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Cost-effectiveness analysis of chromoendoscopy for colorectal cancer surveillance in patients with ulcerative colitis

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Abstract

Background—Recent studies report that the risk of colorectal cancer (CRC) among patients with ulcerative colitis (UC) may be lower than previously estimated. Although white-light endoscopy (WLE) with random biopsies is recommended for dysplasia detection in patients with UC, several studies reported increased detection of dysplasia by chromoendoscopy.

Objective—To analyze the cost effectiveness of chromoendoscopy relative to WLE or no endoscopy for CRC surveillance in patients with UC.

Design—Decision-analytic state-transition (Markov) model with Monte Carlo simulation.

Setting—To simulate the clinical course of chronic UC, we estimated dysplasia and CRC incidence and progression, endoscopic test characteristics, stage-specific mortality rates, and costs from published literature and Medicare reimbursement data.

Patients—Patients from a population-based age distribution with ulcerative colitis for 8 years.

Intervention—We compared 3 different strategies at various surveillance intervals: chromoendoscopy with targeted biopsies, WLE with random biopsies, and no surveillance. The robustness of the model was assessed by using probabilistic sensitivity analysis. One-way sensitivity analyses were performed to evaluate individual variables, and 3-dimensional analysis was used to examine the effects of varying screening intervals.

Main Outcome Measurements—Incremental cost-effectiveness ratio (ICER).

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Results—Chromoendoscopy was found to be more effective and less costly than WLE at all surveillance intervals. However, compared with no surveillance, chromoendoscopy was cost effective only at surveillance intervals of at least 7 years, with an ICER of \$77,176. Chromoendoscopy was the most cost effective strategy at sensitivity levels >0.23 for dysplasia detection and cost <\$2200, regardless of the level of sensitivity of WLE for dysplasia detection. The estimated population lifetime risk of developing CRC ranged from 2.5% (annual chromoendoscopy) to 5.9% (chromoendoscopy every 10 years).

Limitations—Estimates used for the model are based on best available data in the literature.

Conclusion—Chromoendoscopy is both more effective and less costly than WLE and becomes cost effective relative to no surveillance when performed at intervals of 7 years.

Individuals with ulcerative colitis (UC) have an increased likelihood of developing colorectal cancer (CRC). U.S. guidelines recommend initial screening colonoscopy 8 years after the onset of UC symptoms, with surveillance endoscopies every 1 to 2 years to detect dysplasia.¹ Current dysplasia surveillance relies on white-light endoscopy (WLE) with random biopsies throughout the colon and targeted biopsies of macroscopically suspicious lesions. The presence of high-grade dysplasia (HGD) typically prompts a recommendation for total proctocolectomy to prevent progression to CRC. Although patients with low-grade dysplasia (LGD) alone often undergo surgery, there remains controversy as to whether such patients can be managed by more intensive surveillance.^{1,2} Moreover, recent studies suggest that the incidence of CRC among patients with UC may be more modest than previously estimated.³⁻⁵

Based on evidence demonstrating its higher sensitivity for detecting dysplasia,¹ chromoendoscopy with dye-targeted biopsies is recommended by most guidelines as an alternative to WLE for surveillance. In clinical practice, widespread use of chromoendoscopy has been constrained by the perceived need for additional training, higher costs, and longer procedure times.⁶ However, a formal cost-effectiveness analysis comparing chromoendoscopy with WLE has not been conducted. Moreover, prior decision analyses assessing the cost effectiveness of endoscopic surveillance in patients with UC have relied on estimates of CRC incidence developed more than 10 years ago.⁷⁻⁹

Thus, we analyzed the cost effectiveness of chromoendoscopy relative to WLE or no endoscopy for surveillance in patients with UC, taking into account recent, more conservative estimates of the risk of CRC among patients with UC.

