


Cost-effectiveness of surveillance with CT colonography after resection of colorectal cancer

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ABSTRACT

Objective Surveillance following colorectal cancer (CRC) resection uses optical colonoscopy (OC) to detect intraluminal disease and CT to detect extracolonic recurrence. CT colonography (CTC) might be an efficient use of resources in this situation because it allows for intraluminal and extraluminal evaluations with one test. **Design** We developed a simulation model to compare lifetime costs and benefits for a cohort of patients with resected CRC. Standard of care involved annual CT for 3 years and OC for years 1, 4 and every 5 years thereafter. For the CTC-based strategy, we replace CT+OC at year 1 with CTC. Patients with lesions greater than 6 mm detected by CTC underwent OC. Detection of an adenoma 10 mm or larger was followed by OC at 1 year, then every 3 years thereafter. Test characteristics and costs for CTC were derived from a clinical study. Medicare costs were used for cancer care costs as well as alternative test costs. We discounted costs and effects at 3% per year. **Results** For persons with resected stage III CRC, the standard-of-care strategy was more costly (US\$293) and effective (2.6 averted CRC cases and 1.1 averted cancer deaths per 1000) than the CTC-based strategy, with an incremental cost-effectiveness ratio of US\$55 500 per quality-adjusted life-year gained. Our analysis was most sensitive to the sensitivity of CTC for detecting polyps 10 mm or larger and assumptions about disease progression.

Conclusion In a simulation model, we found that replacing the standard-of-care approach to postdiagnostic surveillance with a CTC-based strategy is not an efficient use of resources in most situations.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer among both men and women in the USA.¹ Approximately 115 000 Americans are projected to be diagnosed with non-metastatic CRC in 2020 and undergo curative resection of their disease,¹ with possible adjuvant and neoadjuvant therapy. Regardless of initial treatment(s), these patients face an increased risk of developing colorectal adenomas, second primary cancers and metastatic recurrence over time. Several guidelines exist for multicomponent,

Summary box

What is already known about this subject?

- Patients with colorectal cancer are at increased risk of developing adenomas, second cancers and metastatic recurrence.
- Surveillance at 1 year includes CT to detect extraluminal disease and optical colonoscopy to detect intraluminal disease.
- CT colonography allows for intraluminal and extraluminal evaluations with one test.

What are the new findings?

- Replacing standard-of-care surveillance with a CT colonography-based strategy is not an efficient use of resources in most situations.
- A CT colonography-based surveillance strategy may be cost-effective for older patients or with higher values of CT colonography sensitivity for detecting large polyps.

How might it impact on clinical practice in the foreseeable future?

- Findings from our model suggest that replacing optical colonoscopy and CT with CT colonography at 1 year after resection for older patients with colorectal cancer could be a cost-effective strategy.

postresection surveillance for patients with CRC,^{2–6} although the evidence for which approach is optimal is mixed.^{7–11} Recommended surveillance includes an abdominal/pelvic CT scan annually for the first 3–5 years after resection—as well as more frequent carcinoembryonic antigen assays that could lead to CT—and endoscopic surveillance for the detection of adenomatous polyps and metachronous cancers.

Because postdiagnostic surveillance 1 year after a CRC resection involves optical colonoscopy (OC) to detect intraluminal disease and abdominal CT to detect extraluminal metastatic disease, CT colonography (CTC) may be an efficient use of resources in this setting because it allows for simultaneous intraluminal and extraluminal evaluation. Weinberg

and colleagues¹² conducted a prospective, multicentre study to determine whether CTC, relative to OC (ie, the gold standard approach to identifying CRC polyps and cancer), could effectively identify adenomas and cancers in patients 1 year following CRC resection. They found that the sensitivity of CTC was significantly lower than that of OC; however, it is unclear if the increased efficacy of OC is worth its increased cost. Beck and colleagues¹³ conducted a short-term analysis of the costs and diagnostic yield from the Weinberg study but did not report health and economic outcomes over patients' lifetimes, as recommended by the Panel on Cost-Effectiveness in Health and Medicine.¹⁴ Accordingly, we conducted a cost-effectiveness analysis of a CTC-based surveillance strategy for patients with surgically resected CRC using a lifetime time horizon, incorporating data on test characteristics and costs from a clinical study of 231 patients evaluated with CTC and OC 1 year postresection.¹²

