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Stool DNA Analysis is Cost Effective for Colorectal Cancer Surveillance in Patients with Ulcerative Colitis

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Abstract

Background & Aims—Patients with chronic ulcerative colitis are at increased risk for colorectal neoplasia (CRN). Surveillance by white-light endoscopy (WLE) or chromoendoscopy may reduce risk of CRN, but these strategies are underused. Analysis of DNA from stool samples (sDNA) can detect CRN with high levels of sensitivity, but it is not clear if this approach is cost

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Andrew J. Piscitello: analysis and interpretation of data, statistical analysis, critical revision of manuscript, technical support
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Ashwin N. Ananthakrishnan: study design, analysis and interpretation of data, critical revision of manuscript

effective. We simulated these strategies for CRN detection to determine which approach is most cost effective.

Methods—We adapted a previously published Markov model to simulate the clinical course of chronic ulcerative colitis, the incidence of cancer or dysplasia, and costs and benefits of care with 4 surveillance strategies. These strategies were: analysis of sDNA and diagnostic chromoendoscopy for patients with positive results, analysis of sDNA with diagnostic WLE for patients with positive results, chromoendoscopy with targeted collection of biopsies, or WLE with random collection of biopsies. Costs were based on 2014 Medicare reimbursement. The primary outcome was the incremental cost effectiveness ratio (incremental cost/incremental difference in quality-adjusted life years) compared with no surveillance and a willingness to pay threshold of $50,000.

Results—All strategies fell below the willingness to pay threshold at 2 year intervals. Incremental cost effectiveness ratios were $16,362 per quality-adjusted life year for sDNA analysis with diagnostic chromoendoscopy; $18,643 per quality-adjusted life year for sDNA analysis with diagnostic WLE; $23,830 per quality-adjusted life year for chromoendoscopy alone; and $27,907 per quality-adjusted life year for WLE alone. In sensitivity analyses, sDNA analysis with diagnostic chromoendoscopy was more cost effective than chromoendoscopy alone, up to a cost of $1135 per sDNA test. sDNA analysis remained cost effective at all rates of compliance; when combined with diagnostic chromoendoscopy, this approach was preferred over chromoendoscopy alone, when the specificity of the sDNA test for CRN was above 65%.

Conclusion—Based on a Markov model, surveillance for CRN is cost effective for patients with chronic ulcerative colitis. Analysis of sDNA with chromoendoscopies for patients with positive results was more cost effective than chromoendoscopy or WLE alone.

Keywords

ICER; QALY; cost benefit analysis; inflammatory bowel diseases

Introduction

Population-level data show an increased incidence of colorectal cancer (CRC) in inflammatory bowel disease (IBD), specifically among patients with extensive, long-standing ulcerative colitis (UC)[1] and Crohn's disease (CD) of the colon.[2] Recent data show that CRC incidence and mortality in patients with UC is reduced with surveillance colonoscopy by white light endoscopy (WLE).[3] Even prior to this evidence, surveillance colonoscopy became standard of care, based on several smaller scale case-control and cohort studies, which in aggregate, suggested a benefit from earlier-stage CRC diagnosis.[4] Over the last decade, a growing body of literature suggests that dye-spray-enhanced surveillance with chromoendoscopy may be superior for the detection of dysplastic precursors to CRC. While multiple specialty society guidelines endorse surveillance colonoscopy with WLE,[5] the recent SCENIC consensus statement, jointly issued by the American Gastroenterology Association and the American Society for Gastrointestinal Endoscopy, now recommends chromoendoscopy over standard definition WLE for CRC surveillance in UC patients.[6]

Since its introduction over a decade ago[7] uptake of chromoendoscopy has been slow, due to the requirement for additional training, perceived increased procedure time, and higher costs.[8] A recent study showed that chromoendoscopy might be more cost-effective than WLE but both modalities appeared to be above societal willingness to pay thresholds when used at currently recommended intervals.[9] Complicating matters, patient compliance with CRC surveillance is unacceptably low, even among commercially-insured UC patients.[10] Non-invasive testing by stool DNA (sDNA) is a new potential strategy, hypothesized to reduce costs and improve surveillance adherence.[11-13] Multi-target sDNA has recently been approved by the United States Food and Drug Administration for average-risk CRC screening following a pivotal study in which sensitivity and specificity of sDNA for CRC were similar to gold-standard WLE.[14]

The approved multi-target sDNA test, commercialized as Cologuard™ (Exact Sciences, Madison WI), assays mutant *KRAS*, methylated *BMP3*, methylated *NDRG4* and a fecal immunochemical test (FIT). FIT cannot logically be applied in CD and UC as test specificity may be compromised by hemorrhagic inflammatory activity. However, recent case-control data show that stool assay of aberrant DNA methylation markers, achieved >90% sensitivity at 90% specificity for CRC in patients with IBD.[15, 16]

Several important questions remain that must be addressed before sDNA can be used for CRC surveillance in patients with UC and CD. What sensitivity and specificity thresholds should be required of an sDNA test in this setting? How frequently should the test be applied? Will sDNA be cost-effective, and if so, at what price? We approached these knowledge gaps by modeling the cost-effectiveness of sDNA in comparison to WLE, chromoendoscopy or no surveillance in a hypothetical cohort of UC patients. Further, we sought to inform test design by 1-way sensitivity analyses of test performance, interval and cost. Lastly, probabilistic sensitivity analyses were performed to assess the reliability of model outputs.

Methods

This study was exempt from Institutional Review Board review.