METHODS

Model design

We created a decision-analytic state-transition (Markov) model with Monte Carlo simulation by using TreeAge Pro 2009 (TreeAge, Williamstown, Mass). Patients could enter 1 of 3 pathways: no surveillance (natural history), WLE, or chromoendoscopy. Health states included chronic UC, chronic UC with dysplasia, post-colectomy, CRC, and death (Fig. 1). Possible causes of death included baseline mortality or mortality related to colonoscopy, surgery, or CRC. The Markov cycle length was 1 year. The simulation followed patients

from a population-based age distribution⁵ with an 8-year history of UC to age 90 or death, whichever occurred first. We did not differentiate between pancolitis and left-sided colitis because current guidelines are consistent for both timing and frequency of surveillance for both conditions.¹ Base case values and ranges for transition probabilities, costs, and utilities (Table 1) were taken from a PubMed electronic database search of English-language studies published between January 1, 1992 and December 31, 2012 by using the key words “dysplasia,” “colorectal cancer,” “inflammatory bowel disease,” “ulcerative colitis,” “chromoendoscopy,” “chromoscopy,” “white light endoscopy,” “endoscopy,” and “surveillance.”

Risk of colorectal cancer

For our primary analysis, we modeled the risk of CRC in patients with UC based on the recent meta-analysis of population-based cohorts by Jess et al,⁴ which estimated median cumulative incidences of 2% at 15 years, 3% at 20 years, and 4% at 25 years of disease (Table 1). We assumed that the risk of CRC beyond 25 years of disease was equivalent to 4% at 25 years of disease based on the lack of data over this long-term follow-up. We additionally performed sensitivity analyses by using the Eaden et al⁸ historically higher cumulative CRC incidence estimates of 2% at 10 years, 8% at 20 years, and 18% at 30 years of disease.

Surveillance endoscopy

For our primary analysis, we modeled annual and biennial surveillance as well as surveillance intervals ranging up to 10 years. We estimated test characteristics for WLE and chromoendoscopy by using recently published studies focused on UC and surveillance.^{10,11} For this model, we set the base-case sensitivity of high-definition WLE for dysplasia at 0.695, within the range of previously reported estimates.^{12–16} We limited our analysis to the management of flat dysplasia and dysplasia-associated lesions or masses because studies suggest that the management of adenoma-like masses depends on the presence of coexistent dysplasia elsewhere in the colon.^{17,18} To address differences in the likelihood of each subtype progressing to cancer, we performed sensitivity analyses varying the overall rates of progression from dysplasia to cancer. We assumed that patients diagnosed with high-grade dysplasia (HGD) received total proctocolectomy. Consistent with published practice patterns, patients with low-grade dysplasia (LGD) received either total proctocolectomy (60%) or surveillance every 6 months (40%).^{1,19} Based on available data, we assumed (1) no spontaneous regression of detected dysplasia, (2) similar sensitivity and specificity of chromoendoscopy and WLE for detection of invasive CRC,²⁰ and (3) similar rates of progression to CRC in chromoendoscopy-detected and WLE-detected dysplasia.

We estimated the CRC stage distribution at diagnosis based on Herrinton et al.³ Patients with false-positive CRC detected by colonoscopy were assumed to have subsequent negative CRC staging evaluations but did proceed to colectomy. Patients with false-negative surveillance examinations for CRC were assumed to eventually develop symptoms or signs and to be diagnosed with CRC within 1 year. Based on recommendations from the U.S. Panel on Cost Effectiveness,^{21,22} our analysis was performed from the societal perspective, by using surveillance adherence rates of about 74%.^{23,24}

Colectomy

We modeled colectomy for the following clinical indications: UC flare refractory to medical management, HGD detected by surveillance, diagnosis of CRC, or perforation related to endoscopy.²⁵ Because some patients with dysplasia, particularly LGD, do not undergo total proctocolectomy,¹⁹ we assumed that such patients returned to surveillance colonoscopy. Costs for colectomy, including the 6-month postoperative period, were used to account for various postoperative morbidities.²⁶

Adverse events from colonoscopy or colectomy

We included costs of acute adverse events from colonoscopy or colectomy, including morbidity and mortality.^{7,27,28} Aggregated colonoscopy adverse events included cardiopulmonary events, bleeding, and other morbidities.²⁹ Given underlying UC, we assumed that endoscopic perforations resulted in proctocolectomy rather than segmental colectomy. We assigned the same estimates for mortality probability from emergent colectomy for perforation as for UC flare.²⁷ We estimated 1-time additional costs and 1-month tolls on health state utility associated with endoscopic or surgical adverse events to account for decreased quality of life in the immediate post-procedure period (Table 1). The probability of death related to other causes among patients with UC was consistent across all Markov states.³

Health utility states

We derived utilities for different health states from previously published literature listed in Table 1.^{30–32} All utilities were discounted at a rate of 3% per year.

