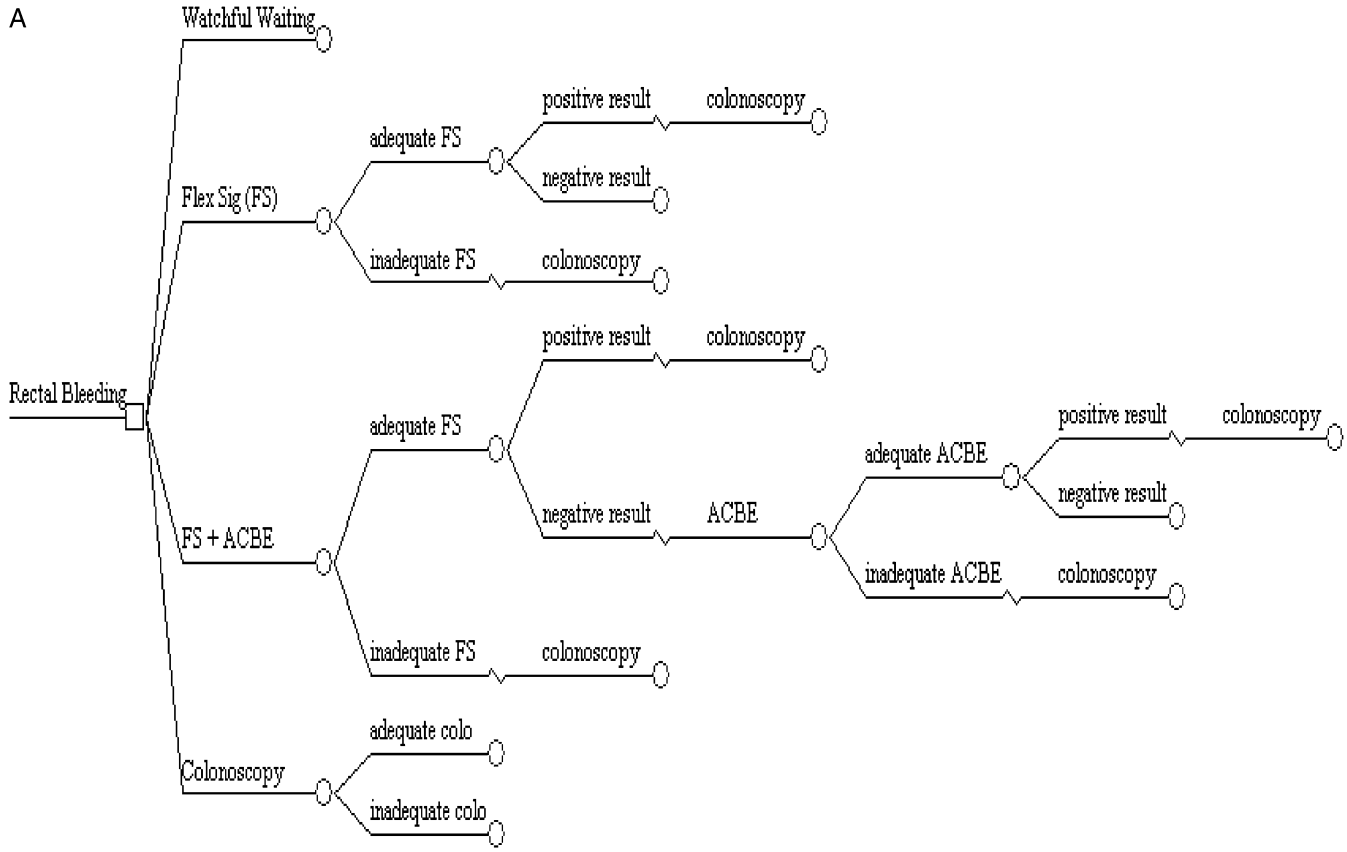
The optimal evaluation strategy for rectal bleeding is unknown. Neither historical information nor the presence or absence of hemorrhoids has been shown to reliably differentiate benign from serious disease.[6–11] Fecal hemoccult testing is not a viable evaluation option for these patients as by definition they have observed blood in or on their stools. Potential strategies for investigation include watchful waiting, flexible sigmoidoscopy, flexible sigmoidoscopy followed by air contrast barium enema, or colonoscopy. Each of these strategies carries with it cost, discomfort, risk for complication, and a chance for false positive and negative results. Ultimately the choice of strategy depends on whether or not making an accurate diagnosis of serious disease will prolong life at an acceptable cost.

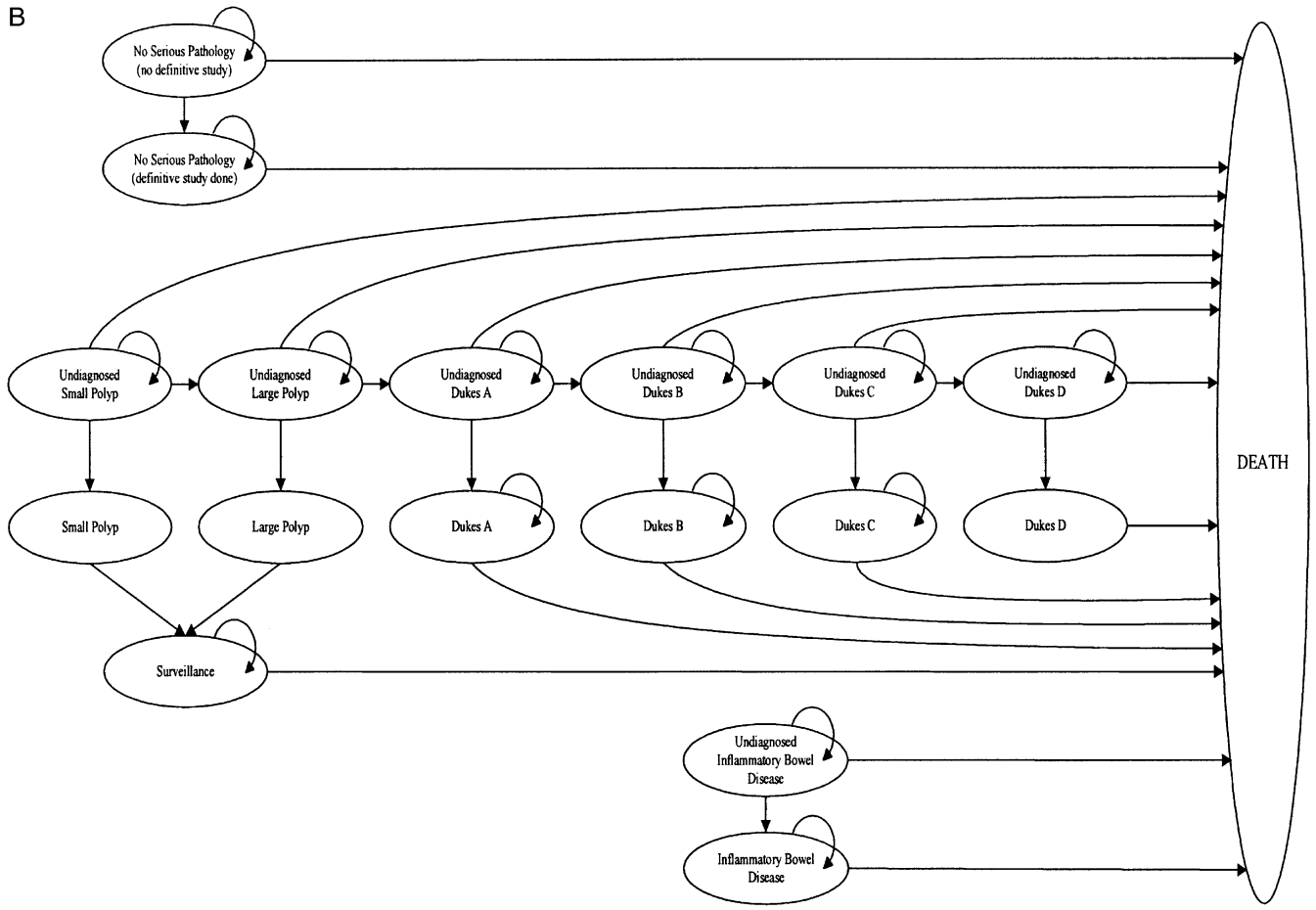
Little is known about the relative cost implications of the evaluation strategies for patients over the age of 40 with rectal bleeding. Our objective was to compare the cost-effectiveness of four commonly employed diagnostic strategies for the evaluation of rectal bleeding.