Model Design

We adapted a previously published Markov model with Monte Carlo simulations[9] and imputed a clinical course of UC, the incidence of colorectal neoplasia (CRN, cancer + dysplasia), and costs & benefits of care with patients committed to one of four surveillance strategies: sDNA with diagnostic chromoendoscopy for sDNA test positives, sDNA with diagnostic WLE for sDNA positives, chromoendoscopy with targeted biopsies only, or WLE with random biopsies. The model was originally created with TreeAge Pro 2009 (TreeAge, Williamstown, MA) and updated with TreeAge 2015. The Markov cycle length was 1 year. The simulation sampled hypothetical patients, 8 years after population-based age distribution of UC diagnosis, the recommended duration to begin surveillance for dysplasia.[17] Termination criteria were death or a patient age greater than 90 years with 10 years of surveillance. Pancolitis and left-sided disease were treated equally according to current guidelines for surveillance.[5] Health states included chronic UC, chronic UC with

dysplasia, status post-colectomy, CRC, and death due to either baseline mortality or mortality related to colonoscopy, surgery, or CRC (Figure 1). Base case values and ranges for transition probabilities and health state utilities (Supplemental Table 1) were obtained from a systematic literature search as previously described.[9] Several key adaptations were included to address the specific aims of this study (Table 1).

Risk of colorectal cancer and benefit of surveillance

Patients in the simulation cohort entered the model at an age consistent with population-level measurements of natural history.[17] The probability of developing CRC, given no prior dysplasia, was modeled on population-level estimates; patients entered the simulation at 8 years after diagnosis with a 1.07% incidence of CRC to match cumulative incidence estimates of 2% at 15 years, 3% at 20 years and 4% at 25 years.[18] Surveillance colonoscopy has been recently shown to reduce colorectal cancer incidence and all-cause mortality.[3] To reflect this benefit, the model was designed to confer improved survival from CRC if detected by surveillance in accordance with previously published estimates.[19]

Stool DNA test performance in ulcerative colitis

Base-case sDNA performance estimates were derived from average-risk sDNA test performance,[14] which are more conservative than those available from the limited literature in IBD patient populations.[15, 16] Also, each surveillance strategy assumed base case compliance of 0.5, consistent with US surveillance adherence estimates.[10]

Costs and utilities

Care and procedure expenditures were based on 2014 Medicare reimbursement for specific procedures (Table 1) or updated to 2014 United States dollars from literature estimates (Supplemental Table 1) [20-22] using published medical Consumer Price Index inflation factors. Because sDNA cost for use in UC has not been determined, and because Medicare has not issued a national coverage determination for sDNA testing in IBD, the base cost was set at $599, the current price billed to commercial insurance for the Cologuard multi-target sDNA test for average-risk CRC screening (Exact Sciences, Madison WI). All costs were estimated from the payer perspective and did not include indirect patient expenses (e.g., travel, lost work time).

Transient utilities included UC flare requiring colectomy, immediate postoperative state, and adverse events from either surgery or colonoscopy; these were modeled with 1 month duration. In patients simulated to have those events, yearly utilities were adjusted by a weighted average of the transient utility and the underlying utility attributed to chronic UC, post-IPAA state or cancer (Dukes stage A/B vs C vs D).

All costs and utilities were discounted at a rate of 3% per year.

Analyses

Base-case analysis was conducted by Markov modeling with Monte Carlo microsimulation which sampled all costs, utilities and probabilities to create 500,000 hypothetical patients and disease courses. The primary outcome was the incremental cost effectiveness ratio

(ICER, incremental cost/incremental difference in quality adjusted life years [QALY]) for each surveillance strategy at two year intervals compared to no surveillance. A willingness to pay (WTP) threshold of $50,000 per QALY was used to estimate cost-effectiveness.[23]

One-way sensitivity analyses evaluated the impact of surveillance compliance, sDNA test cost, and sDNA sensitivity & specificity. A second set of sensitivity analyses studied cost thresholds for a 1-year sDNA surveillance program, compared to 2-year intervals for chromoendoscopy and WLE.

To estimate the degree of uncertainty around the model assumptions, p*robabilistic sensitivity analysis (PSA)* was then performed by simulating 100 separate cohorts of 100,000 patients. Cost, utility and probability variable inputs were sampled by the simulation software according to the distribution type and margin of error around the base-case point estimates (Table 1). Model uncertainty was also examined using cost-effectiveness acceptability curves which utilize a net monetary benefit calculation (NMB) that combines cost, effectiveness and WTP into a single measurement (NMB = effectiveness × WTP − cost). The strategy with the highest NMB is the most cost-effective given the fixed WTP parameter. The sampling variation in the PSA was used to estimate the probability that a surveillance strategy is cost-effective for a given WTP (i.e. the decision maker's threshold ICER). Where the probabilistic sensitivity analysis disagreed with the results of the base case analysis, additional acceptability curves were generated to identify input variables which might potentially disrupt to the expected outcome.

Results

Base Case Analysis

Relative to no surveillance, the primary cost-effectiveness analysis demonstrated that ICERs for annual, biennial and every 3 year sDNA, chromoendoscopy and WLE fell below the WTP threshold of $50,000 (Figure 2). While all options were cost-effective, the ICERs for sDNA-based surveillance were lower than and not dominated by endoscopic-based options. Consistent with prior results,[9] chromoendoscopy modalities were more cost-effective that WLE.

In the no surveillance strategy on 500,000 hypothetical patients, the model generated 95,987 CRC cases, resulting in 81,502 CRC-related deaths over the full duration of the simulation. Biennial WLE reduced CRC cases by 53,800 and associated fatalities by 42,274. To prevent one additional CRC case, 9 patients would have to participate in programmatic WLE surveillance. Biennial chromoendoscopy prevented 52,539 cases and 42,104 hypothetical deaths with 10 surveillance program participants needed to prevent one additional CRC. Though less costly, sDNA with diagnostic chromoendoscopy, and sDNA with diagnostic WLE, prevented 17,681 and 16,230 hypothetical CRC fatalities, respectively. To prevent one additional CRC case, 18 and 19 patients would have to participate in programmatic surveillance with sDNA with diagnostic chromoendoscopy or diagnostic WLE, respectively. Assuming 50% base-case compliance with colonoscopy-based surveillance, and that non-compliant patients used sDNA, 58,504 to 59,785 CRC fatalities would be prevented. For this

combination approach, only 5-8 patients would need to participate in programmatic surveillance with to prevent 1 additional CRC fatality.