METHODS

Overview

We developed a state-transition Markov model with annual cycles to simulate the downstream events for patients with resected CRC to evaluate the clinical utility of incorporating CTC as part of postdiagnosis surveillance. In any year, simulated patients could reside in a number of health states: no lesion, small (1–5 mm), medium (6–9 mm) or large (10 mm or larger) adenoma, hyperplastic polyp only (by size), preclinical cancer (by stage; localised, regional or distant), clinical cancer (by stage), diagnosed metastatic recurrence and dead. Over time adenomas can develop or progress in size, large adenomas can progress to preclinical localised cancer, preclinical cancer can progress in stage or be detected through symptoms and new clinical cancers can result in cancer-related deaths. Patients can also experience metastatic recurrence from their initial CRC—either through symptoms or CT—and face a cancer-specific mortality risk. A schematic of the model is shown in [figure 1](#).

Primary outcomes were discounted lifetime medical costs, quality-adjusted life years (QALYs) and incremental

cost-effectiveness ratios (ICERs). Secondary outcomes were number of lifetime OCs, number of new CRCs and number of CRC-related deaths. Costs were calculated from a US healthcare sector perspective. Both costs and outcomes were assessed over a lifetime time horizon and discounted 3% per year.¹⁴

Surveillance strategies

We compared two surveillance strategies for a hypothetical cohort of 60-year-old patients with resected stage II or stage III CRC based primarily on the American Cancer Society guidelines.⁵ We did not model a differential surveillance strategy for rectal cancer as recommended by some guidelines due to our focus on prevention of metachronous cancers and the assumption that patients with rectal cancer would all receive optimal care and thus have much lower local recurrence rates.^{6 15} The standard-of-care strategy involved an annual CT for 3 years and OC for years 1, 4 and every 5 years thereafter. The comparison strategy involved contrast-enhanced CTC (including the CT examination) at year 1, CT only at years 2 and 3, and OC at year 4 and every 5 years thereafter (CTC-based strategy). Patients with lesions greater than 6 mm detected by CTC underwent follow-up OC, whereas patients with lesions less than 6 mm did not undergo follow-up OC as is the CTC practice.¹⁶ Patients with an adenoma 10 mm or larger diagnosed by OC, considered high risk,¹⁷ underwent OC at 1 year and then every 3 years thereafter. Adenomas <10 mm were followed according to the initial schedule ([table 1](#)). We assumed surveillance would stop at age 80 and that individuals would be perfectly adherent to the surveillance schedule.

We examined two alternative CTC-based strategies in scenario analyses: a strategy where CT would be performed annually for the first 5 years and thus CTC would be used in year 4 as a single test instead of performing CT and OC separately and a strategy where we assumed that those with non-high-risk findings would get OC every 5 years after the initial OC. A schematic of the strategies is shown in [table 1](#).

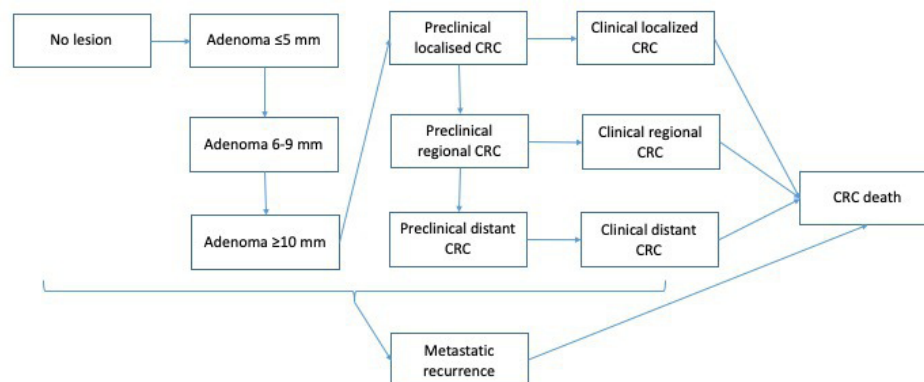


Figure 1 Model diagram showing the intraluminal progression of adenomas to cancer of patients with resected colorectal cancer (CRC). We also allowed for the presence of hyperplastic polyps by size but they could not progress but could lead to colonoscopy if found by CT colonography.