METHODS

Model Overview

We developed a Markov decision model (Fig. 1) to simulate the natural history of patients with rectal bleeding. An explanation of the disease states included in the model is available in Appendix 1 (available online at http://www.blackwellpublishing.com/products/journals/suppmat/jgi40077/jgi40077.htm). The base case consisted of a 55-year-old patient presenting with one or more episodes of rectal bleeding, defined as blood on toilet paper, in toilet bowl, mixed in stool, or on stool. Patients with melena were not included. The time horizon was the patient's lifetime. The patient was asymptomatic with no family or personal history of colon cancer or polyps and no screening within the last 10 years. We considered four diagnostic strategies: watchful waiting (WW), flexible sigmoidoscopy (FS), flexible sigmoidoscopy followed by air contrast barium enema (FS+ACBE), and colonoscopy. The model assumed that patients in the WW arm would only be worked up with colonoscopy if they had recurrent bleeding after 1 year. Patients in both the FS and FS+ACBE arms proceeded to colonoscopy if they had positive findings on FS, ACBE, or an incomplete exam. For FS, an incomplete exam


A
Watchful Waiting
Flex Sig (FS)
adequate FS
positive result
colonoscopy
negative result
inadequate FS
colonoscopy
Rectal Bleeding
FS + ACBE
adequate FS
positive result
colonoscopy
negative result
ACBE
adequate ACBE
positive result
colonoscopy
negative result
inadequate ACBE
colonoscopy
inadequate FS
colonoscopy
Colonoscopy
adequate colo
inadequate colo


B
No Serious Pathology (no definitive study)
No Serious Pathology (definitive study done)
Undiagnosed Small Polyp
Undiagnosed Large Polyp
Undiagnosed Dukes A
Undiagnosed Dukes B
Undiagnosed Dukes C
Undiagnosed Dukes D
DEATH
Small Polyp
Large Polyp
Dukes A
Dukes B
Dukes C
Dukes D
Surveillance
Undiagnosed Inflammatory Bowel Disease
Inflammatory Bowel Disease

was defined as visualization of less than 45 cm of the colon. For ACBE, it was defined as inability of the patient to tolerate the exam or films of sufficiently poor quality as to preclude interpretation. Discovery of adenomatous polyps, colorectal cancer, or IBD constituted a positive exam. In the FS+ACBE arm a negative FS was followed by an ACBE.

Model Estimates

We conducted a systematic review of the literature to estimate the prevalence of serious disease in patients with rectal bleeding and the accuracy of the diagnostic tests being considered in each of the strategies. The methods used to perform this review are described in Appendix 2 (available online at http://www.blackwellpublishing.com/products/journals/suppmat/jgi/jgi40077/jgi40077.htm). Appendix 3 (available online at www.jgim.org) details the results of each of these systematic reviews. When possible, we pooled data using a random-effects model and based point estimates for the base-case scenario on these pooled data. In cases where pooling was not possible, we based point estimates for the base-case scenario on data from an expert panel review.[5] Ranges around point estimates reflect all values we identified in the literature even if the studies did not meet inclusion criteria for the systematic review. Table 1 outlines our base-case probability estimates, range around these estimates, and sources included in the model. We assumed that patients without serious disease had an annual chance of recurrent rectal bleeding of 5% and underwent colonoscopy if they had never successfully completed one. Given uncertainty about rates of recurrent bleeding, we ranged this percentage from 1% to 30% in the sensitivity analysis. Patients diagnosed with small adenomatous polyps (polyps <1 cm without villous or high-grade dysplastic features) were assumed to have a surveillance colonoscopy every 5 years and those with large adenomatous polyps (≥ 1 cm or with villous or high-grade dysplastic features) every 3 years. Surveillance continued life long.

We defined serious disease as colorectal cancer, adenomatous polyps of any size, and IBD. We estimated the probability of serious disease in adult patients over the age of 40 presenting to their primary care providers with rectal bleeding from 6 prospective studies.[6,7,9–12] Patients with anorectal disease such as hemorrhoids and fissures and those with diverticula were not considered to have serious disease. Patients could die from other causes while in any state of the model. The probability of dying of other causes was based on 1997 life tables.[13] Patients remained in the model until age 100 or death.

Natural History

As there is no widely agreed-upon strategy to estimate how quickly adenomatous polyps progress to invasive cancers, we assumed that smaller adenomatous polyps would progress to large polyps in an average of 10 years and that large adenomatous polyps would progress to invasive cancer in an average of 10 years.[5,14–20] We ranged average progression time from 5 to 15 years in the sensitivity analysis. Once invasive cancer was present we assumed average transition times of 2 years, 1 year, and 1 year between Dukes A, B, C, and D cancers, respectively, in undiagnosed patients.[14–16] Mortality within each stage of cancer was estimated from the Surveillance, Epidemiology, and End Results (SEER) cancer registry. We did not take into account the development of new polyps over time, and thus we modeled only the effects of the diagnostic strategies on disease present at the time of initial evaluation.

FIGURE 1. Overview of model. (A). The Markov decision model depicts the four diagnostic strategies a patient with rectal bleeding could potentially undergo. (B). Disease states at entry to the model and progression over time. Patients enter with the undiagnosed version of their disease state and can stay in that state and be diagnosed at a later date, progress to the next most advanced disease state and be diagnosed at that time, be diagnosed initially and appropriately treated, or die from other causes. See Appendix 1 (available online at http://www.blackwellpublishing.com/products/journals/suppmat/jgi/jgi40077/jgi40077.htm).

Diagnostic Strategies

When available, we obtained sensitivity and specificity estimates as well as completion rates for each of the tests based on a review of prospective diagnostic studies in patients with rectal bleeding. For ranges around these estimates we used all information we could find in the literature. In the FS+ACBE arm, we considered the sensitivity and specificity of FS and ACBE separately so as to allow a patient with an inadequate or positive FS to go straight to colonoscopy without first getting an ACBE. As in other cost-effectiveness analyses,[21,22] we assumed that patients with missed cancers, polyps, or IBD would ultimately become symptomatic, prompting further diagnostic evaluation by colonoscopy. We estimated that 90% of polyps would be diagnosed within 7 years, and 90% of Dukes A, B, C, and D cancers by 2, 2, 1, and 1 years, respectively. We estimated that 90% of patients with IBD would be diagnosed within 2 years.

