

Cost-effectiveness of a Single Colonoscopy in Screening for Colorectal Cancer

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Background: A single colonoscopy at the age of 65 years has been recommended as a potential option to screen for colorectal cancer. This study compares the cost-effectiveness of 2 screening programs based on a single or repeated colonoscopy.

Methods: The cost-effectiveness of screening is analyzed with a computer model of a Markov process. A hypothetical population of 100000 subjects aged 50 years undergoes a single colonoscopy at the age of 65 years or repeated colonoscopy every 10 years starting at the age of 50. Transition rates are estimated from US vital statistics and cancer statistics and published data on polyp incidence, patient compliance, and efficacy of colonoscopy plus polypectomy in cancer prevention. Costs of screening and cancer care are estimated from the 1998 Medicare reimbursement data using the perspective of a third-party payer.

Results: Compared with no screening, the incremental cost-effectiveness ratio of a single or repeated colonoscopy amounts to \$2981 or to \$10983 per life year saved, respectively. A single colonoscopy saves most life years if done at the age of 60, but becomes most cost-effective after the age of 70. Depending on the level of compliance, repeated colonoscopies save 2 to 3 times more lives than a screening program based on a single colonoscopy.

Conclusions: A repeated colonoscopy every 10 years offers better prevention against colorectal cancer and represents a medically more desirable screening option. If high costs or low patient compliance renders this option not feasible, a single colonoscopy at the age of 65 would represent a highly cost-effective alternative.

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SEVERAL ECONOMIC analyses¹⁻⁵ have shown that screening of asymptomatic elderly subjects by colonoscopy would represent a cost-effective means to reduce mortality from colorectal cancer (CRC) in the general population. In a head-to-head comparison,⁵ colonoscopy once per 10 years was found to be more cost-effective than a screening strategy based on flexible sigmoidoscopy every 5 or 10 years and annual fecal occult blood tests. Although screening with either flexible sigmoidoscopy or fecal occult blood testing was cheaper than screening with colonoscopy, in the long run colonoscopy prevented more cancers and saved more life years. The seeming cost advantage of the 2 cheaper screening programs became negated by subsequent costs for care of cancers that the initial screening by fecal occult blood testing or flexible sigmoidoscopy failed to prevent. The cost advantage of colonoscopy over the other screening options held up under a wide range of medi-

cal and economic conditions. Even if performed every 10 years, however, screening colonoscopy of the entire adult population older than 50 years would lead to appreciable health care expenditures.^{5,6} Because of the high costs, predicted low patient compliance, and potential for complications associated with repeated colonoscopies, some researchers^{2,7,8} have recommended a 1-time only screening colonoscopy during the entire lifetime. The highest yield in life years by preventing death from CRC would be achieved if the only colonoscopy per lifetime were scheduled between the ages of 65 and 70 years.⁸ To our knowledge, the outcomes of 2 screening strategies based on a single or repeated colonoscopy have not been compared in a head-to-head comparison. The present study, therefore, aims to evaluate the cost-effectiveness of a screening program for CRC based on a single colonoscopy. The 2 screening methods, single vs repeated colonoscopy, are compared for the number of prevented CRCs and the costs spent per life year saved.