Table 1 Schedule of the surveillance strategies*

Year after diagnosis	1	2	3	4	5	6	9	11	14	16	19
Base-case strategies (assumes 3 years of CT)											
Standard of care	OC+CT	CT	CT	OC			OC		OC		OC
CTC-based	CTC	CT	CT	OC			OC		OC		OC
Scenario analysis strategies (assumes 5 years of CT)											
Standard of care	OC+CT	CT	CT	OC+CT	CT		OC		OC		OC
CTC-based	CTC	CT	CT	CTC	CT		OC		OC		OC
Scenario analysis strategies (assumes less intensive OC follow-up)											
Standard of care	OC+CT	CT	CT			OC		OC		OC	
CTC-based	CTC	CT	CT			OC		OC		OC	

*Schedule assumes that all test results show no lesion, hyperplastic polyp or adenoma <10 mm. Persons with adenomas 10 mm or larger get OC after 1 year and the 3 yearly thereafter.

CTC, CT colonography; OC, optical colonoscopy.

Clinical data

Natural history of colorectal disease among patients with resected CRC

The risk of developing an adenoma and the growth rate of each adenoma are greater among patients with resected CRC compared with a screening population.¹⁸ We used structural assumptions typically used in CRC screening models,¹⁹ calibrated the model parameters to average-risk (cancer-free) population targets (eg, adenoma prevalence, CRC incidence)^{20 21} and then increased the transition probabilities by factors in order to match endpoints found in studies of patients following colonoscopic polypectomy of high-risk lesions or resected CRC (online supplementary appendix).^{22–27}

We assumed that patients die from their initial CRC by being diagnosed with metastatic recurrence or extramural pelvic disease first and calibrated to the relative survival curves from the Surveillance, Epidemiology, and End Results (SEER) Program,²⁸ assuming that the cancer-specific mortality rate among persons with extramural disease was the same as for persons presenting with stage IV CRC.²⁹ Annual probabilities of death from other causes were from US life tables.³⁰ Disease progression parameters are shown in the online supplementary appendix.

Misclassification of disease at CRC diagnosis

We estimated the underlying prevalence of residual disease (eg, missed large adenomas) at the time of initial diagnosis so that an OC 1 year after resection would yield the findings reported by Weinberg and colleagues.¹² The relatively high yield of adenomas observed in that study (30.8%) would be from either adenomas missed at initial diagnosis or newly formed adenomas within the first year. We assumed that most adenomas found at 1 year were residual disease, an assumption that is supported by the US Multi-Society Task Force on Colon Cancer.⁶

Test characteristics

Per-person sensitivity estimates for CTC were determined based on the most advanced lesion found (by size

among adenomas, CRC considered more advanced than adenomas, adenomas considered more advanced than hyperplastic polyps, regardless of size) and a CTC was deemed positive if it led to a follow-up OC (table 2).¹² Specificity was estimated among subjects with no adenomas found by OC. Per-person sensitivity estimates for OC by sizes was based on the literature (table 2).^{31 32} We assumed that the specificity of OC was 100% because we modelled hyperplastic polyps separately (using the same size-specific sensitivities for hyperplastic polyps).