Costs

We adopted a modified societal perspective[21] (Lewis 2002) in that all direct medical costs were considered regardless of who incurred them. We did not include indirect costs. Costs relating to testing and treatment are outlined in Table 1. Cost differences between diagnostic strategies result either from the cost of tests and their complications or from the variation in treatment costs due to a delay in diagnosis. We did not consider the cost of other care that may have ensued from missed or undiagnosed serious disease. In the primary analysis, we estimated procedural costs using the 2001 Medicare fee schedule to be consistent with recommendations from the Panel of Cost-effectiveness in Health and Medicine[23–25] and other cost-effectiveness analyses on colon cancer screening.[22,26,27] We obtained estimates for the cost of colorectal cancer treatment from a study using 1990–1994 data from the SEER-Medicare linked database[28] and adjusted them to 2001 dollars using the Medical Care Consumer Price Index from the U.S. Bureau of Labor and Statistics. We performed an alternate scenario analysis to reflect charges for procedures performed in the community setting. These charge estimates were derived from an average of professional and facility fees for procedures performed in 3 hospital systems in our own community. We also performed an alternate scenario analysis using costs of cancer care in the managed care setting.[28–30] Because it is unlikely that patients with early-stage cancers (Dukes A and B) will incur yearly costs related to their cancer throughout their lifetime, we performed a sensitivity analysis in which the cost incurred by these patients was that of

Table 1. Model Assumptions

	Base Case	Sensitivity Analysis Range	References
Causes of rectal bleeding in patients >40 years			
Polyp, %	16	0.7–25.2	(7, 9–12)
Large (≥1 cm)	30	20–50	(8, 11, 21, 43, 44)
Small (<1 cm)	70	59–80	(8, 11, 21, 43, 44)
Colorectal cancer, %	7	0–11.5	(7, 9–12)
Dukes A	47	8–47	(9–11)
Dukes B	20	20–46	(9–11)
Dukes C	26	26–50	(9–11)
Dukes D	7	0–15	(9–11)
IBD	8	3–16	(9–12)
Location of lesions			
Cancers in left colon, %	72	66–82	(45, 46)
Polyps in left colon, %	78	66–86	(45, 46)
Right-sided lesions with associated left-sided lesions, %	48	30–80	(45, 46)
Rate of rebleeding, %	5	1–30	
5-year colorectal cancer mortality, %			
Dukes A	11.12		(47)
Dukes B	24.25		(47)
Dukes C	42.69		(47)
Dukes D	93.69		(47)
Diagnostic test characteristics			
Sensitivity of FS for, %			
Rectosigmoid cancer	95	85–100	(5, 48–52)
Rectosigmoid polyp	85	75–98	(5, 48, 49, 51–53)
IBD	67	50–100	(42, 54)
Specificity of FS	96	92–100	(5, 10, 50, 51)
Sensitivity of ACBE for, %			
Cancer	83	60–100	(5, 42, 48, 49, 51, 52, 54–71)
Polyp	58	27–93	(5, 42, 48-55, 61, 68–79)
IBD	33	23–43	(42, 54, 71, 72)
Specificity of ACBE	93	78–100	(10, 51, 72, 75, 79)
Sensitivity of colonoscopy for, %			
Cancer	95	90–100	(5, 42, 56–60, 80)
Polyp	96	75–100	(5, 42, 61, 72, 73, 80, 81)
IBD	83	83–93	(42)
Procedure complication rates, %			
Colonoscopy: hemorrhage	0.007	0.0024–.046	(82–86)
Colonoscopy: perforation	0.004	0.00001–.0214	(5, 44, 83, 87–98)
Colonoscopy: mortality	0.0001	0.00005–0.0003	(5, 92)
FS: perforation	0.001	0.0001–0.05	(5, 89, 99)
FS: mortality	0.00000006	0–0.00005	(5, 44, 86, 88, 89, 91, 92)
ACBE: perforation	0.0001	0.00004–0.0002	(5, 100, 101)
ACBE: mortality	0.00002	0.000004–0.00002	(100, 101)
Procedure completion rates, %			
FS	75	65–85	(102)
ACBE	85	75–95	
Colonoscopy	90	80–100	(44, 89, 93, 103)
Cost: procedures			
FS	$152	$100–$844	2001 Medicare Physician Fee Schedule
ACBE	$288	$200–$500	2001 Medicare Physician Fee Schedule
Colonoscopy	$620	$200–$2,200	2001 Medicare Physician Fee Schedule
Polypectomy (including pathology)	$216	$150–$500	2001 Medicare Physician Fee Schedule
Costs: cancer care			
Dukes A			
Initial	$19,654	$16,680–$31,744	(28–30)
Incremental	$1,552	$200–$3,183	(28–30)
Dukes B			
Initial	$25,601	$16,680–$31,744	(28–30)
Incremental	$1,552	$200–$3,183	(28–30)
Dukes C			
Initial	$28,705	$19,182–$37,208	(28–30)
Incremental	$2,845	$2,020–$4,038	(28–30)
Dukes D			
Initial	$27,412	$21,921–$39,209	(28–30)
Incremental	$6,724	$6,000–$22,042	(28–30)
Terminal	$19,654	$17,378–$24,800	(28–30)
IBD costs	$9,415	$5,740–$12,915	(104)

(Continued)

Table 1 (continued)

	Base Case	Sensitivity Analysis Range	References
Costs: procedural complications			
Perforation	$13,598	$10,000–$50,000	(22, 27, 32, 44)
Hemorrhage	$4,561	$4,000–$8,000	(27)
Quality of life utilities			
Dukes A	0.74	0.7–0.9	(33–35)
Dukes B	0.74	0.59–0.9	(33–35)
Dukes C	0.63	0.59–0.84	(33–35)
Dukes D	0.27	0.24–0.84	(33–35)
Terminal	0.27	0.24–0.65	(33–35)
IBD	0.85	0.55–0.9	(35, 105)
Undiagnosed IBD	0.65	0.55–0.75	

IBD, inflammatory bowel disease; FS, flexible sigmoidoscopy; ACBE, air contrast barium enema.

surveillance colonoscopy alone. Costs for care of procedural complications including hemorrhage and perforation were also estimated from the literature.[22,27,31,32] All costs and effects were discounted at an annual rate of 3%.

Quality of Life

We based quality of life estimates for patients with cancer on utility valuations derived from a sample of patients who had previously undergone resection of a colorectal polyp[33] (Table 1). The range of utilities includes information derived from a study in patients who had colorectal cancer and from a review study assessing quality of life in various disease states.[33–35] Quality of life estimates for IBD incorporate values from patients with either ulcerative colitis or Crohn's disease.[35] Utility data were highly variable based on the populations studied and methods used to assess quality of life. In the sensitivity analysis, we ranged values broadly to reflect this uncertainty.

Analysis

We used Data 4.0 (TreeAge Software Incorporated, Williamstown, MA) to perform the cost-effectiveness analysis. We report results as cost, effectiveness, and incremental cost-effectiveness, defined as the additional cost per quality-adjusted year of life saved as compared to the alternate strategy (QALY).

Univariate sensitivity analyses were performed on each of the variables, ranging them through all probability estimates found in the literature. When insufficient data existed in the literature we ranged variables widely to include all plausible values. We performed several types of multivariate analyses. First, we performed two-way sensitivity analyses on age with prevalence of polyps and on cost of FS with cost of colonoscopy, as these variables had the greatest impact on the results of the univariate sensitivity analyses. Second, we conducted 4 alternate scenario analyses: 1) adjusting serious disease prevalence to that seen in patients aged 40 to 49,[36] 2) using procedure charges from the community setting, 3) adjusting treatment costs to those seen in managed care, and 4) adjusting quality of life estimates to those seen in colorectal cancer survivors (Table 2).