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MATERIALS AND METHODS

MARKOV MODEL

The cost-effectiveness of cancer screening is analyzed by a Markov process, using a spreadsheet (Excel; Microsoft, Redmond, Wash).⁹ Medical events are modeled as transitions of patients among a set of predefined health states, the occurrence of each transition being governed by a probability value (**Figure 1**). The circles in Figure 1 symbolize the various health states, while the arrows symbolize transition probabilities among them. The time of the analysis is divided into equal increments of 1 year, during which patients may cycle from one state to another. The initial population is composed of 100 000 subjects aged 50 years who at the start are offered the screening colonoscopy. Depending on the initial compliance rate, subjects undergo a colonoscopy or enter the pool of noncompliant persons. After a normal colonoscopy result is obtained (there is no adenomatous polyp), subjects enter a new state labeled "status postcolonoscopy." In subjects compliant with a repeated screening, a colonoscopy is scheduled every 10 years. In the case of an adenomatous polyp, surveillance colonoscopy is repeated every 3 years until adenomatous polyps are no longer found. Subjects in any Markov state can develop CRC, the probability being given by the age-specific incidence rate. The likelihood of developing cancer is reduced in subjects after a normal colonoscopy result or after a polypectomy, depending on the rate of preventive efficacy assigned to the procedure. The time for which colonoscopy plus polypectomy provide protection against CRC is equal to the screening interval. The population in each state is also subjected to the annual age-specific death rate of the US population.¹⁰ Screening by a single colonoscopy at the age of 65 years is modeled similarly to screening by multiple colonoscopies (Figure 1). However, no repeated colonoscopy is scheduled after the initial colonoscopy or after a successful polypectomy. Between the ages of 50 and 64 years and after the age of 75 years, subjects are exposed to the age-specific incidence rate of CRC without any potential protection from colonoscopy and polypectomy.

TRANSITION PROBABILITIES

The transition probabilities built into the model and their range tested in the sensitivity analyses are listed in **Table 1**. Under baseline conditions, subjects are assumed to be compliant with the screening program. In the sensitivity analyses, the compliance rates are varied within the ranges shown in Table 1. In a multicenter trial¹³ of compliance rates, 45%

of a random population accepted the offer of a screening sigmoidoscopy. Because no reliable data on colonoscopy are available, to our knowledge, compliance with the initial colonoscopy is estimated to be similar to that reported for flexible sigmoidoscopy. An 80% compliance rate for repeated colonoscopy is based on similar rates reported for repeated sigmoidoscopy and surveillance colonoscopy after polypectomy.^{11,14} The prevalence rates of adenoma per 10-year age groups are available through autopsy studies.^{12,21} An annual 1% incidence rate is calculated as the average difference between the prevalence rates of 2 consecutive age groups. The annual age-specific incidence rate of CRC is taken from published statistics of the Surveillance, Epidemiology, and End Results Program.¹⁸ The efficacy of colonoscopy in reducing the incidence of CRC is estimated from data of the National Polyp Study.¹⁴ Of all subjects with CRC, 40% are assumed to die of their disease.¹⁸

EFFECTIVENESS AND COSTS

The effectiveness of screening is measured in life years saved through prevention of death from CRC. The life years lost by the age-dependent fractions of patients dying prematurely of CRC are accumulated for each cycle during the entire expected lifetime. The life years saved through screening correspond to the difference in life years lost from cancer-related deaths between 2 Markov models with and without screening.

Medical, surgical, and diagnostic services are assigned code numbers using the physicians' *Current Procedural Terminology*²² or diagnosis-related group²³ to identify the health care resources used for each patient. The code numbers are converted into costs for each health care resource used (Table 1). The costs represent the average payments allowed for each coded procedure by the US Health Care Financing Administration during fiscal year 2000. The cost also includes the possibility of hospitalization for bleeding or perforation after endoscopy with or without polypectomy.^{15-17,24} The most recent cost estimates for the medical care of subjects with CRC range between \$40 000 and \$45 000.^{20,25} All future costs arising from screening or care of CRC and all future life years saved through screening are discounted by an annual rate of 3%.¹⁹

The incremental cost-effectiveness ratio compares each type of intervention with the previous less effective option, including a strategy of no screening. The incremental cost-effectiveness ratio is calculated as the difference in costs divided by the corresponding difference in effectiveness.^{26,27} In the present analysis, a negative incremental cost-effectiveness ratio indicates that a strategy would save lives and cost less than the comparative strategy of no screening.

