

The Impact of Offering Colorectal Cancer Screening

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This report summarizes estimates of health impact and cost-effectiveness that were created to assess the relative value of most of the clinical preventive services recommended by the United States Preventive Services Task Force (USPSTF) and the Advisory Committee on Immunization Practices (ACIP). This ranking of clinical prevention priorities is guided by the National Commission on Prevention Priorities (NCPP).

The results presented in this report are based on earlier analysis and were inflation adjusted to 2012 US dollars to align with other services in the Prevention Priorities project. The report has been reorganized and edited. The model itself was not updated nor rerun for this update of the report.

A. USPSTF Recommendations and screening technologies assessed

This report follows the 2008 recommendation of the USPSTF.¹ The USPSTF most recently updated its colorectal cancer screening recommendation in June 2016. The updated draft recommendation could not be incorporated into this report due to time constraints. Based upon the 2008 recommendation, we assessed screening for colorectal cancer using fecal occult blood testing (FOBT), sigmoidoscopy, or colonoscopy in adults, from ages 50-75 years. In the 2016 update, the USPSTF de-emphasized evaluation of specific screening strategies due to limited direct evidence with which to compare the net benefit of the strategies.² Simulation modeling in support of the USPSTF found small variation in CRC deaths prevented and life years saved among screening strategies.² Those simulation modeling results also indicate that screening strategies that produce greater reductions in death and life years lost to cancer generally have higher risk of harms and require more colonoscopies, thereby reducing the differences in net benefits among screening strategies.

In our evaluation of CRC screening, stool-based tests are represented by annual FOBT and direct visualization is represented by sigmoidoscopy every 5 years and colonoscopy every 10 years. We evaluate screening with patient choice of screening strategy in a simulation model that allows patients to select a test with probabilities consistent with observed utilization as described below. In effect, our estimates represent a weighted average of the modeled screening strategies where the weights are the utilization probabilities representative of the US population.

B. Markov Model of USPSTF Colorectal Cancer Screening Recommendation

Our estimates of the clinically preventable burden (CPB) and cost effectiveness (CE) of colorectal cancer screening are derived from HealthPartners Institute for Education and Research's ModelHealth™: CRC, a Markov microsimulation model. For this analysis, the model simulated a cohort of 20 year olds with sex and race/ethnicity representative of the US population.

The development of this model followed three steps. First, a Markov model simulating the natural history of colorectal cancer was developed. Once the natural history model was developed, it was expanded to account for the current use of screening. Finally, this model was calibrated to SEER data on cancer incidence and mortality.

Natural History Model

We developed a 9-state discrete-time Markov model of the natural progression of colorectal cancer. In this natural history model, detection and treatment occur only in response to symptomatic presentations. A Markov model tracks the progression of individuals through various disease states over time. This model borrows from previous efforts. Figure 1 illustrates histological states and allowed transitions in the natural history model.

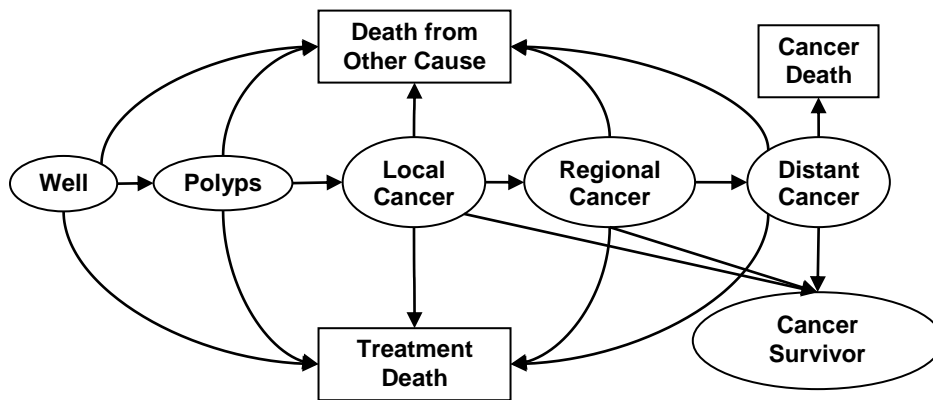


Figure 1: Natural History Model: Markovian states for the natural history of colorectal cancer.