RESULTS

Base-case Analysis

Table 3 shows the results of the base-case 55-year-old patient with rectal bleeding. The least expensive strategy was FS, followed by colonoscopy, and then FS+ACBE. The most expensive strategy was WW. Colonoscopy offered the greatest life expectancy followed by FS+ACBE and then FS alone. The incremental cost-effectiveness for colonoscopy compared to FS was $5,480 per QALY. The incremental cost-effectiveness of FS+ACBE compared to FS alone was $25,107 per QALY. Watchful waiting and FS+ACBE were dominated by colonoscopy, meaning they were more expensive and offered lower life expectancy.

Univariate Sensitivity Analyses

Table 4A shows the results of all univariate sensitivity analyses in which the incremental cost-effectiveness ratio of colonoscopy exceeded $10,000 compared to FS. High preva-

Table 2. Model Assumptions for Alternate Scenario Analyses

Incidence of serious disease in patients aged 40–49, %[36]	Small Polyps 6.25	Large Polyps 4.3	Cancer 0.4	IBD 8.2	
Procedure charges in community setting	FS $844	ACBE $290	Colonoscopy $2,200	Polypectomy $500	
Cost of cancer care in the managed care setting[30]	Dukes A Initial $16,680 Incremental $440	Dukes B Initial $16,680 Incremental $440	Dukes C Initial $19,182 Incremental $2,020	Dukes D Initial $21,921 Incremental $22,041	Terminal $17,378
QOL with cancer based on patients with colorectal cancer: HUI[34]	Dukes A 0.84	Dukes B 0.86	Dukes C 0.85	Dukes D 0.84	Terminal 0.65

IBD, inflammatory bowel disease; QOL, quality of life; HUI, health utilities index; FS, flexible sigmoidoscopy; ACBE, air contrast barium enema.

Table 3. Results of Base-case Analysis

Strategy	Cost	Effectiveness (QALY)	Incremental Cost-effectiveness Compared to FS
FS	$17.1K	14.876	
Colonoscopy	$17.2K	14.890	$5,480
FS+ACBE*	$17.3K	14.885	$25,107
Watchful wait	$17.5K	14.665	Dominated

Flexible sigmoidoscopy followed by ACBE.
QALY, quality-adjusted year of life saved; FS, flexible sigmoidoscopy; ACBE, air contrast barium enema.

lence of IBD and prolonged time to diagnosis of this disease raised the incremental cost-effectiveness ratio of colonoscopy, as did a high sensitivity of FS for polyps, a low sensitivity of FS for IBD, and maximal rates of perforation and hemorrhage during colonoscopy.

Table 4b shows the results from all univariate sensitivity analyses in which the dominance pattern changed and FS was no longer the cheapest option. As age at entry increased, the effectiveness of all invasive strategies began to decrease. By age 78, WW became the least costly strategy (referent) even though other strategies were still associated with a longer life expectancy. Flexible sigmoidoscopy cost an additional $987 per QALY compared to WW. At this older age, colonoscopy became considerably less cost-effective, with an incremental cost-effectiveness of $35,000 per QALY relative to FS. When the prevalence of polyps was minimized to less than 10%, WW once again became the cheapest strategy, with FS offering an incremental cost-effectiveness of $1,876 per QALY and colonoscopy an additional $15,168 compared to FS. When polyp prevalence was maximized, FS returned to being the cheapest strategy and the incremental cost per QALY for colonoscopy came down to $980 compared to FS. Finally, when the cost of colonoscopy was minimized to $200, this became the cheapest and most effective strategy dominating all others. At maximal colonoscopy cost, FS returned to being the cheapest option. The incremental cost-effectiveness as compared to FS was $35,953 for FS+ACBE and $33,955 for colonoscopy. Finally, when the cost of FS was maximized, colonoscopy became the cheapest and most effective strategy dominating all others. Univariate sensitivity analyses of the variables not shown did not significantly alter the results.

Multivariate Analyses

Two-way Sensitivity Analysis. Figure 2 shows the results of an analysis varying both age at entry and prevalence of polyps. The greatest predictor of cost per effectiveness was age. As age increased, the cost per effectiveness of all strategies increased. At any age, the prevalence of polyps had the greatest effect on WW. Except for the youngest cohort, FS was always more cost-effective than colonoscopy. The difference between FS and colonoscopy decreased with increasing polyp prevalence and increased with age. In the older cohorts, WW became the most cost-effective strategy at lower polyp prevalence, but this was only the case when the prevalence of polyps was less than 12% at age 75 and less than 8% at age 65. In the youngest cohort, the cost-effectiveness of colonoscopy and FS are almost identical and are always better than WW. A two-way sensitivity analysis varying the cost of colonoscopy and FS produced results that were relatively similar to those discussed in the univariate analyses.

Table 4A. Results of Univariate Sensitivity Analyses

Variable	Range	Incremental Cost-effectiveness of Colonoscopy Compared to FS
Base case		$5,480
Prevalence of IBD	2.2%	$2,738
	20%	$10,097
Time at which 90% IBD cases diagnosed	0.5 years	$1,057
	3.5 years	$10,021
Risk for perforation with colonoscopy	0.001%	$3,229
	2.14%	$15,296
Risk for hemorrhage with colonoscopy	0.24%	$4,609
	4.6%	$12,860
Sensitivity of FS for IBD	25%	$11,263
	80%	$3,415
Sensitivity of FS for rectosigmoid polyp	75%	$2,840
	98%	$10,369

FS, flexible sigmoidoscopy; IBD, inflammatory bowel disease.

Table 4B. Results of Univariate Sensitivity Analyses

Variable	Range	Incremental Cost-effectiveness Ratio			
		WW	FS	FS+ACBE	Colo
Base case		Dominated	Referent	Dominated	$5,480
Age at entry	40 years	Dominated	Dominated	Dominated	Referent
	80 years	Referent	$987	Dominated	$35,532
Prevalence of polyps	7%	Referent	$1,876	Dominated	$15,168
	27%	Dominated	Referent	Dominated	$980
Cost of colo	$200	Dominated	Dominated	Dominated	Referent
	$2,200	Dominated	Referent	$35,954	$33,955
Cost of FS	$100	Dominated	Referent	Dominated	$9360
	$844	Dominated	Dominated	Dominated	Referent

WW, watchful waiting; FS, flexible sigmoidoscopy; FS+ACBE, flexible sigmoidoscopy followed by air contrast barium enema; colo, colonoscopy.

Alternate Scenarios. In the analysis using disease prevalence data from patients aged 40 to 49 (Table 5A), the incremental cost-effectiveness of colonoscopy decreased to $1,686 per QALY compared to FS. In the analysis using procedure charges in the community setting (Table 5B), WW became the cheapest strategy followed by colonoscopy. Colonoscopy remained the most effective strategy. Both FS and FS+ACBE were dominated in this scenario. The incremental cost-effectiveness for colonoscopy compared to WW was $1,246 per QALY. Secondary analyses using cost data from the Group Health Healthcare system (Table 5C) and adjustment of quality of life data to reflect estimates obtained from cancer survivors did not significantly alter the results.