Sensitivity Analyses on Individual Variables

All biennial surveillance modalities became more expensive as patient compliance increased, but at all levels of compliance at sDNA remained cost-effective. Unless the specificity of sDNA fell below 0.65, sDNA with diagnostic chromoendoscopy was preferred over chromoendoscopy alone. Diagnostic sensitivity of sDNA did not impact cost-effectiveness across a wide range of performance (0.25-0.99) for any target lesion, which included low-grade dysplasia (LGD), high-grade dysplasia (HGD) or CRC. Test cost for sDNA was prohibitive above $1,135 at which point chromoendoscopy became more cost-effective (Table 2). Similarly, in comparison of sDNA with diagnostic WLE against WLE alone, sDNA remained preferred unless the specificity of sDNA fell below 0.66 or cost of sDNA exceeded $1,109.

If sDNA testing were to be performed annually, the threshold cost for sDNA would decrease to $601 and $675 in order to remain cost-effective when compared to biennial interval chromoendoscopy or WLE, respectively.

Probabilistic Sensitivity Analysis

Probabilistic sensitivity analyses supported the findings of the base-case analysis (Figure 3, Supplemental Figure 1). Compared to no surveillance, sDNA with diagnostic chromoendoscopy was below the WTP threshold of $50,000 per QALY or dominant in 71 of 100 hypothetical patient cohorts. Stool DNA with diagnostic WLE or chromoendoscopy alone were below the WTP of $50,000 per QALY or dominant in 66 of the cohorts; WLE alone was below the WTP threshold or dominant 55% of the time.

Base case analyses anticipated that sDNA-based options would show maximal NMB if payers were willing to pay $18,000-$45,000 per QALY (Supplemental Table 2); however, acceptability curves for the full set of input variables provided contradictory results to the base case. To determine why this PSA was discordant with base case expectations, the PSA repeated with stratified sampling by each of the combined utility, cost and probability variables to identify those that might be disruptive when sampled across the entire Monte Carlo distribution. With this approach, the output of all utility and cost variables remained consistent with base-case expectations, while results based on probability variables appeared contradictory (Figure 4, A-C). Sampling by individual probability variables generated curves which were each consistent with base case, therefore interaction among probability variables was suspected. To further investigate this, all probability inputs were sampled in clusters of 2-4 variables at a time in combination with the CRC incidence variable; however, each of these acceptability curves matched base-case expectations (Figure 4 D, Supplemental Figure 2).

Discussion

In this analysis of CRC surveillance strategies, sDNA appears to be more cost-effective when used with either diagnostic chromoendoscopy or diagnostic WLE than

chromoendoscopy alone or WLE alone. Though chromoendoscopy has recently been endorsed by the SCENIC consensus statement,[6] this modality is not yet widely utilized, leaving many patients and providers to rely on WLE. Endoscopy-based surveillance could become more cost-effective if sDNA specificity falls below 0.65 in comparison to chromoendoscopy surveillance alone or below 0.66 in comparison to WLE. These specificity thresholds are well below currently published estimates of sDNA performance in either IBD patients[15, 16] or in the average risk population.[14] The relative cost-effectiveness of sDNA was maintained across a wide spectrum of patient compliance, test sensitivity, and test costs. Even annual sDNA testing was cost-effective in comparison to either annual or biennial endoscopy-based options.

Regardless of test strategy, surveillance for dysplasia and CRC in UC patients appears cost-effective. These findings shed new light on a long-standing clinical uncertainty as previous economic analyses of endoscopic surveillance for CRC in UC patients have yielded mixed results. Provanzale, and colleagues performed a cost-effectiveness analysis of WLE colonoscopy in UC at 1-5 year intervals in comparison to no surveillance.[24] While surveillance at intervals shorter than 5 years appeared to exceed WTP, the ICERs for all intervals were comparable to other commonly performed screening tests, such as cervical cancer screening.[24] Subsequent threshold analyses and critical reviews on surveillance cost-effectiveness have highlighted that test cost, CRC incidence, mortality reduction from surveillance and quality of life after proctocolectomy are critical factors, whereas diagnostic accuracy of colonoscopy did not greatly impact results.[9, 25-27] Consistent with these model outputs, our present analysis did not reveal significant threshold effects when varying the sensitivity of sDNA, though thresholds for specificity and cost were observed.

The present results also update a recent economic analysis of chromoendoscopy and WLE strategies which found dominance by chromoendoscopy but at costs exceeding a WTP of $100,000.[9] The substantial relative QALY gains we observed were most likely due to the incorporation of recent data showing that WLE lowers CRC incidence and improves mortality.[3] Surveillance of UC patients with WLE has only been shown to reduce CRC incidence in one observational study; two others showed earlier stage CRC diagnosis with corresponding mortality benefit.[19, 28] There has been further concern that chromoendoscopy may overestimate risk of subsequent advanced neoplasia in patients with LGD by finding more lesions with uncertain natural history.[13, 29] A recent update of the St. Mark's Hospital surveillance cohort in the United Kingdom showed that the rate of progression from LGD to CRC was similar across each of 4 decades suggesting that the more recent introduction of chromoendoscopy has not changed the apparent risk attributable to LGD.[28] The present model also relied on encouraging but preliminary available data on sDNA performance in IBD.[15, 16] Because small sample size and single-center experience should prompt a cautious approach, we opted to use more conservative sDNA performance inputs from a large clinical trial of average-risk, asymptomatic patients in the general population,[14] and utilized 1-way and probabilistic sensitivity analyses to evaluate sDNA cost-effectiveness across wide hypothesized ranges of test performance. Results from a large multi-center case-control study on sDNA performance in IBD patients are eagerly anticipated (ClinicalTrials.gov identifier NCT01819766).