RESULTS

BASELINE ASSUMPTIONS

Table 2 shows the outcomes of modeling screening programs to prevent CRC. The total number of CRCs represents all cancers to be expected during the remaining lifetime of a cohort of 50-year-old persons without screening. Under baseline conditions, screening by a single colonoscopy prevents 23% of all CRCs, compared with 75%

prevented by screening with multiple colonoscopies. The higher fraction of cancers prevented through screening with repeated vs single colonoscopy also results in more life years saved. The fewer colonoscopies in single vs repeated screening translates into fewer complications. In the repeated colonoscopy program, 85% of the total costs arise from the endoscopic procedure itself. By contrast, the endoscopic procedure contributes only 28% to the total costs of the single colonoscopy screening program. In the latter program, the largest fraction of costs stems

from care for unprevented cancer. The total costs of managing CRC increase going from no screening to single and then to repeated colonoscopy. At the same time, the effectiveness of screening, as evidenced by the number of life years saved, increases in the same order. Compared with no screening, single colonoscopy represents a cost-effective screening strategy of less than \$3000 per life year saved. Repeated colonoscopy triples the overall amount of life years saved at the added expense of \$14878 per additional life year saved compared with a single screening colonoscopy (Table 2). Compared with no screening, repeated colonoscopy is associated with an incremental cost-effectiveness ratio of \$10983. In subsequent 1-way sensitivity analyses, the outcomes of the 2 screen-

ing strategies are further evaluated by systematically varying all assumptions built into the models.

VARIATIONS OF COMPLIANCE RATES

Because the initial compliance determines how many persons enter the screening program, it influences in a linear fashion the overall number of cancers prevented and the total costs of the screening program. The incremental cost-effectiveness remains unaffected. For obvious reasons, any decrease in the repeated compliance rate affects only the program composed of multiple endoscopies. It reduces the overall number of cancers prevented and the number of life years saved through colonoscopy. The loss in compliance for test repetition makes the program of multiple colonoscopies become more similar to the program of a single colonoscopy. Because the incidence of CRC is characterized by an age-dependent increase, the yield of screening colonoscopy increases with age. The program of multiple colonoscopies initiated at the age of 50 years is especially hurt if many subjects leave the screening program after the first or second colonoscopy, before they come to benefit from the higher effectiveness of the screening program at an older age. Assuming a compliance rate of 80% with repeated colonoscopy results in an incremental cost-effectiveness ratio of \$20 533 per additional life year saved compared with a single screening colonoscopy and \$13 081 compared with no screening.

VARIATIONS OF COSTS

A lesser efficacy of colonoscopy plus polypectomy in preventing CRC reduces the overall effectiveness of both programs similarly, ie, fewer life years are saved. Because the

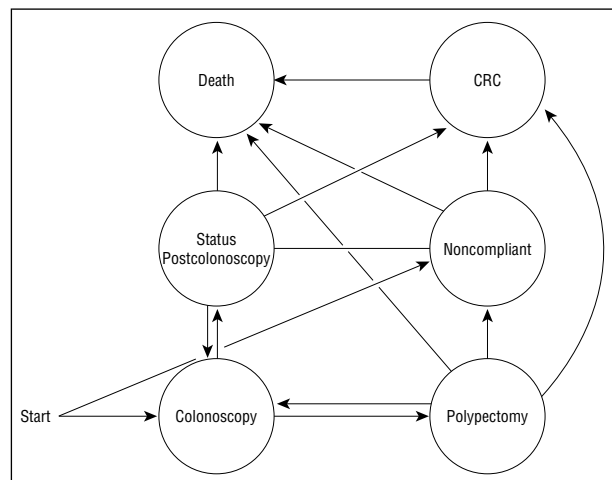


Figure 1. Markov state diagram of screening for colorectal cancer (CRC) by repeated colonoscopy. Circles indicate various health states; arrows, transitions between the various states; and noncompliant, subjects noncompliant with initial or repeated colonoscopy.