DISCUSSION

We compared four commonly used diagnostic strategies for the evaluation of patients aged 40–80 with rectal bleeding. We found FS to be the cheapest test and colonoscopy to be the

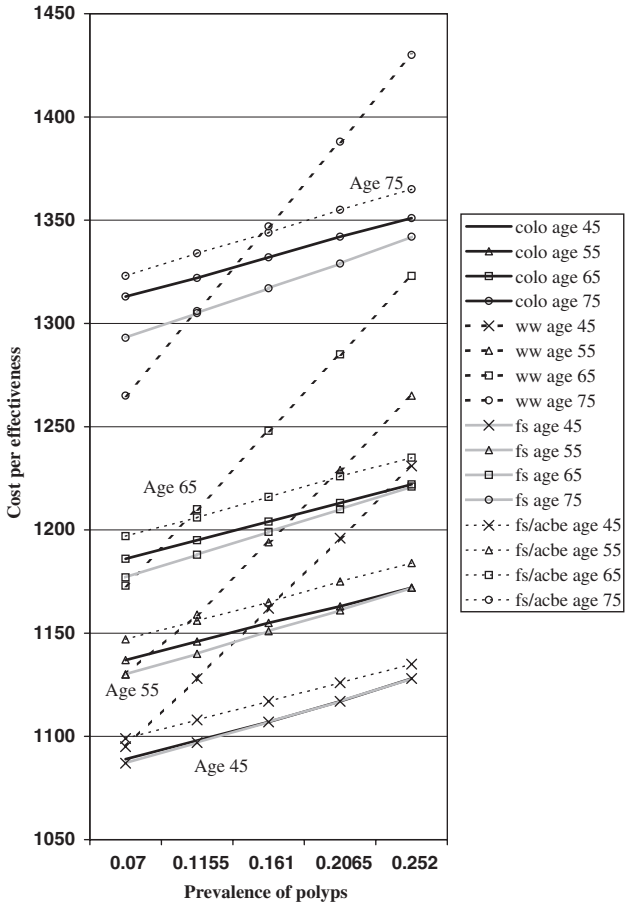


FIGURE 2. Two-way sensitivity analysis varying prevalence of polyps and age at entry. The y axis represents cost per effectiveness and the x axis represents prevalence of polyps. Separate analyses are shown for cohorts starting at ages 45, 55, 65, and 75. Results for the age 45 cohort are marked with X, age 55 with triangles, age 65 with squares, and age 75 with circles. The strategy of colonoscopy is depicted by a solid line, flexible sigmoidoscopy by a shaded line, flexible sigmoidoscopy followed by air contrast barium enema by a dotted line, and watchful waiting by a dashed line.

most effective initial test with a relatively low cost per additional year of life saved compared to FS. We found FS followed by ACBE to be both more expensive and less effective than colonoscopy.

There is currently no set standard of care for the evaluation of rectal bleeding. Though practice patterns have not been formally studied, our perception is that clinicians are often influenced by patient history and examination findings and thus employ a WW strategy in selected patients. Similarly, there appear to be significant practice variations in the use of FS, ACBE, and colonoscopy. One may use the argument that because screening with colonoscopy is cost-effective[22,26,27,37–39] it should remain so in patients presenting with rectal bleeding. However, uncertainty remains on which evaluation strategy is most cost-effective in screening patients,[40] and the latest report from the U.S. Preventive Services Task Force suggests there is insufficient evidence to recommend one strategy over another.[41] Our analysis demonstrates initial colonoscopy has a very low incremental cost per QALY compared to FS. Additionally, the strategy of WW is both more costly and less

Table 5. Results of Alternate Scenario Analyses

A. Base-case Age 45

Strategy	Cost	Effectiveness (QALY)	Incremental C/E
FS	$19.2K	18.990	
Colonoscopy	$19.2K	19.004	$1,686
FS+ACBE	$19.4K	18.999	Dominated
Watchful wait	$19.5K	18.881	Dominated

B. Procedure Charges in the Community Setting

Strategy	Cost	Effectiveness	Incremental C/E
Watchful wait	19.7K	14.665	
Colonoscopy	19.9K	14.890	$1,246
FS	20.2K	14.876	Dominated
FS+ACBE	20.5K	14.885	Dominated

C. Group Health Treatment Cost

Strategy	Cost	Effectiveness	Incremental C/E
FS	$16.1K	14.876	
Colonoscopy	$16.1K	14.890	$5,421
FS+ACBE	$16.3K	14.885	Dominated
Watchful wait	$16.3K	14.665	Dominated

QALY, quality-adjusted year of life saved; C/E, cost-effectiveness; FS+ACBE, flexible sigmoidoscopy followed by air contrast barium enema.

effective than an initial invasive strategy, except in elderly patients with very low prevalence of polyps.

Our study revealed an unexpected finding that lowering the age of subjects entering the analysis to 40–49 while simultaneously lowering serious disease rates to those seen in this age group made colonoscopy appear even more cost-effective than in older patients. We had anticipated that lower rates of serious disease in younger patients would increase the incremental cost-effectiveness ratio for colonoscopy. However, as is demonstrated in the two-way sensitivity analysis of age and polyp prevalence, age at entry has a much greater impact on the cost-effectiveness of all strategies than does polyp prevalence, presumably due to a greater potential for years of life saved in patients with a greater life expectancy. As age decreases, the incremental cost of colonoscopy compared to FS decreases. As polyp prevalence decreases the incremental cost of colonoscopy compared to FS increases but to a lesser degree. Thus, in our alternate scenario representing the cohort of patients aged 40–49, colonoscopy is even more cost-effective than in our base-case scenario. As full colonoscopic evaluation is not routinely recommended to patients with rectal bleeding in this younger age group, this finding has potential policy implications.

A recent cost-effectiveness analysis of younger patients with rectal bleeding also found that as patients approached the age of 40, full colonic evaluation became more cost-effective, but in that analysis FS+ACBE was less expensive and more effective than colonoscopy.[21] In this study, Lewis et al. found the incremental cost of colonoscopy relative to FS for a 45-year-old patient was $9,360 per year of life gained as opposed to $3,858 when comparing FS+ACBE to FS alone. The reasons for this disparity are unclear. In all our analyses, we found colonoscopy to be associated with a longer life expectancy than FS+ACBE, whereas the Lewis study found

the reverse. Because in both studies colonoscopy is more sensitive than FS or ACBE and the risk of death from colonoscopy is extremely low, one would intuitively expect that colonoscopy results in longer life expectancy. Regardless, in both studies full colonic evaluation is favored, and the incremental cost-effectiveness of colonoscopy compared to FS remains under $10,000.

Another interesting finding was the change in dominance patterns when using community procedure charge data in place of Medicare procedure cost data. In this scenario, WW became the cheapest strategy, with an incremental cost per QALY for colonoscopy compared to WW of only $1,246. While the procedural cost for colonoscopy increased by a greater absolute dollar amount than it did for FS, it was a proportionally smaller increase. As a result, the FS and FS+ACBE strategies became much more expensive and were dominated by the colonoscopy strategy. Of note, all strategies in this scenario were considerably more expensive than in the base-case scenario. It is the difference between strategies that decreased, not the overall cost per effectiveness in absolute terms.