There are several potential limitations to this study. The acceptability curve generated from the full set of variables appeared contrary to the base-case results. Stratifying by inputs of utilities, costs and probabilities appeared to isolate probability variables; however, despite sampling probability variables individually and in groups of 2-4 at a time, we were unable to identify any potentially disruptive inputs. Therefore, we remain confident in the base-case findings. There is also the potential to under estimate costs. Inputs for costs of endoscopic procedures, complications, surgery and cancer care were modeled from the Medicare perspective, and may be lower than reimbursement rates from commercial insurance carriers. Also, the model did not include any indirect costs. While there is precedent for their exclusion due the difficulty of accurate measurement,[24, 25, 27] this may under-estimate the total burden to society.

We are encouraged that surveillance for CRC in UC patients appears cost-effective, as the ICER estimates of all options fell below a WTP of $50,000. Based on our modeling, sDNA was most cost-effective relative to no surveillance. The user-friendly features of sDNA may improve patient compliance,[30] and its addition as an option in the surveillance arsenal may enhance overall effectiveness.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

CRC	Colorectal cancer
CRN	Colorectal neoplasia
HGD	High-grade dysplasia
ICER	Incremental cost-effectiveness ratio
IPAA	Ileal pouch anal anastomosis
LGD	Low-grade dysplasia
QALY	Quality-adjusted life-year
sDNA	Stool DNA
WLE	White light endoscopy
WTP	Willingness to pay threshold

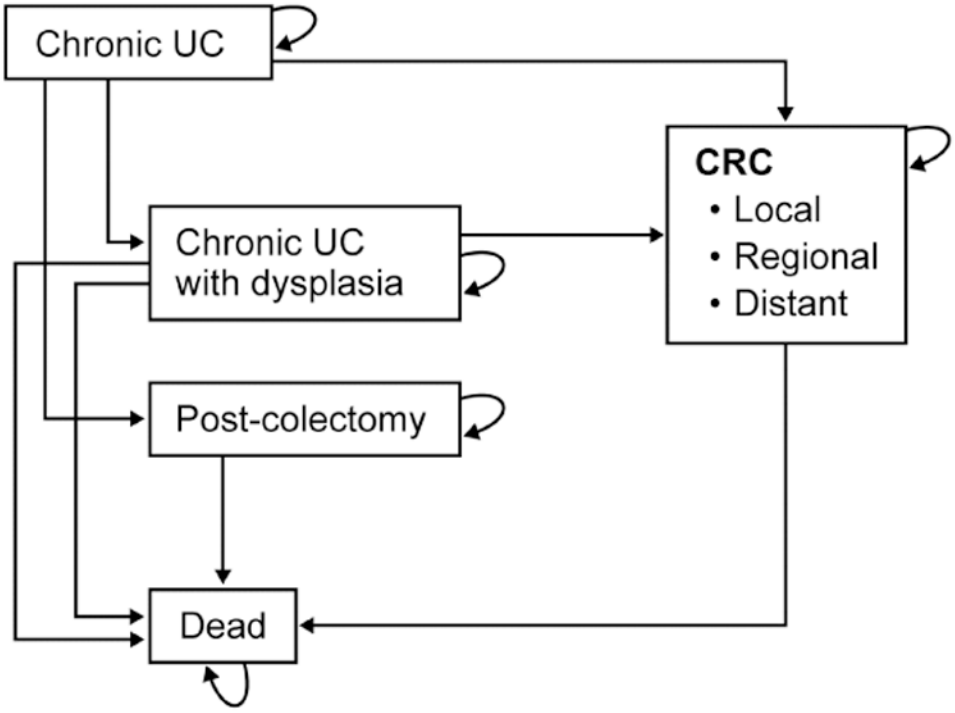
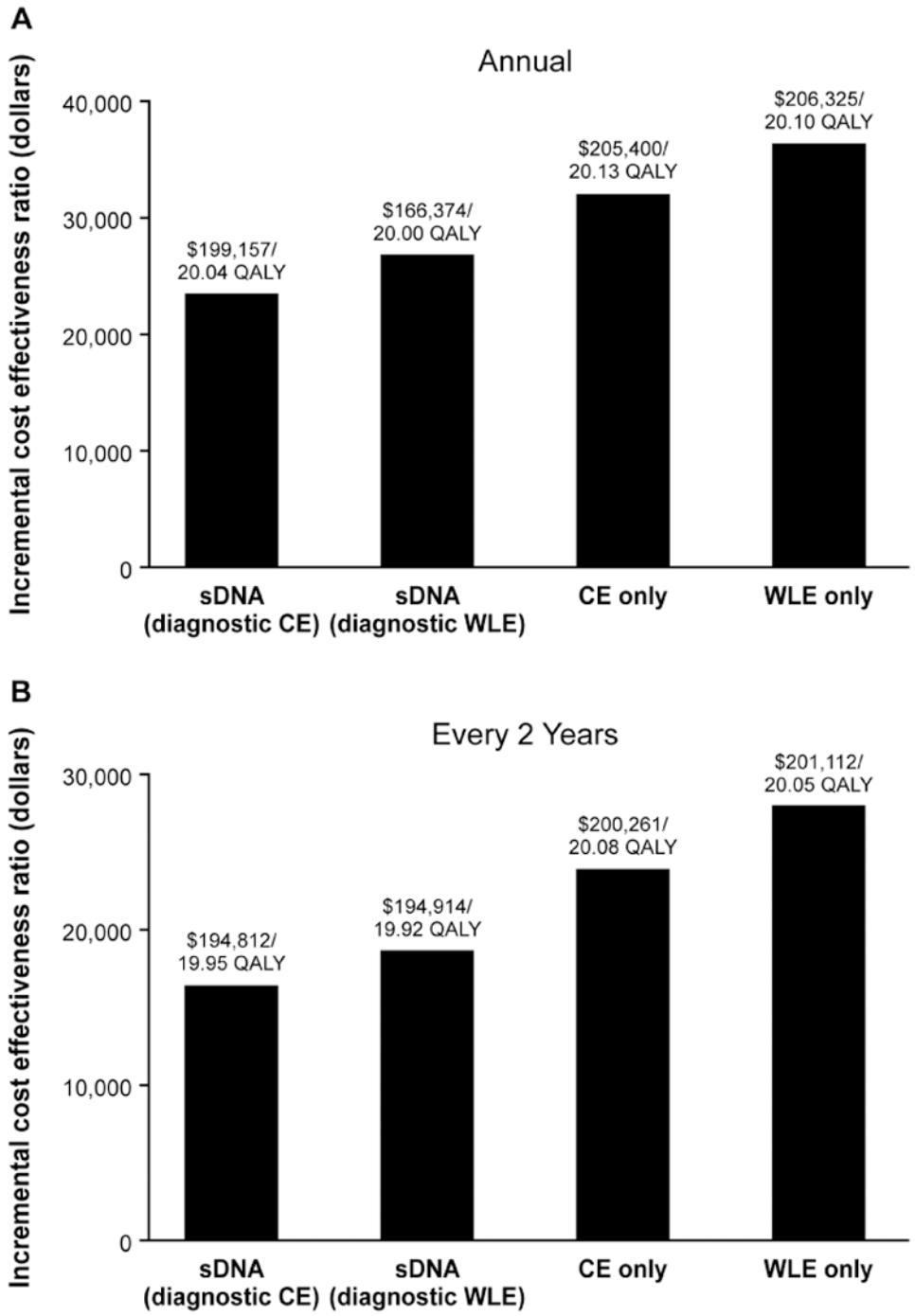