Costs

All costs were adjusted to 2011 U.S. dollars by using the overall Consumer Price Index and discounted at a rate of 3% per year.^{33–36} We used Medicare Surveillance, Epidemiology, and End Results data to derive estimates for cancer-related costs by CRC stage.³⁴ Local CRC cost was averaged between the stage 1 and 2 estimates. We adjusted costs for a population aged <65 years by using methods of Mariotto et al.³⁵ Costs of colectomy for CRC at any stage were based on estimates in Lang et al.³⁴ We did not include friction costs (effects of lost productivity borne by others).

Presently, colonoscopy reimbursement for WLE and chromoendoscopy from the Centers for Medicare and Medicaid Services are the same. The recommended method for surveillance by WLE is 4-quadrant, random biopsies every 10 cm, in addition to targeted biopsies of macroscopically suspicious lesions.¹ Thus, we set a minimum of 8 pathology bottles as our base case for WLE. Because the number of chromoendoscopy biopsies varies according to the number of lesions visualized with dye, we set our base case as 4 bottles sent for histologic evaluation. Despite limited data regarding the length and cost of training required to perform chromoendoscopy, we assumed in our base model a relatively circumscribed training period without significant costs. For all other costs and probabilities in which ranges were not available, the range for sensitivity analysis varied between 25% below and above their average values.^{37–42}

Outcomes and data analysis

The primary outcome from a base-case analysis by using a Markov model with Monte Carlo microsimulation of 10,000 independent trials was the incremental cost-effectiveness ratio (ICER) among strategies of no surveillance, annual WLE, and annual chromoendoscopy. We also performed the same analysis at various surveillance intervals. A willingness-to-pay (WTP) threshold of \$100,000 per quality-adjusted life year (QALY) was used to determine cost effectiveness.⁴³ Probabilistic sensitivity analysis was performed by using 100-fold distribution sampling of all variables, to account for uncertainty in the model assumptions and assess the robustness of the results. The incremental cost-effectiveness scatter plots display the uncertainty of the expected incremental cost and incremental effect between two competing surveillance strategies resulting from the probabilistic sensitivity analysis. A 95% confidence ellipse is drawn in each incremental cost-effectiveness scatter plot, with the dashed line indicating the WTP threshold of \$100,000 per QALY. Finally, 3-dimensional analysis was done by using Monte Carlo microsimulation of 10,000 trials, with probabilistic sensitivity analysis with 100-fold distribution sampling of all variables in order to assess the effect of screening at various intervals. Univariate sensitivity analyses were performed on transition probabilities, costs, and utilities to analyze the impact of changes in model estimates on the preferred strategy.

RESULTS

Base-case analyses

Our primary cost-effectiveness analysis showed that annual chromoendoscopy and WLE were dominated by no surveillance, and the ICER for biennial chromoendoscopy relative to no surveillance was cost prohibitive in the setting of updated CRC estimates among patients with UC (Table 2). By using a WTP threshold of \$100,000 per QALY, chromoendoscopy became cost effective only at a surveillance interval of 7 years, with an ICER of \$77,176 (Table 2). In a competing strategy analysis, in which we compared surveillance intervals by type of endoscopy, we found that surveillance by chromoendoscopy every 10 years was the most cost-effective strategy compared with chromoendoscopy at other intervals. Likewise, surveillance by WLE every 10 years was the most cost-effective strategy compared with WLE at other intervals.

When we used the higher cumulative incidence rates of CRC of Eaden et al⁸ for all 3 strategies (no surveillance, chromoendoscopy, and WLE), chromoendoscopy continued to dominate WLE, with an ICER of chromoendoscopy against no surveillance that fell from \$157,405 with annual surveillance to \$87,935 with surveillance every 3 years.