Colonoscopy-specific complications

The probability of perforation was 0.6 per 1000 individuals and given a perforation the risk of death was 5.2%, based on a population-based study of colonoscopies performed between 1991 and 1998.^{33 34} We also modelled non-fatal perforation events and gastrointestinal bleeding or transfusion and assigned a cost and disutility associated with these events.³³

Quality of life

To calculate QALYs, each year of life spent in a health state was weighted by value (utility) between 0 and 1 to reflect the health-related quality of life of that state, where 0 represents death and 1 represents perfect health. Utilities for cancer by stage and phase of care were derived from Ness and colleagues³⁵ (table 2). We assigned a utility of 0.67 for all individuals until they experienced metastatic recurrence and were assigned the utility associated with distant CRC (0.25). For patients who developed metachronous CRC, we applied a linear index for predicting utilities of joint health states (eg, stage II CRC and metastatic recurrence).³⁶ We assigned utility decrements of 0.038 (ie, assuming a utility of 0 for 2 weeks) for colonoscopy-related morbidity events (perforation or gastrointestinal bleeding).³⁷

Costs

The costs of surveillance tests were derived from the study by Weinberg and colleagues (table 2).^{12 13} We used alternative cost estimates of surveillance tests derived

**Table 2** Model parameters

Variable	Estimate (range)	Distribution	Source
Residual adenoma prevalence at initial CRC diagnosis (most advanced lesion)			12
Adenoma 1–5 mm	0.15 (0.11–0.20)	Beta (35, 196)	
Adenoma 6–9 mm	0.11 (0.08–0.16)	Beta (26, 205)	
Adenoma 10 mm or larger	0.04 (0.02–0.07)	Beta (10, 221)	
Preclinical localised CRC	0.001*	Uniform (0, 0.002)	
Hyperplastic polyp 1–5 mm	0.130 (0.09–0.18)	Beta (30, 201)	
Hyperplastic polyp 6–9 mm	0.048 (0.02–0.08)	Beta (11, 220)	
Hyperplastic polyp 10 mm or larger	0.013 (0.003–0.03)	Beta (3, 228)	
Test characteristics (person-based; for most advanced lesion)			
Sensitivity (CTC)			12
Polyp 1–5 mm	0.31 (0.17–0.47)†	Beta (11, 24)	
Polyp 6–9 mm	0.38 (0.21–0.57)	Beta (10, 16)	
Polyp 10 mm or larger, or CRC	0.80 (0.52–0.97)	Beta (8, 2)	
Specificity (CTC)	0.84 (0.78–0.89)	Beta (134, 26)	12
Sensitivity (OC)			
Polyp 1–5 mm	0.55 (0.45–0.64)	Beta (56, 46)	29
Polyp 6–9 mm	0.67 (0.54–0.79)	Beta (35, 17)	28
Polyp 10 mm or larger, or CRC	0.95 (0.84–1.00)	Beta (21, 1)	28
Specificity for adenomas (OC)	1.00	Assumed constant	
Colonoscopy risks (per 1000 polypectomies)			
Death	0.033 (0.00003–0.166)	Beta (0.493, 14 994)	30 31
Nonfatal perforation	0.60 (0.36–0.91)	Beta (18, 29 988)	30
GI bleed	6.66 (5.77–7.61)	Beta (201, 29 988)	30
Quality-of-life weights			
Utilities			32
Localised cancer	0.74 (0.69–0.79)	Normal (0.74, 0.026)	
Regional cancer	0.63 (0.58–0.68)	Normal (0.11, 0.008)‡	
Distant cancer	0.25 (0.20–0.30)	Normal (0.25, 0.026)	
Disutility			33
Perforation or GI bleed	0.038 (0.001–0.075)	Uniform (0.001, 0.075)	
Costs			13
Tests			
OC without polypectomy	US\$700 (US\$684–US\$717)	Normal (700, 8.2)	
OC with polypectomy	US\$1033 (US\$930–US\$1156)	Normal (1033, 60.7)	
CTC	US\$244 (US\$228–US\$275)	Normal (244, 7.7)	
Colonoscopy complications			34
Perforation	US\$14 949 (US\$12 019–US\$17 879)	Normal (14949, 1494.9)	
Serious gastrointestinal event	US\$6256 (US\$4849–US\$7213)	Normal (6256, 625.6)	
Cancer care			34 35
Initial year, localised CRC	US\$33 629 (US\$32 745–US\$34 538)	LN (10.42, 0.0136)	
Initial year, regional CRC	US\$48 053 (US\$47 065–US\$49 062)	LN (10.78, 0.0106)	
Initial year, distant CRC	US\$66 327 (US\$63 375–US\$47 301)	LN (11.00, 0.0188)	
Continuing, localised CRC	US\$2352 (US\$2071–US\$2483)	LN (7.76, 0.0463)	
Continuing, regional CRC	US\$2912 (US\$2573–US\$3063)	LN (7.98, 0.0445)	
Continuing, distant CRC	US\$9920 (US\$8489–US\$10 638)	LN (9.20, 0.0576)	
Death from distant CRC	US\$76 310 (US\$74 555–US\$78 086)	LN (11.24, 0.0119)	

*Assumption.