Figure 1.

Model health state transition diagram from chronic ulcerative colitis (UC) to dysplasia, colorectal cancer (CRC), surgery or death

Adapted from Konijeti GG, Shrime MG, Ananthakrishnan AN, Chan AT. Cost-effectiveness analysis of chromoendoscopy for colorectal cancer surveillance in patients with ulcerative colitis. Gastrointest Endosc. 2014 Mar;79(3):455-65 and used with permission.



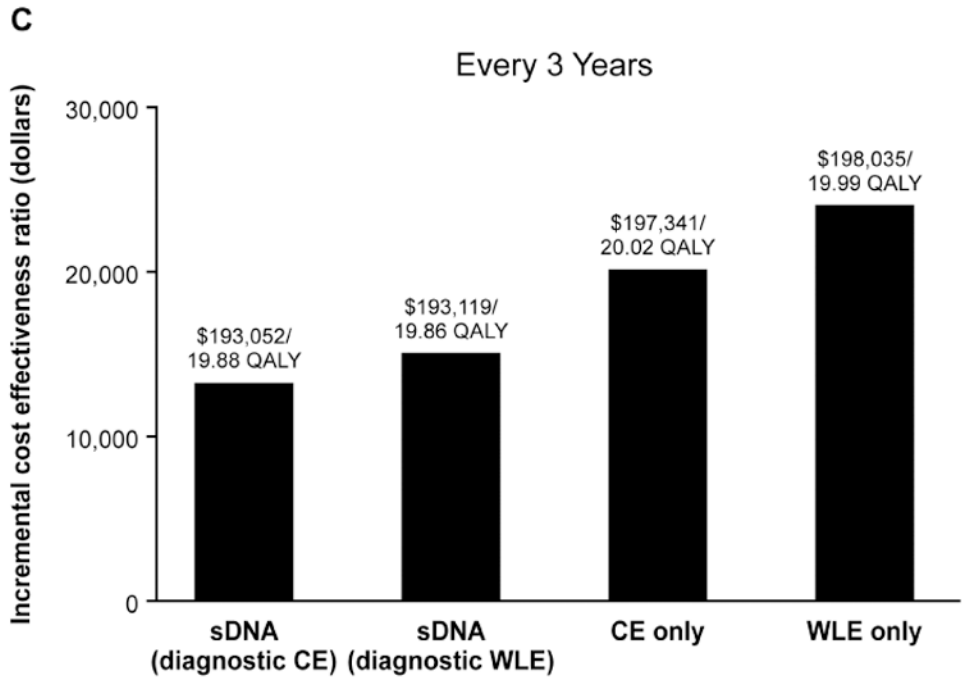
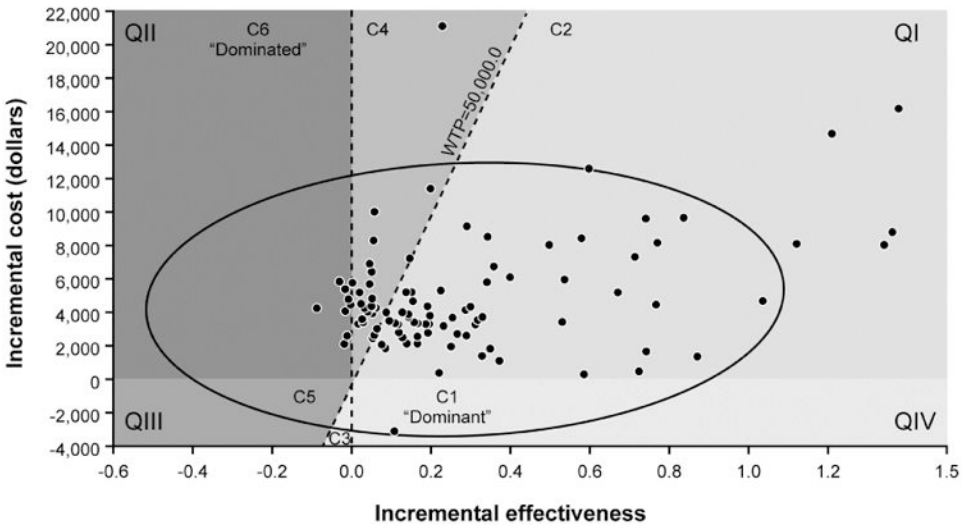


Figure 2.