Probabilistic sensitivity analysis

Probabilistic sensitivity analyses of endoscopic surveillance every 7 years supported findings from the base-case analyses, with chromoendoscopy dominating WLE and an ICER of \$107,929 for chromoendoscopy relative to no surveillance. Figure 2 shows the results of the acceptability curve, which illustrates the probabilities of an intervention (eg, chromoendoscopy, WLE, or no surveillance) being cost effective across a range of WTP thresholds. The acceptability curve indicates that chromoendoscopy every 7 years is more

likely to be cost effective than no surveillance at a WTP threshold $> \$69,141$. Below this threshold, chromoendoscopy is less likely to be cost effective. According to the acceptability curve, WLE is less likely to be cost effective than either chromoendoscopy or no surveillance.

Figure 3 shows the incremental cost-effectiveness scatter plots for chromoendoscopy versus no surveillance or WLE at 7-year surveillance intervals. By using a WTP of \$100,000 per QALY, chromoendoscopy was the optimal strategy in 55% of trials compared with no surveillance, and in 66% of trials compared with WLE.

Sensitivity analysis by varying screening interval

In a 3-dimensional analysis of the Markov model at varying screening intervals, the lifetime cumulative risk of the population of patients with UC developing CRC was 2.5% with annual endoscopy and 7.3% with no surveillance. The lifetime cumulative risk of developing CRC despite endoscopic surveillance gradually increased with longer screening intervals, reaching 5.9% with chromoendoscopy performed every 10 years.

Sensitivity analyses on individual variables

We performed 1-way sensitivity analyses to determine the preferred endoscopic strategy across variable values in the setting of biennial surveillance, consistent with current guidelines¹ (Table 3). All other factors equal, chromoendoscopy was the preferred strategy when, for dysplasia detection, its sensitivity was over 0.23 or specificity over 0.89. Across all levels of compliance with surveillance colonoscopy and sensitivities of WLE for dysplasia detection, chromoendoscopy was the preferred strategy. In regard to costs, WLE became the preferred strategy only when the cost of chromoendoscopy rose above \$2200. Chromoendoscopy remained the preferred strategy across all probabilities of dysplasia in patients with chronic UC and probabilities of dysplasia progression ranging from 0 to 1 (Table 3).

We also examined the sensitivity threshold of chromoendoscopy to detect dysplasia if the cost of chromoendoscopy were equal to the cost of WLE. In this case, chromoendoscopy was the preferred strategy when its sensitivity was > 0.38 . At discount rates ranging from 0% to 5%, chromoendoscopy still dominated WLE at a screening interval of every 7 years, with an ICER of chromoendoscopy relative to no surveillance of \$103,971 by using a discount rate of 5% and \$84,672 when no discounting was applied.

DISCUSSION

Our analysis indicates that chromoendoscopy is more effective and less costly than WLE for CRC surveillance in patients with UC but becomes cost effective only compared with no surveillance at surveillance intervals of at least 7 years, with a resultant ICER of less than a WTP threshold of \$100,000 per QALY. After accounting for lower CRC incidence rates among patients with chronic UC, CRC surveillance every 1 to 2 years does not appear to be cost effective. To our knowledge, this is the first decision analysis comparing different surveillance endoscopy strategies among patients with UC by using updated CRC estimates in patients with UC.

A higher risk of CRC among patients with UC is well-established. However, recent studies suggest that the magnitude of this increased risk is lower compared with earlier estimates. For our primary analysis, we used these lower CRC incidence estimates⁴ across all 3 strategies (chromoendoscopy, WLE, or no surveillance) performed at intervals ranging from every 1 to 10 years. We found that, compared with no surveillance, neither chromoendoscopy nor WLE were cost effective unless surveillance intervals were lengthened to 7 to 10 years. Thus, if these lower CRC incidence estimates are indeed confirmed in other populations, the optimal surveillance intervals among patients with chronic UC may be more similar to recommended screening intervals among average-risk individuals without UC.⁴⁴ This is perhaps not unexpected because we observed that the lifetime cumulative risk of developing CRC among patients with UC despite surveillance with chromoendoscopy performed every 10 years was 5.9%, comparable to the lifetime cumulative risk of CRC of approximately 5% among average-risk individuals without UC.³⁷ When we conducted sensitivity analyses by using historically higher cumulative CRC incidence estimates published by Eaden et al,⁸ the ICER decreased significantly. This suggests that shorter surveillance intervals, particularly using chromoendoscopy, may be even more cost effective if CRC incidence among patients with UC is higher than recent estimates would support or among subgroups of patients with UC at higher risk of CRC (eg, coexistent primary sclerosing cholangitis).