†Assumed to be 0 in base case.

‡Models the difference between the utility of localised and regional CRC.

CRC, colorectal cancer; CTC, CT colonography; GI, gastrointestinal; LN, Lognormal; OC, optical colonoscopy.

from Medicare reimbursement data in sensitivity analysis: US\$259 for CTC, US\$878 for OC without polypectomy and US\$1291 for OC with polypectomy.^{38 39} The net costs of CRC-related care were derived from an analysis of CRC cases relative to those of matched controls in the SEER-Medicare linked data (ie, these costs represent cancer-specific costs).^{40 41} We used phase-specific (ie, last year of life, initial year postdiagnosis and years in between) costs of CRC based on a previous analysis of SEER-Medicare data. All costs were updated to 2019 dollars using the personal consumption expenditure price index.

Analysis

The model was used to project discounted QALYs and discounted lifetime medical costs for both strategies. We calculated the ICER for the more costly and more effective strategy, defined as the ratio of the difference in cost divided by the differences in QALYs. While cost-effectiveness thresholds between US\$50 000 and US\$200 000/QALY are in the range that is considered cost-effective,^{42 43} we used a threshold of US\$100 000/QALY for our analysis. We performed deterministic and probabilistic sensitivity analyses to test the robustness of our results. The model was programmed in TreeAge Pro (V.2018, TreeAge Software, Williamstown, Massachusetts, USA).

RESULTS

Base case

Compared with using CTC as a combined intraluminal/extraluminal evaluation at 1 year, the standard-of-care strategy increased both lifetime average costs (US\$293 additional discounted dollars) and QALYs (0.0053 QALYs, discounted) for 60-year-old patients with stage III resected CRC (table 3). The ICER of standard of care compared with the CTC-based strategy was US\$55 500/QALY gained. For patients with resected stage II CRC, the standard-of-care option resulted in an ICER of US\$40 200/QALY gained (table 3). Table 4 shows the intermediate outcomes for each strategy. Compared with the CTC-based strategy, the standard-of-care strategy is associated with 789 additional colonoscopies, 2.6 averted CRC

Table 4 Expected outcomes per 1000 individuals with resected stage III colorectal cancer

Outcome	Strategy		Difference†
	CTC-based*	Standard of care	
Number of colonoscopies	3124.1	3912.8	788.7
Number of new CRC cases	12.5	9.9	-2.6
Number of CRC deaths‡	318.1	317.0	-1.1

*Assuming 3 yearly CT scans.
 †Standard of care minus CTC-based strategy; values could be off due to rounding.
 ‡Includes cancer deaths associated with the initial cancer diagnosis.
 CRC, colorectal cancer; CTC, CT colonography.

cases and 1.1 averted cancer deaths per 1000 persons with resected stage III CRC.

Sensitivity analyses

In one-way sensitivity analyses, our results were most sensitive to the sensitivity of CTC for detecting adenomas 10mm or larger and assumptions about the speed of disease progression (figure 2). If the CTC sensitivity for detecting adenomas 10mm or larger was as high as 0.97, then the ICER for standard of care compared with the CTC-based strategy was US\$210 800/QALY. If we assumed that the annual probabilities of progression through the adenoma states (ie, 1–5 to 6–9 mm, 6–9 to 10 mm or larger, 10 mm or larger to preclinical CRC) was 50% of our base-case estimates, the ICER for standard of care versus CTC-based strategy was US\$163 400/QALY. The ICER for standard of care compared with the CTC-based strategy increased to US\$81 000/QALY for stage III CRC and US\$60 600/QALY for stage II CRC when we used Medicare costs for the surveillance tests. The ICER for standard of care compared with the CTC-based strategy decreased if we assumed lower adherence with all surveillance testing. However, if we assumed that