Cycle lengths are 1 year. The model assumes a disease progression similar to previous models of colorectal cancer. All persons start in a polyp-free well state at age 20. Each year, an individual has a risk of developing a polyp in the colon. The probability of that individual developing a polyp is determined by age, gender, and race/ethnicity specific probabilities. Given the growth of a polyp, its location in the colon and type are determined. A person may have multiple polyps, and each polyp may have different characteristics and progression rates. In the model, all colorectal cancers develop from an adenomatous polyp that progressed to a local cancer. The probability of progression is determined by age-specific dwell times. There are three cancer states in the model: local, regional, and distant. Time in each cancer state following a polyp’s progression is stage-specific. Once a cancer becomes symptomatic and a diagnosis is made, the probability of survival is stage-specific. Death rates for causes other than colorectal cancer were from condition-adjusted death tables.

There is growing evidence that colorectal cancer significantly differs across population groups. These differences are seen in differences in age-specific polyp incidence as well that the types and location of polyps in the colon. Similar to other studies of differences in colorectal incidence and disease burden, we estimated age- and group-specific polyp incidence. We did not find strong evidence of group-specific differences in disease progression, and therefore these are held constant across groups in the model. We used cancer incidence and progression rates to calibrate our model to Surveillance, Epidemiology, and End Results (SEER) data with the model populated with reported screening utilization rates. Transitional probabilities between model states are listed in Table 1.

Model of Screening, Diagnosis and Treatment

From the histological state at the beginning of a cycle (e.g. at the beginning of the year) the histological state at the end of the cycle (e.g. at the end of the year) is determined based on applicable transitional probabilities. In the model these state transitions are conditioned on intra-cycle actions such as screening, diagnosis and treatment received during the year. For example, a person’s cancer status at the end of any year is partly determined by actions during that year (i.e. what treatments were received and their effectiveness). Persons who are screened have a higher likelihood of being detected at an earlier stage, and those detected in early stages have a higher survival probability than those detected at later stages. This conceptual approach is presented in Figure 2.

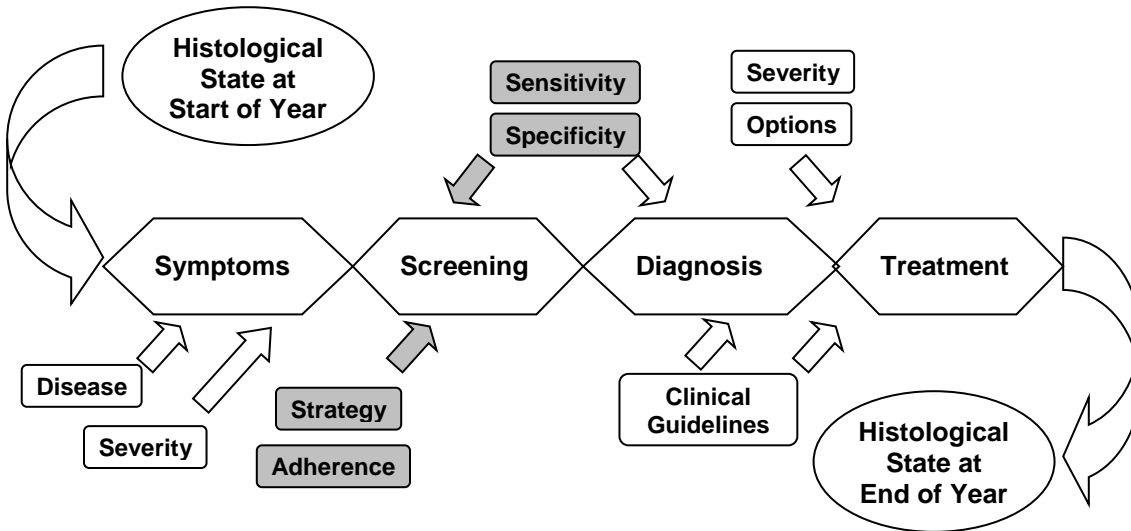


Figure 2: Within-State model of colon cancer screening: Screening recommendations are reflected by altering specific model parameters.