Our model shows that, all other factors being equal, chromoendoscopy is preferred at costs up to \$2200. This suggests that the overall cost of chromoendoscopy could be increased by over \$1200 before WLE would become more cost effective at a WTP threshold of \$100,000 per QALY. This incremental cost is approximately equivalent to a strategy of random biopsies yielding 8 bottles and dye-targeted biopsies yielding an additional 7 bottles for pathology assessment. These data suggest that even chromoendoscopy that includes both random biopsies and targeted biopsies of dye-highlighted lesions would be preferred compared with WLE alone. Furthermore, our findings support the use of chromoendoscopy regardless of patient compliance with surveillance guidelines.

Because probabilistic sensitivity analyses supported the use of chromoendoscopy in most, but not all trials, our results support the need for further studies to determine whether chromoendoscopy always should be the preferred strategy for surveillance. Moreover, our findings have implications for other emerging imaging modalities, such as narrow-band imaging or chromoendoscopy-guided confocal endomicroscopy. If we assume a cost that is similar to that of chromoendoscopy, our data suggest that any new technology platform would require a sensitivity for detection of dysplasia of 0.23 to be cost effective relative to WLE and no surveillance. If the cost were as high as that of WLE with random biopsy, an alternative imaging modality would require a sensitivity for dysplasia detection of 0.38 or higher.

The strengths of our study include the use of updated CRC estimates in UC, particularly considering the sensitivity of the ICER to these estimates. Robustness of the findings was demonstrated by the consistency of the primary findings despite changes in important variables. We chose to model this analysis from a societal perspective, by using a population-based age distribution rather than a predefined patient with a given age and sex.

In doing so, we believe that our study has greater generalizability and external validity, enabling us to assess the overall utility and cost of chromoendoscopy relative to that of WLE.

Our analysis has limitations. First, as with any decision analysis, we relied on model inputs that require the simplification of parameters and events inherently susceptible to uncertainty. However, sensitivity analyses demonstrated robust results across a range of plausible inputs. Second, we recognize that adherence to current surveillance guidelines is not optimal and often is modified according to individual patient characteristics. However, there are no data to estimate the impact of practice variation on dysplasia incidence or progression to CRC. Because deviation from current guidelines would lower efficacy for CRC prevention, the results of our model likely underestimate the additional utility of chromoendoscopy compared with that of WLE. Third, based on the lack of data in the literature, we could not account for potential differences in the specific rates of progression to CRC according to lesion type (eg, flat dysplasia and dysplasia-associated lesions or masses vs adenoma-like mass), lesion distribution, detection method (eg, chromoendoscopy-detected vs WLE-detected dysplasia), or the extent of the dysplastic field. However, sensitivity analysis demonstrated that chromoendoscopy remained the preferred strategy across all probabilities of dysplasia in chronic UC and rates of progression of dysplasia to CRC. Finally, we recognize that studies published more recently show higher false-positive rates for chromoendoscopy.^{45,46} However, these studies estimated specificity by using data comparing chromoendoscopy with other modalities, such as narrow-band imaging or confocal endomicroscopy, rather than WLE. For our analyses, we estimated specificity based only on studies comparing chromoendoscopy with WLE.

In summary, we found that endoscopic surveillance at an interval of 1 to 2 years for chronic UC did not appear cost effective after accounting for lower, more recent estimates of CRC incidence among patients with chronic UC. Chromoendoscopy dominates WLE but becomes cost effective only at surveillance intervals of 7 years. Although chromoendoscopy has been consistently shown to enhance the detection of dysplasia over WLE, it has not been widely adopted mainly because of perceptions about the need for additional resources.⁶ The results of our analysis, which incorporates the additional costs associated with these possible hindrances, support wider use of chromoendoscopy as the primary mode of surveillance in patients with UC. Our results also suggest that current guidelines for endoscopic surveillance in UC may require re-evaluation. Finally, although our study offers an estimate for a threshold level of sensitivity for other emerging technologies to be cost effective, further research is needed to assess the comparative effectiveness of these platforms.