Incremental cost-effectiveness ratios for each surveillance strategy at (A) annual, (B) biennial and (C) every 3-years surveillance intervals in comparison to no surveillance, which cost $189,960 for 19.65 quality-adjusted life years (QALY). CE, chromoendoscopy; sDNA, stool DNA; WLE, white light endoscopy

A



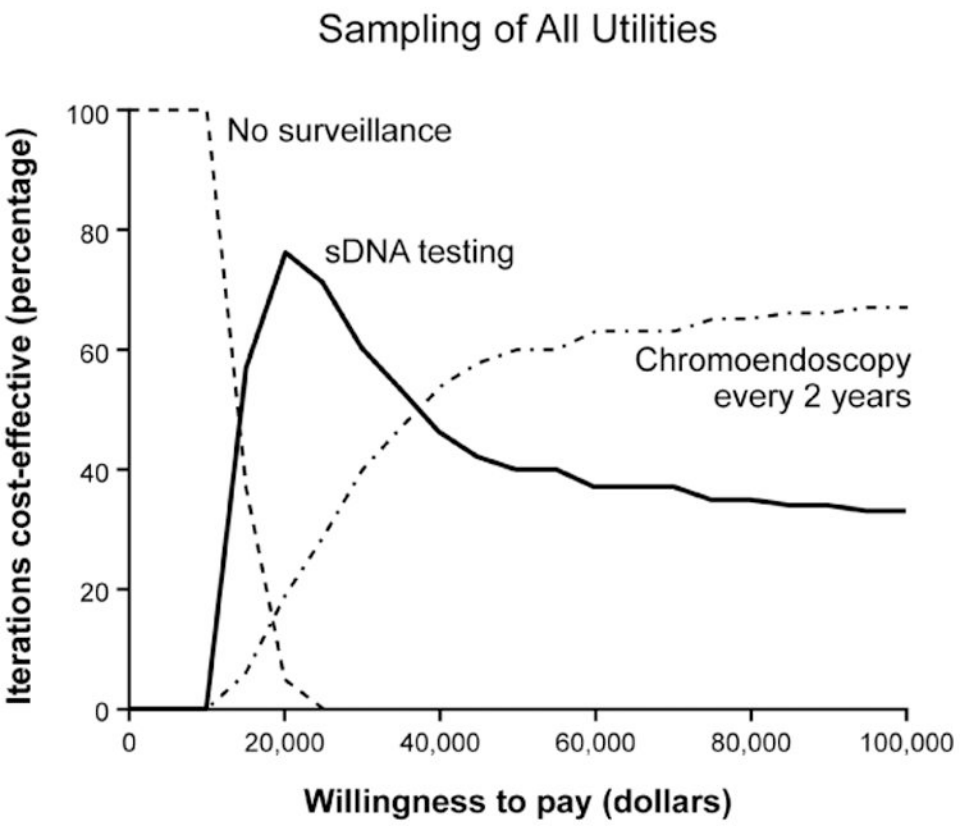
B

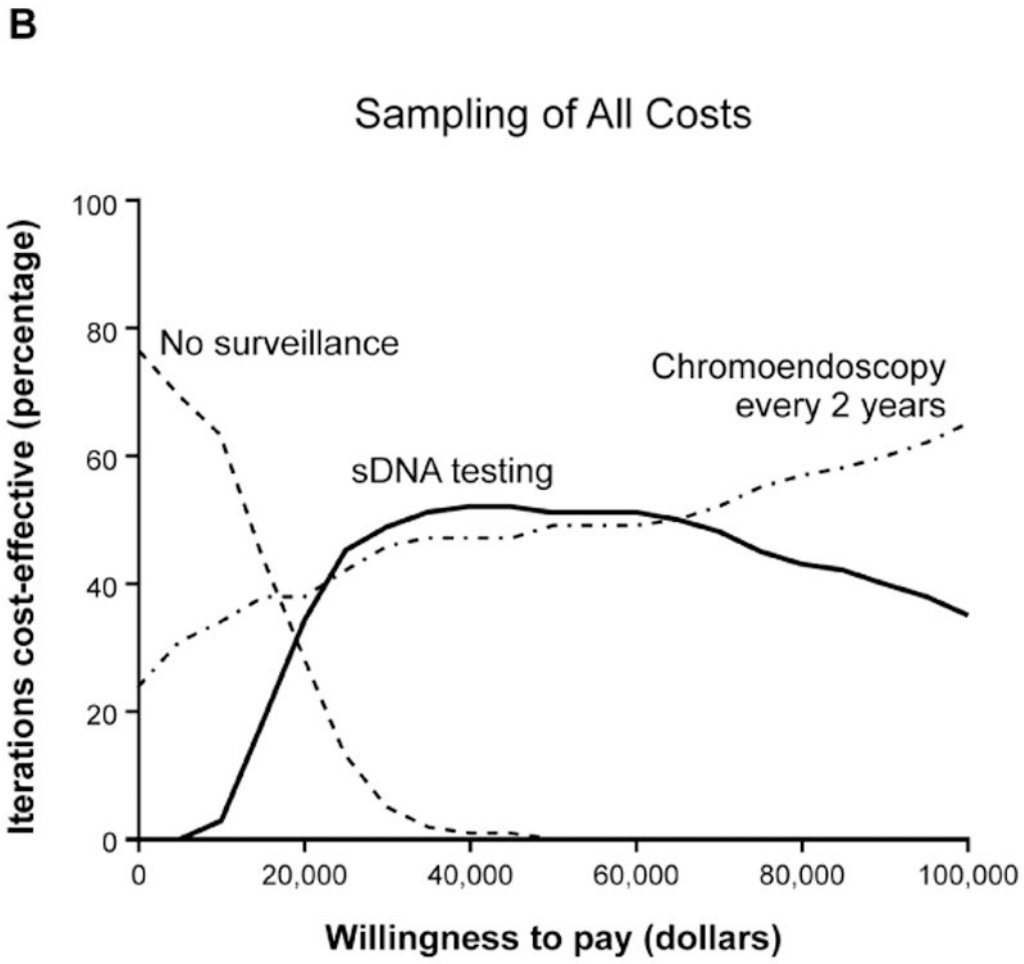
Component (C)	Quadrant (Q)	Overall % (n=100)	Interpretation
C1	QIV	1	Screening strategy is less costly and more effective than no surveillance. **Screening strategy recommended** because it absolutely dominates no surveillance.
C2	QI	70	Screening strategy is more costly and more effective than no surveillance. **Screening strategy recommended** because its ICER does not exceed WTP.
C3	QIII	0	Screening strategy is less costly and less effective than no surveillance. **Screening strategy recommended** because its ICER does not exceed WTP.
C4	QI	22	Screening strategy is more costly and more effective than no surveillance. Screening strategy not recommended because its ICER exceeds WTP.
C5	QIII	0	Screening strategy is less costly and less effective than no surveillance. Screening strategy not recommended because its ICER exceeds WTP.
C6	QII	7	Screening strategy is more costly and less effective than no surveillance. Screening strategy not recommended because it is absolutely dominated by no surveillance.