Four general factors impact an individual’s year-end histological state in the model: symptoms, screening, diagnosis, and treatment. The impact of each is determined by the specifics of that factor. For example, a person with distant colorectal cancer is much more likely to be symptomatic than one with local colorectal cancer. Similarly, the likelihood of being screened is dependent on the screening strategy, adherence rates and individual modifiers of adherence (age, race/ethnicity, and prior screening behavior). Further, the likelihood of a correct screening outcome (i.e. a true positive or true negative) depends on the number and location of polyps within the colon as well as the sensitivity and specificity of the screening technology. These model parameters and their sources are presented in Table 1.

**C. Model outcomes for Prevention Priorities
Clinically Preventable Burden (CPB)**

Conceptually, CPB is the burden addressed by the service multiplied by the effectiveness of the service at preventing that burden. The Prevention Priorities project expresses the prevented burden in terms of quality adjusted life years (QALYs) saved, which are a measure of the total years of additional life gained as well as the quality of those life years. A year of cancer-free life is given a higher quality of life than one with distant cancer. For each service including in the Prevention Priorities ranking, CPB is estimated as the difference in QALYs between offering the preventive service to 100% of the population compared to no utilization of the service. This provides an indication of each service’s total value rather than the value of improving delivery rates over current levels for the U.S. population. Realistic adherence rates are factored in. Therefore offering a preventive service to 100% of the population does not mean that all eligible persons are screened or immunized or that they follow-through with recommended behavior change, medication use or diagnostic testing and treatments.

Several factors impact the estimated effectiveness of the USPSTF’s recommended service regarding colorectal cancer screening. Among these are differences in disease morphology among population groups, screening delivery rates, the selection of screening technology, the sensitivity and specificity of that screening technology, the effectiveness of treatments, and assumptions made regarding a disease’s

impact on quality of life. Data regarding these parameters were obtained from published literature and are summarized Table 1. The “Base Case” column shows the best available estimate while the “Upper” and “Lower” columns cover the range over which the parameters were varied in sensitivity analysis.

Cost-Effectiveness (CE)

We used the same methods for producing estimates of CE across preventive services.³⁻⁸ These methods are consistent with the ‘reference case’ of the Panel of Cost-Effectiveness in Health and Medicine.⁹⁻¹¹ Our methods include the use of a 3% discount rate for both cost and health benefits, the exclusion of productivity losses from disease costs, and the exclusion of medical costs that are not related to the conditions prevented by the service. We use year 2005 dollars for all cost data used in model inputs; results are inflation-adjusted to 2012 dollars.

Screening Costs Direct medical costs including the costs of administering and processing the screen as well as any office time associated with that screen. Direct non-medical costs including patient time and transportation costs were collected from other published sources. Summed estimates of all these values and their sources are provided in Table 1.

Diagnostic and Confirmatory Costs Following the onset of symptoms or a positive screening using either FOBT or a flexible sigmoidoscopy, a diagnostic colonoscopy along with a polypectomy is common. The model accounts for these diagnostic colonoscopies separately from a colonoscopy screen.

Treatment Costs by Histological State

Treatments and subsequent costs are state-dependent. Rather than model the multitude of potential treatment pathways as would be done for a model focused on treatment alternatives, we constructed annual treatment costs by diagnosed histological state based on weighted averages of procedure costs. Further, we attempted to capture the differences between initial, ongoing, and terminal cancer treatments. In the model, an individual incurs initial treatment costs the first year in a cancer state. During any subsequent years in that state in which they do not die, they incur ongoing cancer costs. For those who die of cancer, they incur terminal costs in the year of death.

Utilization Rates

In the simulation model, when a patient is due for a colorectal screen (i.e. at age 50 or when the recommended interval of a prior screen has expired), they are offered screening in a clinical setting. They decide whether or not to be screened. Given a choice to screen, the choice of screening technology is based on published estimates as shown in Table 1. The model also allows for the selection of a prior screening technology to impact the current choice of screen; however, because we are aware of no data regarding correlation in choice of screening over time, our base case estimate assumes choice of screening technology is independent of previous choices.

Utilization rate estimates are based on reports from national surveys conducted at various times from 1992 – 2001. Four reports¹²⁻¹⁵ summarized screening rates from the Behavioral Risk Factor Surveillance Survey (BRFSS) in 1992, 1997, 1999, and 2001, and three reports¹⁶⁻¹⁸ summarized screening rates from the National Health Interview Survey (NHIS) in 1992, 1998 and 2000. The questions in these surveys were not consistent over time, but the responses appear to indicate a slow upward trend in use of FOBT and endoscopy since 1992. The studies using these surveys also provide information regarding different screening rates by population group as well the screening technology used by those groups. These estimates are included in the model.