Table 3 Cost-effectiveness results for cohort of 60-year-old patients with resected colorectal cancer*

Scenario and strategy	Total cost (US\$)	Health effects (QALYs)	Incremental Cost (US\$)	Incremental QALYs	ICER (US\$/QALY)
Stage III patients					
CTC-based strategy	121 099	8.0721			
Standard of care	121 392	8.0774	293	0.0053	55 498
Stage II patients					
CTC-based strategy	112 300	9.3684			
Standard of care	112 557	9.3748	257	0.0064	40 193

*Costs and effects are generated under the assumption of 100% systematic adherence to surveillance. A lower systematic adherence would reduce costs and effects proportionally but ICERs would remain unchanged.
 CTC, CT colonography; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

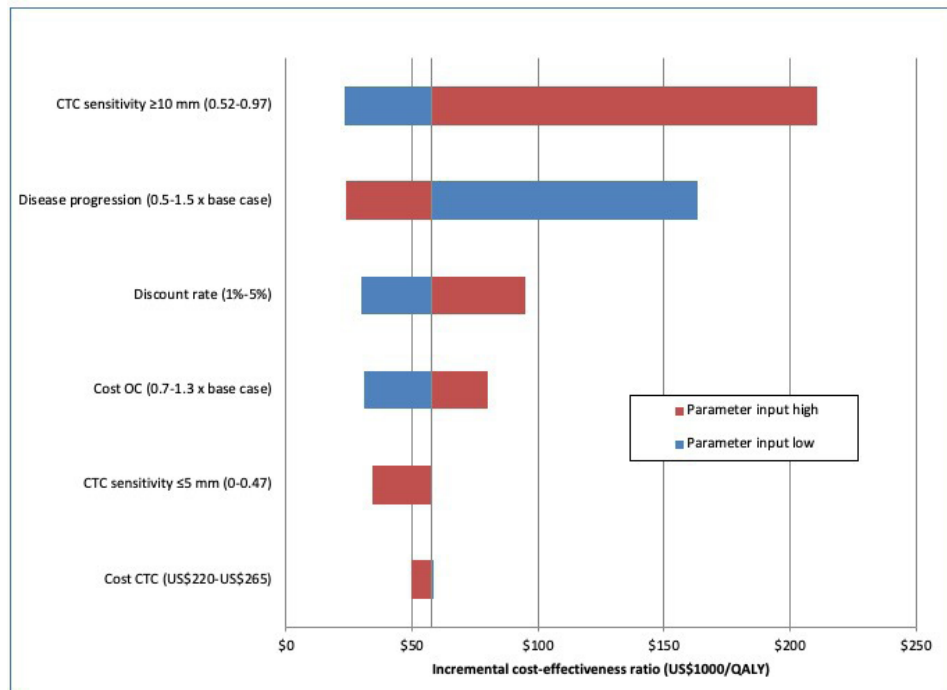


Figure 2 Results from one-way sensitivity analyses. Ranges used to vary each parameter are indicted. Results are for 60-year-old stage III resected colorectal cancer and represent the incremental cost-effectiveness ratio of standard of care compared with the CT colonography-based strategy.

adherence with CTC was greater than that with OC at the initial follow-up postresection, there were scenarios for which standard of care would no longer be cost-effective at a cost-effectiveness threshold of US\$100 000/QALY. For example, if adherence was 75% with OC and 99% with CTC, then the ICER for standard of care would be greater than US\$100 000/QALY (assuming full compliance with OC follow-up if CTC is positive).

Probabilistic sensitivity analysis

The distributions shown in [table 2](#) represent parameter uncertainty. By running the model for 5000 iterations with random draws from the distributions, we can characterise the overall uncertainty of the cost-effectiveness results. At a cost-effectiveness threshold of US\$100 000/QALY, the standard-of-care strategy was the most cost-effective option in 86% of the iterations ([figure 3](#)). The 95% credible interval for the ICER for standard of care relative to the CTC-based strategy was US\$12 207–US\$207 659/QALY.