Table 1. Baseline Assumptions and Range Tested in the Sensitivity Analysis*

Variable	Baseline Model	Sensitivity Analysis	Source
Incidence of adenomas per year, %	1	0-6	Riff et al ¹¹ and Williams et al ¹²
Screening interval for colonoscopy, y	10	3-10	Winawer et al ⁴
Surveillance interval after polypectomy, y	3	1-5	Winawer et al ⁴
Compliance, %			
With initial colonoscopy	100	45	Atkin et al ¹³
With repeated colonoscopy	100	80	Winawer et al ¹⁴
Efficacy of colonoscopy in preventing CRC, %	75	50-100	Winawer et al ¹⁴
Bleeding, %			
Colonoscopy	0.15	...	Haert and Classen ¹⁵
Polypectomy	2.00	...	Waye et al ¹⁶
Perforation, %			
Colonoscopy	0.20	...	Haert and Classen ¹⁵
Polypectomy	0.38	...	Waye et al ¹⁶
Sigmoidoscopy	0.01	...	Waye et al ¹⁷
Mortality from CRC, %	40	...	Ries et al ¹⁸
Annual discount, %	3	...	Weinstein and Stason ¹⁹
Expenditures, \$†			
Colonoscopy	696	100-1000	...
Polypectomy	1004	150-1500	...
Bleeding	4360
Perforation	13 000
Medical care for incurable CRC	45 228	60 000	Lee et al ²⁰

*CRC indicates colorectal cancer; ellipses, unchanged data in the sensitivity analysis or absence of particular references for cost data.

†Includes professional fees and facility costs.

Table 2. Outcome of Screening Programs to Prevent CRC*

Variable	Screening Option		
	No Screening	Single Colonoscopy	Multiple Colonoscopies
Expected No. of CRCs without screening	5904	5904	5904
No. of prevented CRCs	0	1352	4428
Prevented/total CRCs, %	0	23	75
Life years saved	0	2604	7952
No. of colonoscopies	0	86 184	365 457
Diagnostic (without polypectomy)	0	77 566	328 911
Therapeutic (with polypectomy)	0	8618	36 546
No. of bleeding complications	0	289	1224
No. of screening-related perforations	0	188	797
No. of screening-related deaths	0	9	37
Costs, \$			
Colonoscopy	0	41 091 209	189 667 598
Care for CRC	136 452 922	103 124 901	34 113 230
Total	136 452 922	144 216 110	223 780 828
Increment of costs/saved life year†	...	2981	14 878
Increment of many colonoscopies vs none	10 983

*CRC indicates colorectal cancer; ellipses, data not applicable.

†Incremental cost-effectiveness ratio, comparing each 2 consecutive screening options.

costs of colonoscopy remain unaffected by changes in effectiveness, the incremental cost-effectiveness ratios of both programs increase. For instance, a decrease of the efficacy rate from baseline of 75% to 50% increases the incremental cost-effectiveness ratio of single and repeated screening to \$10872 and \$22909, respectively, compared with no screening.

The incremental cost-effectiveness ratio of both screening programs (compared with no screening) decreases with decreasing cost of colonoscopy. If the colonoscopy cost decreases below a certain threshold, screening saves more money from preventing cancer than the money spent on the screening procedure itself. For instance, varying the cost of colonoscopy between \$100 and \$1000 changes the incremental cost-effectiveness ratio of a single colonoscopy between -\$5664 and \$19309, the threshold for the cost per colonoscopy being \$304. Secondary to the larger number of colonoscopies involved, the program of repeated screening is more sensitive to changes in the colonoscopy cost. Varying the cost of colonoscopy to between \$100 and \$1000 changes the incremental cost-effectiveness ratio of repeated colonoscopy to between -\$2086 and \$35661. The threshold cost per colonoscopy is \$150. Because complications of colonoscopy make the procedure overall more expensive, changes in the incidence or the cost of complications affect the outcome as similarly as the colonoscopy cost. Secondary to their relatively infrequent occurrence, however, the overall impact of complications on the cost-effectiveness ratio is rather small.

The introduction of new and expensive chemotherapy for advanced CRCs, such as raltitrexed, irinotecan hydrochloride, and oxaliplatin, may increase the costs associated with cancer care.²⁸ As a general rule, more expensive cancer care renders prevention a more cost-effective medical option. Fewer cancers are prevented and more costs arise from cancer care in the single vs the repeated screening program. Therefore, screening with a

single colonoscopy is more sensitive to changes in the costs of cancer care than is screening with repeated colonoscopies. Assuming a higher cost of cancer care, such as \$60000 per case, decreases the incremental cost-effectiveness ratio of single colonoscopy to -\$1199 and of multiple colonoscopies to \$6779.