Abbreviations

CRC	colorectal cancer
HGD	high-grade dysplasia
ICER	incremental cost-effectiveness ratio
LGD	low-grade dysplasia

QALY	quality-adjusted life year
UC	ulcerative colitis
WLE	white-light endoscopy
WTP	willingness to pay

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Take-home Message

- Chromoendoscopy appears both more effective and less costly than white-light endoscopy for the surveillance of colorectal cancer among patients with chronic ulcerative colitis.

Figure 1.
State transition diagram.

Figure 2.
Acceptability curve.

Figure 3. Incremental cost-effectiveness scatter plots (willing to pay \$100,000). *ICER*, incremental cost-effectiveness ratio.

TABLE 1

Transition probabilities, costs, and utilities

Variable	Base case	Range	Monte Carlo distribution (base case, 95% CI)	References
UC				
Annual rate of UC flare requiring colectomy	0.0023	0.0016–0.0075	Beta (0.0023; 0.0015)	7, 25
Percent adhering to surveillance colonoscopy	0.74	0.60–1.00	Beta (0.74; SD 0.1)	23, 24
Probability of death due to other causes in UC	0.0013	0.0001–0.003	Beta (0.0013; SD 0.0007)	3
Colonoscopy test characteristic				
WLE sensitivity for dysplasia	0.695	0.00–1.00	Beta (0.695, SD 0.100)	12–15
WLE specificity for dysplasia	0.9	0.00–1.00	Beta (0.90, SD 0.15)	10, 12, 15
WLE or chromoendoscopy sensitivity for CRC	0.9	0.80–1.00	Beta (0.9; SD 0.05)	12, 14, 20
WLE or chromoendoscopy specificity for CRC	0.999	.90–1.00	Beta (0.999; SD 0.025)	7, 12
Chromoendoscopy sensitivity for dysplasia in UC	0.833	0.36–1.00	Beta (0.833, SD 0.159)	11, 15
Chromoendoscopy specificity for dysplasia in UC	0.913	0.44–1.00	Beta (0.913, SD 0.141)	10, 11
Colorectal cancer risk in patients with UC				
Annual incidence of CRC in patients with UC (2012 published estimates)				
8–15 y	0.001345941		Beta	4
16–20 y	0.001521801		Beta	4
>21 y	0.001631547		Beta	4
Annual incidence of CRC in patients with UC (2001 published estimates)				
8–15 y	0.00416040		Beta	8
16–20 y	0.00416040		Beta	8
21–25 y	0.05555700		Beta	8
>26 y	0.05555700		Beta	8
Dysplasia				
Probability of LGD if dysplasia on surveillance colonoscopy	0.75	0.61–0.80	Beta (0.75; SD 0.048)	15, 18
Probability of HGD if dysplasia on surveillance colonoscopy	0.25	0.20–0.38	Beta (0.25; SD 0.045)	15, 18
Proportion proceeding to colectomy if LGD	0.60	0–1.00	Beta (0.60; SD 0.25)	19
Probability of synchronous CRC if LGD	0.19	0.04–0.46	Beta (0.19, SD 0.105)	39, 42
Probability of developing CRC given LGD	0.14	0.090–0.314	Beta (0.140; SD 0.056)	42
Probability of synchronous CRC if HGD	0.53	0.42–0.67	Beta (0.53, 0.06)	39, 40
Probability of dysplasia in chronic UC	0.0036	0.0008–0.015	Beta (0.0036, SD 0.004)	41
Colorectal cancer				
Cancer stage at diagnosis				
Local cancer (Dukes A/B, stage 1–2)	0.472	0.354–0.637	Beta (0.472; 0.071)	3
Regional cancer (Dukes C, stage 3)	0.377	0.295–0.471	Beta (0.377; 0.044)	3
Distant cancer (Dukes D, stage 4)	0.151	0.069–0.165	Beta (0.151; 0.024)	3