We believe the results favoring colonoscopy are robust. We made several assumptions that biased the results against colonoscopy. We assumed very low rebleeding rates in patients without serious disease, thus minimizing the number of unnecessary colonoscopies in the WW, FS, and FS+ACBE arms. Also, patients found to have polyps were placed in a surveillance state indefinitely where they continued to accrue the cost and risks of repeated colonoscopies without any benefit because we did not model the appearance of new lesions over time. This assumption biases against colonoscopy because this strategy is most likely to put patients in the surveillance state for the longest period of time. Additionally, we did not account for the cost of increased physician visits that would result from undetected disease. As we would expect more missed disease in the strategies that do not begin with colonoscopy, colonoscopy benefits the least from this omission. Finally, we considered the sensitivity and specificity of FS and ACBE separately so as to allow patients with a positive FS to go to colonoscopy without getting an ACBE first. In our model, if both ACBE and FS are successfully completed, the sensitivity for polyps of the tests performed in series is 90%. This estimate is higher than what has been found in studies that assessed the sensitivity of the combined strategy.[10,42] Improved sensitivity for polyps would likely make the FS+ACBE strategy appear more effective than it actually is.

This study has several limitations. First, while we systematically sought the best available evidence, we had no reliable information on the natural progression of disease, rebleeding rates, and time to diagnosis of missed disease. To compensate, we ranged our estimates very broadly across all values that seemed plausible. The sensitivity analysis demonstrated that there was no appreciable change in our basic conclusion even at the extremes of the estimates. Second, we did not include indirect costs of procedures and cancer care, which may have biased the model in favor of colonoscopy. Third, it is unlikely that a physician in practice would relegate all adult patients presenting with rectal bleeding into a WW strategy. Rather, based on history, physical, and anoscopy findings, the decision to pursue invasive work-up would be made for some patients and not for others. A more accurate reflection of this process would be a strategy in which those patients found to have hemorrhoids or fissures on anoscopy were treated with conservative measures and only evaluated invasively if symptoms persisted. Those without findings on anoscopy would go on to immediate work-up. However, there is a considerable body of information suggesting that historical information and results of anoscopy correlate poorly with actual findings at colonoscopy.[6–11] A patient referred for invasive evaluation based on initial clinical findings is no more or less likely to have disease than one who lacks clinical findings. Thus, distribution of patients into an early work-up versus work-up based on symptoms or anoscopy results would put equal numbers of diseased patients into each arm, mirroring what already occurs in the model.

Despite these limitations, our study has several important implications. All patients over the age of 40 presenting with rectal bleeding should have at least a partial evaluation of the colon. Colonoscopy offers additional prolongation of life at relatively low cost. These recommendations are even stronger in patients aged 40–49 as they have the most to lose from missed diagnoses. While patients at the upper end of the age spectrum have less benefit from evaluation of the entire colon, the cost per QALY is still lower than many other interventions commonly performed in this age group. In situations where colonoscopy is not readily available, FS followed by ACBE provides very similar prolongation of life expectancy at a slightly higher cost. Until the time when we have data from prospective clinical trials comparing the costs and effects of these strategies in patients with rectal bleeding, our cost-effectiveness model allows clinicians and health care payors to feel more secure in their choice of an early invasive strategy to evaluate adult patients with rectal bleeding.

Acknowledgment goes to Benjamin Chan, MS of the Division of Medical Informatics and Outcomes Research, OHSU for help with statistical work and to Som Saha, MD, MPH for help with reviewing this manuscript.

REFERENCES

1. **Nelson RL, Abcarian H, Davis FG, Persky V.** Prevalence of benign anorectal disease in a randomly selected population. Dis Colon Rectum. 1995;38:341–4.
2. **Talley NJ, Jones M.** Self-reported rectal bleeding in a United States community: prevalence, risk factors, and health care seeking. Am J Gastroenterol. 1998;93:2179–83.
3. **Crosland A, Jones R.** Rectal bleeding: prevalence and consultation behaviour. BMJ. 1995;311:486–8.
4. **Johnson DA, Gurney MS, Volpe RJ, et al.** A prospective study of the prevalence of colonic neoplasms in asymptomatic patients with an age-related risk. Am J Gastroenterol. 1990;85:969–74.
5. **Winawer SJ, Fletcher RH, Miller L, et al.** Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology. 1997;112:594–642.
6. **Mant A, Bokey EL, Chapuis PH, et al.** Rectal bleeding. Do other symptoms aid in diagnosis? Dis Colon Rectum. 1989;32:191–6.
7. **Norrelund N, Norrelund H.** Colorectal cancer and polyps in patients aged 40 years and over who consult a GP with rectal bleeding. Fam Pract. 1996;13:160–5.
8. **Segal WN, Greenberg PD, Rockey DC, Cello JP, McQuaid KR.** The outpatient evaluation of hematochezia. Am J Gastroenterol. 1998;93:179–82.
9. **Metcalf JV, Smith J, Jones R, Record CO.** Incidence and causes of rectal bleeding in general practice as detected by colonoscopy. Br J Gen Pract. 1996;46:161–4.
10. **Helfand M, Marton KI, Zimmer-Gembeck MJ, Sox HC Jr.** History of visible rectal bleeding in a primary care population. Initial assessment and 10-year follow-up. JAMA. 1997;277:44–8.