VARIATIONS OF SCREENING AGE

The effectiveness of any type of screening is directly correlated with the incidence of the disease for which it is designed. Because the incidence rate of CRC shows a marked age-dependent increase, the number of cancers prevented per single colonoscopy is higher in an older than a younger population of screenees. If repeated screening is started at ages older than 50, the less effective initial colonoscopy (at the age of 50) is saved at the expense of missing some CRCs affecting relatively few subjects between the ages of 50 and 60. The subsequent colonoscopies performed every 10 years will still be able to prevent most cancers that occur in the older age groups. Screening by a single colonoscopy is far more likely to lose its preventive power if scheduled too early or too late. **Figure 2** shows the relationship between the age at a single screening and the effectiveness of the program for the percentage of life years saved. The analyses are based on the assumption of a 100% compliance rate. It appears that most life years could be saved by a single colonoscopy done at the age of 60. As subjects grow older, their risk of developing CRC increases, but the benefit of cancer prevention decreases because of the concomitant decrease in life expectancy. Preventing cancer in subjects much younger than 60 may be associated with an appreciable increase in life expectancy for the individual patient, but the chance of actually being able to do so is limited by the overall low incidence rate of CRC.

Figure 3 shows the relationship between the age at screening and the incremental cost-effectiveness ra-

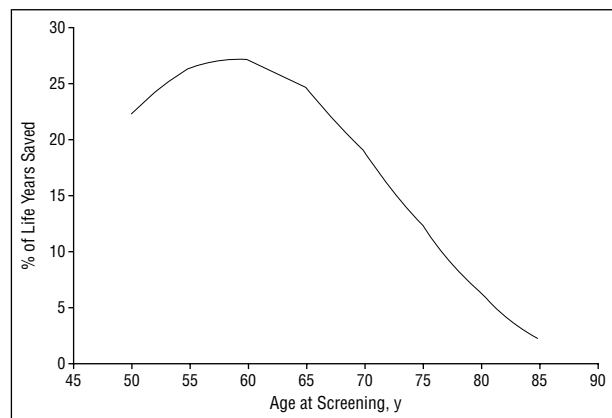


Figure 2. Influence of age at the single colonoscopy on the percentage of life years saved.

tio of a single colonoscopy screening program. The curve exhibits a steady decline that crosses the 0 line at the age of 70. The negative ratios indicate that beyond the age of 70, screening costs less than no screening. The costs spent on screening are more than outweighed by the costs saved by less cancer care. From a strictly money-saving perspective, the best age for a single screening colonoscopy lies between 75 and 80, because the screening program may actually save rather than incur costs.

COMMENT

In previous studies,¹⁻⁵ the use of colonoscopy every 10 years has been demonstrated to be a cost-effective means to prevent mortality from CRC that compares favorably with flexible sigmoidoscopy or annual fecal occult blood testing. When applied to the general population, however, colonoscopic screening every 10 years after the age of 50 becomes a costly health measure.⁵ The aim of the present economic analysis was to provide a head-to-head comparison between 2 screening programs using either a single colonoscopy once per lifetime or repeated colonoscopies every 10 years. Depending on the level of compliance, repeated colonoscopies could save 2 to 3 times more lives than a screening program based on a single colonoscopy. If third-party payers were able to provide the financial resources and subjects were willing to participate, a screening program composed of multiple colonoscopies represents the better yet more expensive alternative. Under tighter economic conditions with only limited funds available for cancer screening, a single colonoscopy between the ages of 65 and 70 offers a relatively cheap and highly cost-effective means of screening for CRC.