Scenario analyses

We evaluated an alternative CT-based strategy where we assumed that the recommended timing for annual CT scans was 5 years instead of 3 years, as is the case for some guidelines. In this scenario, we assumed that CTC would be used in both years 1 and 4. The ICER associated with standard of care was lower than in the case of 3 yearly CTs at US\$51 100/QALY gained for stage III resected patients. We also evaluated a scenario where we assumed that those with non-high-risk findings would get OC every 5 years instead of the one 3 years after the initial

1 year OC. The ICER of standard of care compared with the CTC-based strategy was US\$24 300/QALY (stage III patients).

We varied the age of the cohort between 50 and 70 years for stage III resected patients. For a cohort of 50-year-old patients, the cost-effectiveness of the standard-of-care strategy compared with the CTC-based strategy was US\$34 500/QALY gained. For a cohort of 70-year-old patients, the ICER increased to US\$106 900/QALY.

DISCUSSION

Recommended surveillance for patients 1 year after CRC resection includes an abdominal/pelvic CT scan to detect distant recurrence and endoscopic surveillance to detect adenomatous polyps or metachronous CRC. Offering patients a single test to accomplish both extraluminal and intraluminal detection may result in both a reduction of testing burden for patients, which could affect adherence to surveillance testing, and an efficient use of resources. We used the methods of decision analysis to determine the differences in lifetime costs and benefits of a strategy that replaces the currently recommended two tests at 1 year (OC+CT) with a strategy that involves only one initial test (CTC). Health outcomes of new CRC cases detected and cancer-specific deaths were improved with the standard-of-care approach but with an increase in direct medical costs. We sought to determine which strategy was cost-effective for patients with CRC as part of a long-term surveillance protocol. We found that standard-of-care surveillance, when compared with a CTC-based approach, provided a potentially high-value

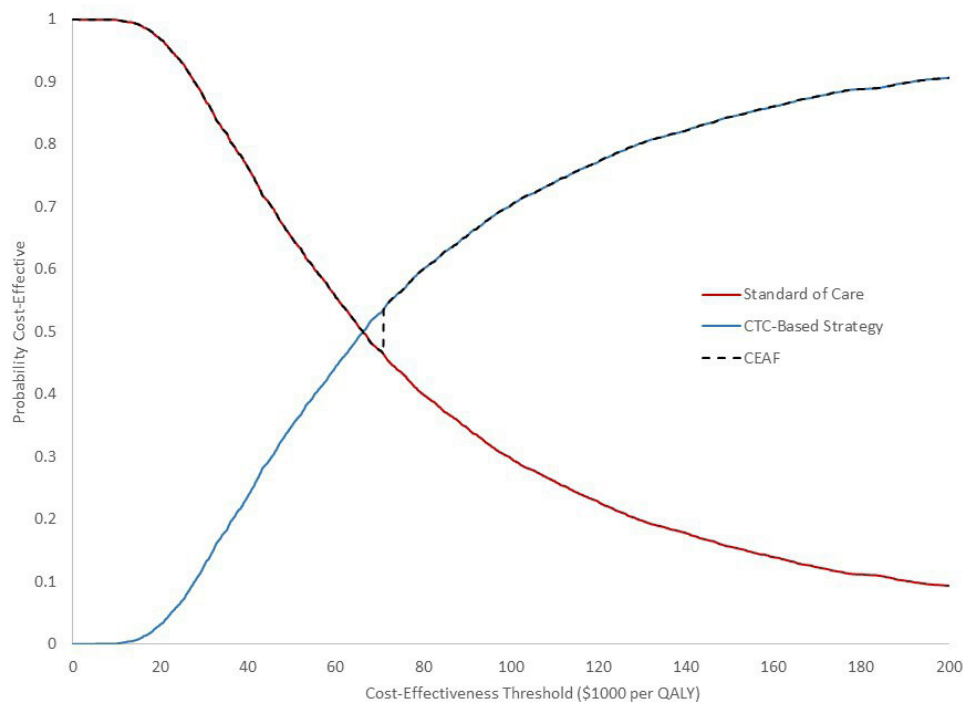


Figure 3 Cost-effectiveness acceptability curve showing the probabilities of standard of care and the CT colonography (CTC)-based strategy being cost-effective in 60-year-old patients with stage III resected colorectal cancer as the cost-effectiveness threshold varies. Also shown is the cost-effectiveness acceptability frontier (CEAF) indicating the probability of being cost-effective for the optimal strategy.