D. Results

CPB Estimate

Based on the data points, assumptions, and calculations described above, systematically offering colorectal cancer screening would prevent more than 107,440 cases of colorectal cancer in a U.S. birth cohort of 4 million. In all, 59,320 deaths would be prevented, and 203,000 QALYs saved (Table 2).

Cost-Effectiveness Estimate

The two rightmost rows of Table 2 present the per-person costs and the final cost-effectiveness estimate for the base case scenario. Offering colorectal cancer screening to a hypothetical U.S. birth cohort of 4 million would result in the prevention of 107,440 cases of colorectal cancer at a discounted cost of \$3,509 per person for a final cost effectiveness ratio of \$28,738.

Sensitivity analysis

In single-variable sensitivity analysis, CPB is most sensitive to adherence to screening, the choice of screening technology, and incidence and location of polyps in the colon. CPB decreases by as much as 55% and increases by 35% within the ranges specified in Table 1. CPB is also moderately sensitive to the changes in disease progression, producing a range of 91,000 to 274,000 QALYs saved. The corresponding summary range for the CE ratio is \$15,420/QALY, to \$47,716/QALY.

F. Limitations

Our natural history model of CRC allows for the age-dependent timing, location and type of polyp occurrence and subsequent disease progression to vary according to gender and race/ethnicity. Differences due to race/ethnicity were based on published estimates of observed disease incidence and did not allow robust examination of sub-groups other than blacks and whites. In addition, recent studies indicate a strong hereditary component to CRC risk with CRC incidence linked to a series of genetic markers (i.e. Lynch Syndrome).¹⁹⁻²¹ We did not model genetic aspects of CRC disease risk.

The estimates of CPB and CE were limited to three screening strategies for which data were most complete at the time of the original analysis: FOBT alone, flexible sigmoidoscopy alone, and colonoscopy. The most recent USPSTF recommendations indicate that effective screening options also include FIT, FIT-DNA, and combined FIT and sigmoidoscopy.² In effect, the screenings that would occur using one of these other strategies were represented in our estimates by one of the three included strategies. Therefore, excluding these strategies would result in substantial bias to our estimates only if the strategies are frequently used and they have substantially different efficacy and cost-effectiveness than the included strategies. While we did find our results were sensitive to the mix of screening technologies in ranges shown in Table 1, the range of CE ratios produced in sensitivity analysis were not greater than for other services. The simulation analyses of the CISNET group in support of the USPSTF showed similar net benefit among the screening strategies,² and other CISNET analyses indicate similar cost-effectiveness among recommended strategies as determined by average CE ratios that we calculated from results presented in Table 8 of their report.²²

Finally, utilization data used in the analysis are now dated. Overall CRC screening has increased since the model was specified. Colonoscopy has become more common while the use of sigmoidoscopy has declined. The similarity of impact among the updated screening strategies in the CISNET models' results indicates that changes in the mix of strategies is not likely to substantially impact the overall estimates of CPB and CE. However, reliance on historical utilization rates as a proxy for adherence means that our

CPB is likely to be understated by about 40%. Because scoring ranges are wide in the Prevention Priorities ranking, the CPB estimate for CRC screening could double without affecting its CPB score.