11. **Goulston KJ, Cook I, Dent OF.** How important is rectal bleeding in the diagnosis of bowel cancer and polyps? Lancet. 1986;2:261–5.
12. **Fijten GH, Muris JW, Starmans R, Knottnerus JA, Blijham GH, Krebber TF.** The incidence and outcome of rectal bleeding in general practice. Fam Pract. 1993;10:283–7.
13. **Anderson RN.** United States Life Tables, 1997. Natl Vital Stat Rep. 1999;47:1–37.
14. **Muto T, Bussey HJ, Morson BC.** The evolution of cancer of the colon and rectum. Cancer. 1975;36:2251–70.
15. **Morson BC, Bussey HJ.** Magnitude of risk for cancer in patients with colorectal adenomas. Br J Surg. 1985;72(suppl):S23–S25.
16. **Eddy DM.** Screening for colorectal cancer. Ann Intern Med. 1990; 113:373–84.
17. **Hoff G, Foerster A, Vatn MH, Sauar J, Larsen S.** Epidemiology of polyps in the rectum and colon. Recovery and evaluation of unresected polyps 2 years after detection. Scand J Gastroenterol. 1986;21:853–62.
18. **Hofstad B, Vatn M, Larsen S, Osnes M.** Growth of colorectal polyps: recovery and evaluation of unresected polyps of less than 10 mm, 1 year after detection. Scand J Gastroenterol. 1994;29:640–5.
19. **Hoff G, Larsen S.** Epidemiology of polyps in the rectum and sigmoid colon. Discriminant analysis for identification of individuals at risk of developing colorectal neoplasia. Scand J Gastroenterol. 1986;21:848–52.
20. **Stryker SJ, Wolff BG, Culp CE, Libbe SD, Ilstrup DM, MacCarty RL.** Natural history of untreated colonic polyps. Gastroenterology. 1987;93: 1009–13.
21. **Lewis JD, Brown A, Localio AR, Schwartz JS.** Initial evaluation of rectal bleeding in young persons: a cost-effectiveness analysis. Ann Intern Med. 2002;136:99–110.
22. **Wagner JL, Tunis S, Brown M, et al.** The cost effectiveness of colorectal cancer screening in average risk adults. In: Young GP, Rozen P, Levin B, eds. Prevention and Early Detection of Colorectal Cancer in Young Adults. Philadelphia, PA: W.B. Saunders; 1996.
23. **Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB.** Recommendations of the Panel on Cost-effectiveness in Health and Medicine. JAMA. 1996;276:1253–8.
24. **Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC.** The role of cost-effectiveness analysis in health and medicine. Panel on Cost-Effectiveness in Health and Medicine. JAMA. 1996;276:1172–7.
25. **Siegel JE, Weinstein MC, Russell LB, Gold MR.** Recommendations for reporting cost-effectiveness analyses. Panel on Cost-effectiveness in Health and Medicine. JAMA. 1996;276:1339–41.
26. **Khandker RK, Dulski JD, Kilpatrick JB, Ellis RP, Mitchell JB, Baine WB.** A decision model and cost-effectiveness analysis of colorectal cancer screening and surveillance guidelines for average-risk adults. Int J Technol Assess Health Care. 2000;16:799–810.
27. **Sonnenberg A, Delco F.** Cost-effectiveness of a single colonoscopy in screening for colorectal cancer. Arch Intern Med. 2002;162:163–8.
28. **Brown ML, Riley GF, Potosky AL, Etzioni RD.** Obtaining long-term disease specific costs of care: application to Medicare enrollees diagnosed with colorectal cancer. Med Care. 1999;37:1249–59.
29. **Fireman BH, Quesenberry CP, Somkin CP, et al.** Cost of care for cancer in a health maintenance organization. Health Care Financ Rev. 1997;18:51–76.
30. **Taplin SH, Barlow W, Urban N, et al.** Stage, age, comorbidity, and direct costs of colon, prostate, and breast cancer care. J Natl Cancer Inst. 1995;87:417–26.
31. **Lieberman D.** Cost-effectiveness of colon cancer screening. Am J Gastroenterol. 1991;86:1789–94.
32. **Rex DK, Lehman GA, Hawes RH, Ulbright TM, Smith JJ.** Screening colonoscopy in asymptomatic average-risk persons with negative fecal occult blood tests. Gastroenterology. 1991;100:64–7.
33. **Ness RM, Holmes AM, Klein R, Dittus R.** Utility valuations for outcome states of colorectal cancer. Am J Gastroenterol. 1999;94:1650–7.
34. **Ramsey SD, Andersen MR, Etzioni R, et al.** Quality of life in survivors of colorectal carcinoma. Cancer. 2000;88:1294–303.
35. **Tengs TO, Wallace A.** One thousand health-related quality-of-life estimates. Med Care. 2000;38:583–637.
36. **Lewis JD, Shih CE, Blecker D.** Endoscopy for hematochezia in patients under 50 years of age. Dig Dis Sci. 2001;46:2660–5.
37. **Siba S.** Experience with haemoccult screening in Hungary. A multicenter trial. Hepatogastroenterology. 1983;30:27–9.
38. **Vijan S, Hwang EW, Hofer TP, Hayward RA.** Which colon cancer screening test? A comparison of costs, effectiveness, and compliance. Am J Med. 2001;111:593–601.
39. **Frazier AL, Colditz GA, Fuchs CS, Kuntz KM.** Cost-effectiveness of screening for colorectal cancer in the general population. JAMA. 2000; 284:1954–61.
40. **Pignone M, Saha S, Hoerger T, Mandelblatt J.** Cost-effectiveness analyses of colorectal cancer screening: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2002;137:96–104.
41. **U.S. Preventive Services Task Force.** Screening for colorectal cancer: recommendation and rationale. Ann Intern Med. 2002;137:129–31.
42. **Irvine EJ, O'Connor J, Frost RA, et al.** Prospective comparison of double contrast barium enema plus flexible sigmoidoscopy v colonoscopy in rectal bleeding: barium enema v colonoscopy in rectal bleeding. Gut. 1988;29:1188–93.
43. **Church JM.** Analysis of the colonoscopic findings in patients with rectal bleeding according to the pattern of their presenting symptoms. Dis Colon Rectum. 1991;34:391–5.
44. **Lieberman DA, Smith FW.** Screening for colon malignancy with colonoscopy. Am J Gastroenterol. 1991;86:946–51.
45. **Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G.** Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med. 2000; 343:162–8.
46. **Lieberman D.** Cost-effectiveness of colonoscopy in screening for colorectal cancer; cost-effectiveness of screening colorectal cancer in the general population. Gastrointest Endosc. 2001;54:537–8.
47. **Ries LAG, Eisner MP, Kosary CL, et al., eds.** Surveillance, Epidemiology and End Results Program (SEER) Cancer Statistics Review 1975–2000. Bethesda, MD: National Cancer Institute; 2003.
48. **Kewenter J, Brevinge H, Engaras B, Haglind E.** The yield of flexible sigmoidoscopy and double-contrast barium enema in the diagnosis of neoplasms in the large bowel in patients with a positive hemoccult test. Endoscopy. 1995;27:159–63.
49. **Jensen J, Kewenter J, Asztely M, Lycke G, Wojciechowski J.** Double contrast barium enema and flexible rectosigmoidoscopy: a reliable diagnostic combination for detection of colorectal neoplasm. Br J Surg. 1990;77:270–2.
50. **Farrands PA, Vellacott KD, Amar SS, Balfour TW, Hardcastle JD.** Flexible fiberoptic sigmoidoscopy and double-contrast barium-enema examination in the identification of adenomas and carcinoma of the colon. Dis Colon Rectum. 1983;26:725–7.
51. **Jensen J, Kewenter J, Haglind E, Lycke G, Svensson C, Ahren C.** Diagnostic accuracy of double-contrast enema and rectosigmoidoscopy in connection with faecal occult blood testing for the detection of rectosigmoid neoplasms. Br J Surg. 1986;73:961–4.
52. **Saito Y, Slezak P, Rubio C.** The diagnostic value of combining flexible sigmoidoscopy and double-contrast barium enema as a one-stage procedure. Gastrointest Radiol. 1989;14:357–9.
53. **Thoeni RF, Petras A.** Detection of rectal and rectosigmoid lesions by double-contrast barium enema examination and sigmoidoscopy. Accuracy of technique and efficacy of standard overhead views. Radiology. 1982;142:59–62.
54. **Brewster NT, Grieve DC, Saunders JH.** Double-contrast barium enema and flexible sigmoidoscopy for routine colonic investigation. Br J Surg. 1994;81:445–7.
55. **Vellacott KD, Amar SS, Hardcastle JD.** Comparison of rigid and flexible fibreoptic sigmoidoscopy with double contrast barium enemas. Br J Surg. 1982;69:399–400.
56. **Beggs I, Thomas BM.** Diagnosis of carcinoma of the colon by barium enema. Clin Radiol. 1983;34:423–5.
57. **Brady AP, Stevenson GW, Stevenson I.** Colorectal cancer overlooked at barium enema examination and colonoscopy: a continuing perceptual problem. Radiology. 1994;192:373–8.
58. **Rex DK, Rahmani EY, Haseman JH, Lemmel GT, Kaster S, Buckley JS.** Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. Gastroenterology. 1997;112: 17–23.
59. **Strom E, Larsen JL.** Colon cancer at barium enema examination and colonoscopy: a study from the county of Hordaland, Norway. Radiology. 1999;211:211–4.
60. **Haseman JH, Lemmel GT, Rahmani EY, Rex DK.** Failure of colonoscopy to detect colorectal cancer: evaluation of 47 cases in 20 hospitals. Gastrointest Endosc. 1997;45:451–5.
61. **Fork FT.** Double contrast enema and colonoscopy in polyp detection. Gut. 1981;22:971–7.
62. **Anderson N, Cook HB, Coates R.** Colonoscopically detected colorectal cancer missed on barium enema. Gastrointest Radiol. 1991;16:123–7.