Figure 3.

(A) Incremental cost-effectiveness ratio (ICER) scatter plot and 95% confidence interval ellipse in relationship to $50,000 willingness to pay threshold (WTP) for stool DNA with diagnostic chromoendoscopy in reference to no surveillance. Quadrants (QI-IV) are defined by cost and effectiveness axes and components (C1-6) define where stool DNA is recommended or not in relationship to WTP. (B) Interpretation key shows that stool DNA with diagnostic chromoendoscopy was the recommended surveillance strategy in the majority (71%) of cohorts in which the full range of model parameters was sampled.

A





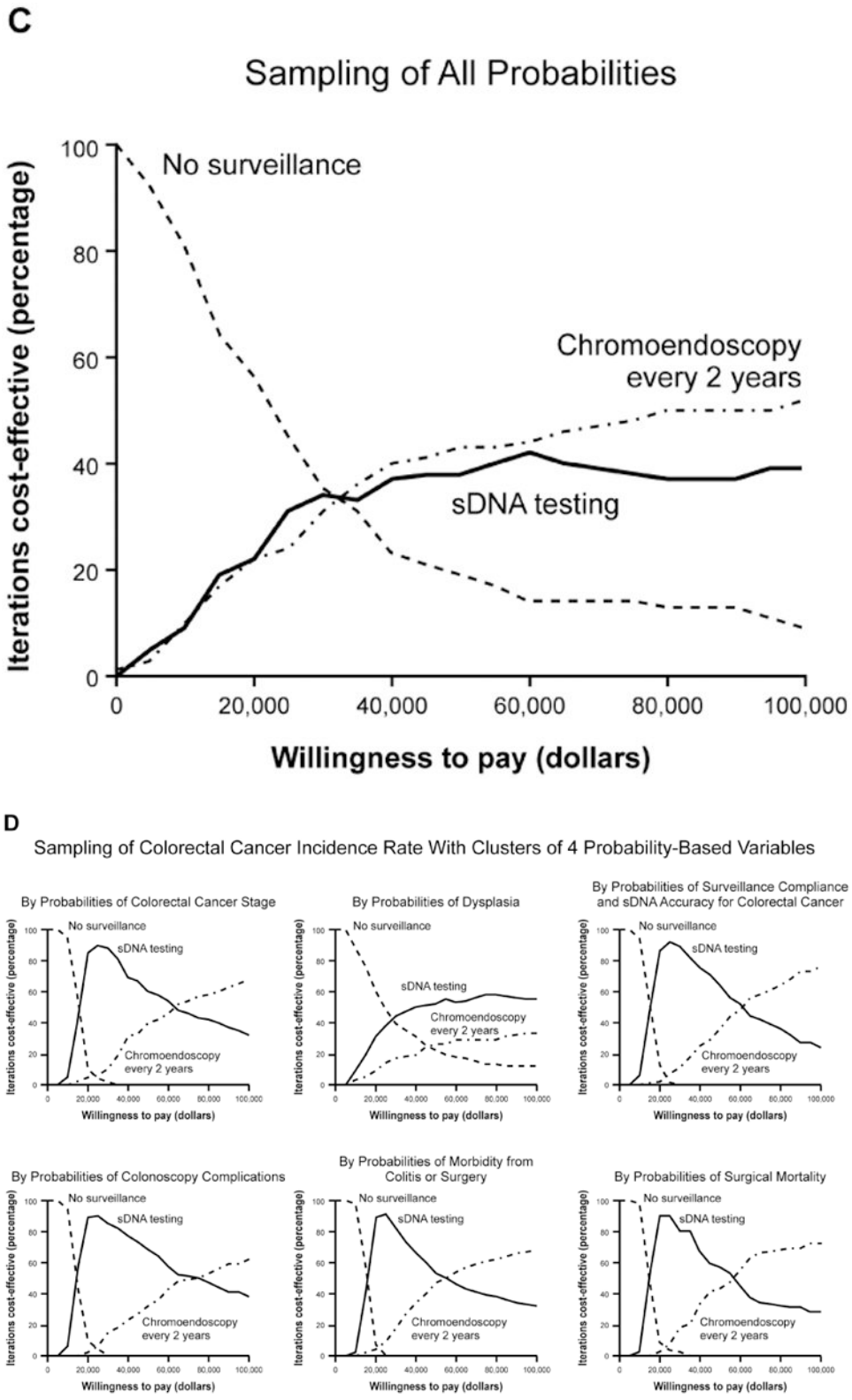


Figure 4.