Table 1: Selected Model Parameters				
Parameter	Base Case	Upper	Lower	Source
Incidence of Polyps	0.10% - 8.00%	0.05% - 4.00%	0.20% - 16%	4,23-37
Location of Polyps in Colon (varies by age, sex and race/ethnicity)				4,23-32,35-40
Ascending	28%-36%	14%-18%	56%-72%	
Transverse	14% - 16%	7%-8%	28-32%	
Descending	4% - 6%	2% - 3%	8% - 12%	
Sigmoid	28% - 32%	14% - 16%	56% - 64%	
Rectum	15% - 22%	7.50% - 11.00 %	30% - 44%	
Probability of Polyp being Adenomatous (Progressive)				4,23-32,37-44
0-64	14.00%	8.50%	34.00%	
65-74	26.00%	16.00%	54.00%	
75+	45.00%	23.50%	74.00%	
Polyp Progression to Local Cancer (yrs)	10	5	20	3,4,23,24,28,33,34,3 9,40,45-60
Local to Regional (yrs)	2	1	5	
Regional to Distant (yrs)	2	1	5	
5-yr Cancer Death Rates				4,5,28,47,61-63
Regional	10.50%	8.00%	13.00%	
Local	35.20%	30.00%	40.00%	
Distant	91.70%	90.00%	93.00%	
Screening Adherence (varies by age, sex and race/ethnicity)	29.18% - 54.18%	21.88% - 40.64%	36.47% - 67.73%	19-21,38,39,45,64-75
Screening Technologies	Base Case	Upper	Lower	
FOBT				44,56,76-87
Polyp Sensitivity	10.00%	8.00%	12.00%	
Cancer Sensitivity	60.00%	48.00%	72.00%	
Specificity	90.00%	80.00%	100.00%	
Screening Cost*	\$40	\$20	\$60	
Sigmoidoscopy				44,50,56,76-78,88-93
Polyp Sensitivity	86.00%	68.80%	100.00%	
Cancer Sensitivity	95.00%	90.00%	100.00%	
Specificity	98.00%	95.00%	100.00%	
Screening Cost*	\$300	\$150	\$450	
Colonoscopy				44,56-58,76-78,83,94-99

Polyp Sensitivity	90.00%	80.00%	100.00%	
Cancer Sensitivity	98.00%	90.00%	100.00%	
Specificity	98.00%	95.00%	100.00%	
Screening Cost*	\$550	\$200	\$1,000	
Risk of Non-Fatal Complication	0.30%	0.20%	0.40%	20,70,71,97,100-110
Cost*	\$8,000	\$4,000	\$12,000	
Risk of Fatal Perforation	0.01%	0.00%	0.01%	20,70,71,88,97,100-111ssssss
Cost*	\$10,000	\$12,000	\$8,000	
Utilization of Screening Technologies				13-16,18,56,87,112-145
FOBT: Varies by age, sex, and race/ethnicity	31.82% - 44.76%	23.87% - 33.57%	39.78% - 55.95%	
Sigmoidoscopy: Varies by age, sex, and race/ethnicity	16.97% - 20.51%	12.73% - 15.38%	21.22% - 25.64%	
Colonoscopy: Varies by age, sex, and race/ethnicity	39.60% - 47.86%	29.70% - 35.90%	49.51% - 59.83%	
Impact of Previous Choice on Current Choice of Screen (Odds Ratio)	<i>Assumed</i>			
FOBT	1	3	0.5	
Sigmoidoscopy	1	3	0.5	
Colonoscopy	1	3	0.5	
Treatment Costs*				39,40,56,146-163
Diagnostic Colonoscopy with Polypectomy	\$1,000	\$500	\$1,500	
Localized Cancer				
Initial	\$25,000	\$18,750	\$31,250	
Ongoing	\$2,500	\$1,875	\$3,125	
Regional Cancer				
Initial	\$44,000	\$33,000	\$55,000	
Ongoing	\$3,100	\$2,325	\$3,875	
Distant Cancer				
Initial	\$60,000	\$45,000	\$75,000	
Ongoing	\$10,000	\$7,500	\$12,500	
Terminal Care Costs	\$61,000	\$45,750	\$76,250	
Quality of Life Weights				164,165
Localized Cancer	0.79	0.85	0.65	
Regional Cancer	0.56	0.65	0.45	
Distant Cancer	0.48	0.60	0.35	
Cancer Remission	0.90	1	0.75	
Discount Rate**	3%	1%	5%	
*Cost inputs are expressed in 2005 US dollars. **Costs and QALYs are discounted in calculating CE ratios; QALYs are not discounted in calculating CPB.				

Table 2: Results of Markov Model of Colorectal Cancer Screening					
	Colorectal Cancer Cases Prevented	Deaths Prevented	CPB (QALYs Saved)	Per Person Costs*	CE Ratio*
Offering CRC screening to a US birth cohort	107,440	49,320	203,280	\$3,509	\$28,738
*Cost and CE ratio results are inflated in 2012 US dollars. **Costs and QALYs are discounted in calculating CE ratios; QALYs are not discounted in calculating CPB.					

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