63. **Bolin S, Franzen L, Nilsson E, Sjodahl R.** Carcinoma of the colon and rectum. Tumors missed by radiologic examination in 61 patients. Cancer. 1988;61:1999–2008.
64. **Evers K, Laufer I, Gordon RL, Kressel HY, Herlinger H, Gohel VK.** Double-contrast enema examination for detection of rectal carcinoma. Radiology. 1981;140:635–9.
65. **Johnson CD, Carlson HC, Taylor WF, Weiland LP.** Barium enemas of carcinoma of the colon: sensitivity of double- and single-contrast studies. AJR Am J Roentgenol. 1983;140:1143–9.
66. **Kelvin FM, Maglinte DD, Stephens BA.** Colorectal carcinoma detected initially with barium enema examination: site distribution and implications. Radiology. 1988;169:649–51.
67. **Kelvin FM, Gardiner R, Vas W, Stevenson GW.** Colorectal carcinoma missed on double contrast barium enema study: a problem in perception. AJR Am J Roentgenol. 1981;137:307–13.
68. **Law RL, Longstaff AJ, Slack N.** A retrospective 5-year study on the accuracy of the barium enema examination performed by radiographers. Clin Radiol. 1999;54:80–3; discussion 83–4.
69. **Ott DJ, Scharling ES, Chen YM, Wu WC, Gelfand DW.** Barium enema examination: sensitivity in detecting colonic polyps and carcinomas. South Med J. 1989;82:197–200.
70. **Morosi C, Ballardini G, Pisani P, et al.** Diagnostic accuracy of the double-contrast enema for colonic polyps in patients with or without diverticular disease. Gastrointest Radiol. 1991;16:345–7.
71. **Jaramillo E, Slezak P.** Comparison between double-contrast barium enema and colonoscopy to investigate lower gastrointestinal bleeding. Gastrointest Radiol. 1992;17:81–3.
72. **Durdey P, Weston PM, Williams NS.** Colonoscopy or barium enema as initial investigation of colonic disease. Lancet. 1987;2:549–51.
73. **Thoeni RF, Petras A.** Double-contrast barium-enema examination and endoscopy in the detection of polypoid lesions in the cecum and ascending colon. Radiology. 1982;144:257–60.
74. **de Roos A, Hermans J, Shaw PC, Kroon H.** Colon polyps and carcinomas: prospective comparison of the single- and double-contrast examination in the same patients. Radiology. 1985;154:11–3.
75. **Fork FT.** Reliability of routine double contrast examination of the large bowel: a prospective study of 2590 patients. Gut. 1983;24:672–7.
76. **Rex DK, Lehman GA, Lappas JC, Miller RE.** Sensitivity of double-contrast barium study for left-colon polyps. Radiology. 1986;158:69–72.
77. **Ott DJ, Gelfand DW, Wu WC, Kerr RM.** Sensitivity of double-contrast barium enema: emphasis on polyp detection. AJR Am J Roentgenol. 1980;135:327–30.
78. **Cheong Y, Farrow R, Frank CS, Stevenson GW.** Utility of flexible sigmoidoscopy as an adjunct to double-contrast barium enema examination. Abdom Imaging. 1998;23:138–40.
79. **Winawer SJ, Stewart ET, Zauber AG, et al.** A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. National Polyp Study Work Group. N Engl J Med. 2000;342:1766–72.
80. **Hixson LJ, Fennerty MB, Sampliner RE, McGee D, Garewal H.** Prospective study of the frequency and size distribution of polyps missed by colonoscopy. J Natl Cancer Inst. 1990;82:1769–72.
81. **Rex DK, Cutler CS, Lemmel GT, et al.** Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology. 1997;112:24–8.
82. **Eckardt VF, Kanzler G, Schmitt T, Eckardt AJ, Bernhard G.** Complications and adverse effects of colonoscopy with selective sedation. Gastrointest Endosc. 1999;49:560–5.
83. **Isbister WH.** Colonoscopy—a ten year Wellington experience. N Z Med J. 1987;100:74–7.
84. **Ure T, Dehghan K, Vernava AMD, Longo WE, Andrus CA, Daniel GL.** Colonoscopy in the elderly. Low risk, high yield. Surgical Endoscopy. 1995;9:505–8.
85. **Atkin WS, Hart A, Edwards R, et al.** Uptake, yield of neoplasia, and adverse effects of flexible sigmoidoscopy screening. Gut. 1998;42: 560–5.
86. **Kewenter J, Brevinge H.** Endoscopic and surgical complications of work-up in screening for colorectal cancer. Dis Colon Rectum. 1996;39:676–80.
87. **Lieberman D.** Endoscopic screening for colorectal cancer. Gastroenterol Clin North Am. 1997;26:71–83.
88. **Cowen AE, Macrae FA.** Gastrointestinal endoscopy: an accurate and safe primary diagnostic and therapeutic modality. Med J Aust. 1992;157:52–7.
89. **Waye JD, Kahn O, Auerbach ME.** Complications of colonoscopy and flexible sigmoidoscopy. Gastrointest Endosc Clin N Am. 1996;6: 343–77.
90. **Basson MD, Etter L, Panzini LA.** Rates of colonoscopic perforation in current practice. Gastroenterology. 1998;114:1115.
91. **Damore LJ II, Rantis PC, Vernava AM III, Longo WE.** Colonoscopic perforations. Etiology, diagnosis, and management. Dis Colon Rectum. 1996;39:1308–14.
92. **Orsoni P, Berdah S, Verrier C, et al.** Colonic perforation due to colonoscopy: a retrospective study of 48 cases. Endoscopy. 1997;29:160–4.
93. **Church JM.** Complete colonoscopy: how often? And if not, why not? Am J Gastroenterol. 1994;89:556–60.
94. **Lo AY, Beaton HL.** Selective management of colonoscopic perforations. J Am Coll Surg. 1994;179:333–7.
95. **Hureau J, Avtan L, Germain M, Blanc D, Chaussade G.** [Colonic perforation during colonoscopy. 100 cases]. Chirurgie. 1992;118:703–15; discussion 715–6. French.
96. **Heath B, Rogers A, Taylor A, Lavergne J.** Splenic rupture: an unusual complication of colonoscopy. Am J Gastroenterol. 1994;89: 449–50.
97. **Waye JD, Lewis BS, Yessayan S.** Colonoscopy: a prospective report of complications. J Clin Gastroenterol. 1992;15:347–51.
98. **Ghazi A, Grossman M.** Complications of colonoscopy and polypectomy. Surg Clin North Am. 1982;62:889–96.
99. **Katon RM, Keeffe EB, Melnyk CS.** Flexible Sigmoidoscopy. Markham, Ontario: Thomas Allen & Son, Limited; 1985.
100. **Blakeborough A, Sheridan MB, Chapman AH.** Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. Clin Radiol. 1997;52:142–8.
101. **Gore RM, Levine MS, Laufer I.** Testbook of Gastrointestinal Radiology. Philadelphia, PA: W.B. Saunder; 1995.
102. **Stewart BT, Keck JO, Duncan AV, Santamaria NM, Allen P.** Difficult or incomplete flexible sigmoidoscopy: implications for a screening programme. Aust N Z J Surg. 1999;69:19–21.
103. **Freeman B, Engel JJ, Fine MS, DiVita DP.** Colonoscopy to the cecum: how often do we get there? Experience in a community hospital. Am J Gastroenterol. 1993;88:789 Letter.
104. **Hay JW, Hay AR.** Inflammatory bowel disease: costs-of-illness. J Clin Gastroenterol. 1992;14:309–17.
105. **Trallori G, Messori A.** Drug treatments for maintaining remission in Crohn's disease. A lifetime cost-utility analysis. Pharmacoeconomics. 1997;11:444–53.