Acceptability curves for the each of the major input variable categories (A) utilities, (B) costs and (C) probabilities. Probabilities were further examined in smaller clusters of variables at a time (D) which all met base-case expectations.

Table 1

Transition probabilities and healthcare costs

Variable	Base case	Standard Deviation (SD)*	Monte Carlo distribution type*	2.5th/97.5th Percentile*	References
Stool DNA					
Sensitivity LGD	0.41	SD 0.018	Beta	0.38 / 0.45	14
Sensitivity HGD	0.69	SD 0.072	Beta	0.56 / 0.85	14
Sensitivity CRC	0.92	SD 0.35	Beta	0.84 / 0.98	14
Specificity	0.87	SD 0.0036	Beta	0.86 / 0.87	14
Ulcerative colitis					
% Adhering to surveillance	0.5	SD 0.11	Beta	0.28 / 0.71	10
Age of UC diagnosis					17
10 years	0.075	-	-	-	17
30 years	0.354	-	-	-	17
50 years	0.279	-	-	-	17
70 years	0.238	-	-	-	17
90 years	0.054	-	-	-	17
Annual rate of CRC incidence by UC duration					
At 8th year	0.0107	-	Beta	0.00045 – 0.044	18
9-15 years	0.00135	-	Beta	0.000032 - 0.0046	18
16-20 years	0.00205	-	Beta	0.000044 – 0.0089	18
≥21years	0.00207		Beta	0.000067 – 0.0075	18
Probability CRC stage at diagnosis					
Surveillance					
Dukes A/B	0.86	0.13	Beta	0.50 / 1.00	19
Dukes C	0.10	0.012	Beta	0.08 / 0.13	19
Dukes D	0.04	0.0065	Beta	0.03 / 0.06	19
No Surveillance					
Dukes A/B	0.47	0.071	Beta	0.33 / 0.60	19, 31
Dukes C	0.38	0.044	Beta	0.29 / 0.49	19, 31
Dukes D	0.15	0.024	Beta	0.11 / 0.20	19, 31

Variable	Base case	Standard Deviation (SD)*	Monte Carlo distribution type*	2.5th/97.5th Percentile*	References
Costs					
Annual care UC	$8,485	$1,061	Gamma	$6,326 / $11,048	20
Stool DNA test	$599	$75	Gamma	$460 / $744	CPT G0464
CE with biopsies	$1,221	$153	Gamma	$932 / $1,589	CPT 88305 CPT 45380
WLE with biopsies	$1,405	$177	Gamma	$978 / $1714	CPT 88305 CPT 45380
Adverse event from colonoscopy	$7,075	$2,653	Gamma	$2,636 / $15,386	27
Colectomy cost + 6 month postoperative care	$62,453	$35,858	Gamma	$17,004 / $153,379	32, 33
Routine care with IPAA (annual)	$6,058	$758	Gamma	$4,540 / $7,238	20
Cancer related expenses, initial					
Local	$48,945	$6,115	Gamma	$37,994 / $64,953	21, 22
Regional	$64,746	$8,091	Gamma	$52,209 / $85,461	21, 22
Distant	$64,384	$8,046	Gamma	$49,446 / $82,898	21, 22
Cancer related expenses, continuing					
Local	$3,796	$475	Gamma	$3,126 / $4,799	21, 22
Regional	$7,887	$986	Gamma	$6,078 / $9,916	21, 22
Distant	$26,570	$3,321	Gamma	$19,531 / $33,248	21, 22
Cancer related expenses, terminal					
Local	$20,453	$2,556	Gamma	$16,126 / $25,261	21, 22
Regional	$36,509	$4,562	Gamma	$27,348 / $47,145	21, 22
Distant	$49,792	$6,223	Gamma	$39,566 / $62,789	21, 22

*Apply to probabilistic sensitivity analysis only

CE, chromoendoscopy; CRC, colorectal cancer; HGD, high-grade dysplasia; IPAA, ileal pouch anal anastomosis; LGD, low-grade dysplasia; SD, standard deviation; UC, ulcerative colitis; WLE, white light endoscopy

Please see Supplemental Table 1 for additional model inputs and distributions

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Table 2

One way sensitivity analyses assuming biennial testing intervals

Comparison strategy	Variable	Base case value	N simulated individual patients	Range of sensitivity analysis	Threshold value
Chromoendoscopy	Percent adhering to sDNA Screening	0.50	500,000	25% to 100%	n/a
	Cost of sDNA Test	$599	100,000	$600 to $1500	**$1,135**
	Specificity of sDNA	0.866	100,000	0.25 - 0.99	**0.65**
	Sensitivity sDNA to CRC	0.923	100,000	0.25 - 0.99	n/a
	Sensitivity sDNA to HGD	0.692	100,000	0.25 - 0.99	n/a
	Sensitivity of sDNA to LGD	0.409	100,000	0.25 - 0.99	n/a
White light endoscopy	Percent adhering to sDNA Screening	0.50	500,000	25% to 100%	n/a
	Cost of sDNA Test	$599	100,000	$600 to $1800	**$1,109**
	Specificity of sDNA	0.866	100,000	0.25 - 0.99	**0.66**
	Sensitivity sDNA to CRC	0.923	100,000	0.25 - 0.99	n/a
	Sensitivity sDNA to HGD	0.692	100,000	0.25 - 0.99	n/a
	Sensitivity of sDNA to LGD	0.409	100,000	0.25 - 0.99	n/a

CRC, colorectal cancer; HGD, high-grade dysplasia; LGD, low-grade dysplasia; sDNA, stool DNA