Variable	Base case	Range	Monte Carlo distribution (base case, 95% CI)	References
Cancer progression (annual transition proportion)				
From local CRC to regional CRC	0.20	0.10–0.30	Beta (0.20; SD 0.05)	38
From regional CRC to distant CRC	0.40	0.20–0.60	Beta (0.40; SD 0.10)	38
Cancer mortality				
Local cancer (Dukes A/B, stage 1–2)	0.0211	0.0158–0.0263	Beta (0.0211; SD 0.0026)	37
Regional cancer (Dukes C, stage 3)	0.0699	0.0524–0.0874	Beta (0.0699; SD 0.0088)	37
Distant cancer (Dukes D, stage 4)	0.3467	0.2600–0.4334	Beta (0.3467; SD 0.0434)	37
Adverse events				
Mortality from emergent colectomy	0.024	0.018–0.16	Beta (0.024; SD 0.036)	27
Mortality from elective colectomy	0.006	0.0035–0.066	Beta (0.006; SD 0.016)	7, 27
Mortality from colectomy for CRC	0.042	0.039–0.057	Beta (0.042; SD 0.005)	28
Morbidity from emergent colectomy	0.421	0.316–0.526	Beta (0.421; SD 0.053)	27
Morbidity from elective colectomy	0.346	0.260–0.433	Beta (0.346; SD 0.043)	27
Morbidity from colectomy for CRC	0.384	0.278–0.405	Beta (0.384; SD 0.032)	28
Mortality from surveillance colonoscopy	0.00007	.00006–.0003	Beta (0.00007; SD 0.00006)	29
Morbid adverse event from surveillance colonoscopy	0.005	0.001–0.009	Beta (0.005; SD 0.002)	29
Perforation from surveillance colonoscopy	0.0001	0.00003–0.003	Beta (0.0001; SD 0.0007)	29
Costs (\$2011 U.S.)				
Annual care of chronic UC	6646	4985–8308	Gamma (6646; SD 831)	33
WLE with surveillance biopsies	1321	990–1655	Gamma (1321; SD 166)	
WLE	473	355–591		CPT 45380 (2011)
Random & targeted biopsies (8 bottles)	848	636–1060		CPT 88305 (2011)
Cost/bottle	106			
Chromoendoscopy with surveillance biopsies	983	737–1229	Gamma (983; SD 123)	
Chromoendoscopy	473	355–591		CPT 45380 (2011)
Chromoendoscopy spray catheter	75	56–93		36
Chromoendoscopy spray (methylene blue)	11	9–13		American Regent
Targeted biopsies (base case: 4 bottles)	424	318–530		CPT 88305 (2011)
Cost per bottle	106			
Morbid adverse event from surveillance colonoscopy	6210	3105–12421	Gamma (6210; SD 2329)	7
Colectomy cost + 6 mo postoperative	54818	SD 31474	Gamma (54818; SD 31474)	26
Routine care with IPAA (annual)	4900	3675–6125	Gamma (4900; SD 613)	2, 33
Cancer-related expenses (\$2011 U.S.)				
Initial costs				
Local	42313	31735–52880	Gamma (31735; 5286)	34, 35
Regional	55973	41971–69952	Gamma (41971; 6995)	34, 35
Distant	55660	41736–69560	Gamma (55660; 6956)	34, 35
Continuing costs				