The same type of Markov process was used to model the impact of single and repeated colonoscopies. In the past, this model was also used to study fecal occult blood testing and flexible sigmoidoscopy.⁵ The comparisons among the different screening strategies are based on the same set of transition probabilities and cost estimates built into the model. This facilitates the direct comparisons between the various screening alternatives, because it eliminates the need to adjust for differences in the assumptions built into various economic models. To be able to compare a screening with a no screening strategy, the

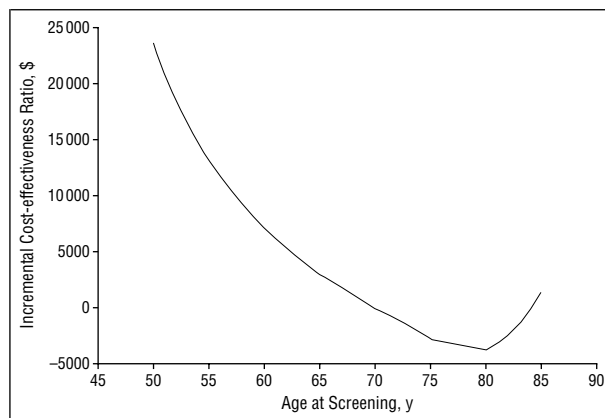


Figure 3. Influence of age at the single colonoscopy on the incremental cost-effectiveness ratio of screening compared with no screening.

cost estimates of cancer care also need to be considered by the economic model. This increases the total costs associated with each program, because each program is penalized for the cancers it fails to prevent.

A previous analysis⁸ suggested that the best age for a single colonoscopy to save most life years from death due to CRC would be between 65 and 70 years. This previous analysis looked at the gains of colonoscopy screening from a strictly medical perspective, with the primary focus on the interests of the individual subject undergoing a single screening procedure. Each remaining year lived at a different age was weighted by an age-weight function that took into account the age-dependent decline in life's social value.^{29,30} In contradistinction, the present analysis looks at the gains of a single screening colonoscopy from a societal perspective, with the primary focus on the amount of life years saved in the total population. This variable is influenced not only by the life expectancy of the individual screenee but also by the total number of subjects within the population who at each age will benefit from cancer prevention. Future gains in life years are discounted by a constant annual rate of 3%, but not by an age-dependent weight function. Despite these differences, both studies reach a similar conclusion. The greatest economic advantage results from screening after the age of 70, while the greatest medical advantage is achieved by screening at the age of 60. Screening at the age of 65 seems to provide a good compromise between the 2 different perspectives. At this age, the number of life years saved is still close to the maximum value, yet the incremental cost-effectiveness ratio is markedly less than at the age of 60. In any case, the incremental cost-effectiveness ratio of a single colonoscopy is far less than that of any other competing screening strategy.

The decision models of the present article are built on the assumption that endoscopic prevention could negate cancer-related loss in life years and that patients would fully benefit from the restored life expectancy of an average population without CRC. The models do not consider the presence of other competing medical risks in some of the subjects undergoing screening at the age of 65 to 70 years. Such subjects may already have serious heart disease, hypertension, or diabetes, which could shorten their life expectancy irrespective of CRC. If re-

relationships existed between CRC and other causes of death and patients with CRC were more likely to die of other diseases as well, they would gain less life years from endoscopic screening for CRC. Screening in general tends to identify slow-growing cancers, which pose less of a lethal threat to older subjects.³¹ Other factors, such as sex-specific compliance or a decrease in the incidence of CRC in the general population, may militate against the effectiveness of screening. Therefore, models only serve as a guide for assessing the potential outcome of a medical strategy. Decision models do not obviate the primacy of clinical data gathered through controlled clinical trials, because they cannot account for all factors that may eventually determine the cost-effectiveness of screening.

In conclusion, the present economic analysis suggests that a single colonoscopy at the age of 65 years represents a cost-effective means to screen for CRC. It is more cost-effective than fecal occult blood testing or flexible sigmoidoscopy every 5 or 10 years. Such screening is, however, less effective in saving life years than a repeated colonoscopy every 10 years. At an incremental increase in cost-effectiveness that would seem still economically feasible, repeated screening offers a much greater potential for prevention and represents a medically more desirable option. For political and economic reasons, however, repeated screening by colonoscopy every 10 years may remain an elusive goal. It also may not be accepted by the general consumer as a worthwhile means to prolong life expectancy. Under such circumstances, a single colonoscopy at the age of 65 would represent the next best alternative.

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