Variable	Base case	Range	Monte Carlo distribution (base case, 95% CI)	References
Local	3282	2460–4102	Gamma (3282; 411)	34, 35
Regional	6818	5112–8520	Gamma (6818; 852)	34, 35
Distant	22970	17224–28707	Gamma (22970; 2871)	34, 35
Terminal costs				
Local	17682	13259–22099	Gamma (17682; 2210)	34, 35
Regional	31562	23667–39444	Gamma (31562; 3944)	34, 35
Distant	43045	32277–53796	Gamma (43045; 5380)	34, 35
Utilities				
Chronic UC, with or without dysplasia	0.94	0.85–1.0	Triangular (0.94, 0.85, 1.0)	2, 32
Post-IPAA	0.9	0.84–0.94	Triangular (0.90, 0.84, 0.94)	30
Local cancer (Dukes A/B, stage 1–2)	0.74	0.69–0.78	Triangular (0.74, 0.69, 0.78)	31
Regional cancer (Dukes C, stage 3)	0.59	0.54–0.69	Triangular (0.59, 0.54, 0.69)	31
Distant cancer (Dukes D, stage 4)	0.25	0.20–0.31	Triangular (0.25, 0.20, 0.31)	31
Severe UC flare resulting in colectomy	0.42 (1 mo)	0.10–0.70	Triangular (0.42, 0.10, 0.70)	30, 32
Surgery (IPAA or other type of colectomy)	0.61 (1 mo)	0.32–0.84	Triangular (0.61, 0.32, 0.84)	32
Colonoscopy adverse events	3.1% (1 mo)	1.0%–12.5%	Triangular (3.1%, 1%, 12.5%)	7
Postoperative adverse events	0.55 (1 mo)	0.30–0.70	Triangular (0.55, 0.30, 0.70)	32
Other variables				
Discount rate	3%			21, 22
Cycle length	1 y	0–10 y		
Willingness to pay threshold	\$100,000/QALY			43

CI, Confidence interval; UC, ulcerative colitis; SD, standard deviation; WLE, white-light endoscopy; CRC, colorectal cancer; LGD, low-grade dysplasia; HGD, high-grade dysplasia; CPT, Current Procedural Terminology; IPAA, ileal pouch anal anastomosis; QALY, quality-adjusted life year.

TABLE 2

Base case results *

Screening interval, y	Screening method	Cost	QALY	Incremental C/E (ICER)
N/A	No surveillance	\$100,200	13.187	
1	Chromoendoscopy	\$125,000	13.101	(Dominated)
	WLE	\$128,000	13.063	(Dominated)
2	Chromoendoscopy	\$116,000	13.203	\$993,711
	WLE	\$118,000	13.167	(Dominated)
3	Chromoendoscopy	\$111,000	13.219	\$338,558
	WLE	\$113,000	13.202	(Dominated)
5	Chromoendoscopy	\$107,000	13.230	\$158,508
	WLE	\$108,000	13.214	(Dominated)
7	Chromoendoscopy	\$104,900	13.248	\$77,176
	WLE	\$105,800	13.239	(Dominated)
8	Chromoendoscopy	\$104,100	13.284	\$40,415
	WLE	\$104,800	13.279	(Dominated)
10	Chromoendoscopy	\$103,100	13.356	\$17,150
	WLE	\$103,900	13.344	(Dominated)

N/A, not applicable; QALY, quality-adjusted life year; C/E, cost effectiveness; ICER, incremental cost-effectiveness ratio; WLE, white-light endoscopy.

* Jess estimates (Table 1).

TABLE 3

One-way sensitivity analyses with biennial surveillance (WTP \$100,000)

Variable	Base case	Sensitivity analysis range	Threshold	Preferred strategy below threshold	Preferred strategy above and equal to threshold
Cost of WLE	\$1134	\$0–\$2500	\$200	WLE	Chromoendoscopy
Cost of chromoendoscopy	\$983	\$0–\$2500	\$2200	Chromoendoscopy	WLE
Sensitivity of chromoendoscopy for dysplasia	0.833	0–1.00	0.23	WLE	Chromoendoscopy
Specificity of chromoendoscopy for dysplasia	0.913	0–1.00	0.89	WLE	Chromoendoscopy
Sensitivity of WLE for dysplasia	0.695	0–1.00	N/A	Chromoendoscopy	Chromoendoscopy
Specificity of WLE for dysplasia	0.90	0–1.00	0.92	Chromoendoscopy	WLE
Annual probability of dysplasia in chronic UC	0.0036	0–1.00	N/A	Chromoendoscopy	Chromoendoscopy
Annual probability of CRC given dysplasia	0.14	0–1.00	N/A	Chromoendoscopy	Chromoendoscopy
Probability of adhering to surveillance colonoscopy	0.74	0.01–1.00	N/A	Chromoendoscopy	Chromoendoscopy

WTP, Willingness-to-pay; WLE, white-light endoscopy; N/A, not applicable; UC, ulcerative colitis; CRC, colorectal cancer.