approach to managing disease for patients diagnosed with CRC (in other words, is an efficient use of resources). Our results were sensitive to assumptions about the sensitivity of CTC for detecting adenomas 10 mm or larger and rate of progression through disease states. We also found that standard of care was not cost-effective for older stage III patients (eg, patients over age 69 using a cost-effectiveness threshold of US\$100 000/QALY). Our results incorporated findings from a prospective, multi-centre study designed to determine the test characteristics of CTC among patients with CRC 1 year following resection.¹² The ICER for standard-of-care surveillance compared with a CTC-based strategy was US\$53 500/QALY, which is generally in the range of cost-effectiveness thresholds considered to be cost-effective, and we found an 86% probability that standard-of-care surveillance is cost-effective.

Our cost-effectiveness results were most sensitive to the sensitivity of CTC for detecting adenomas 10 mm or larger. Our base-case estimate of 0.80 from the clinical study¹² had a wide CI, and we found that if that value were as high as 0.90 that standard of care would no longer be cost-effective using a cost-effectiveness threshold of US\$100 000/QALY. In addition, the sensitivity that would result in the CTC-based strategy being cost-effective would be even lower for older patients (eg, 0.86 for 65-year-old stage III patients). Kim and colleagues⁴⁴ reported a sensitivity of 0.82 for CTC in a postresection setting, which is similar to the estimate we used. Our estimate was lower compared with a meta-analysis of the diagnostic performance of CTC in a screening population (per-person

sensitivity of 0.85).⁴⁵ Our analysis was not sensitive to several parameters, including the sensitivity of CTC for polyps smaller than 10 mm and the risk of death from polypectomy.

We compared two strategies that differed only in the surveillance tests used in the first year following CRC resection. This comparison allowed us to examine the isolated effects related to the use of CTC in this population. Guidelines recommend CT imaging at least yearly for the first 3 to 5 years and for our base-case analysis we assumed CT would be done for the first 3 years, as recommended by the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO).⁴⁶ When we considered the case of a 5 yearly CT scanning (and thus using CTC at years 1 and 4), the ICER for standard-of-care surveillance compared with a CTC-based strategy was lower (US\$51 100/QALY for patients with stage III resected CRC). Because both strategies had equivalent CT scan usage for the detection of extraluminal metastatic disease, the primary difference between the strategies was the ability to detect underlying adenomas or metachronous CRC at the first year (or first and fourth year) after resection. Because of this, we only found minimal impact when we evaluated a scenario where only a 1 year CT was used. Alternatively, we found a much larger effect on the ICER of standard of care compared with the CTC-based strategy when we evaluated a scenario of decreased intensity of OC (eg, every 5 years after year 1). We simulated a lifetime time horizon in order to capture the long-term effects and costs of missing lesions by CTC or overdiagnosis of lesions by OC



(ie, adenomas that never would have progressed to clinical cancer during a patients' lifetime) at 1 year.

Our results show that patients with postresection CRC could experience a significant reduction in the burden associated with OC under a CTC-based strategy. Of the approximately 100 000 patients who undergo CRC resection each year, there would be about 79 000 fewer OC procedures performed collectively over their lifetime. The harms associated with a CTC-based strategy, however, would be that an additional 110 patients (of the 100 000) would die from CRC during their lifetime.

Our study was the first to evaluate the cost-effectiveness of CTC for surveillance in patients after CRC resection. Other studies have evaluated postdiagnosis surveillance strategies. Hassan and colleagues⁴⁷ evaluated the cost-effectiveness of performing OC at 1 year compared with no OC and found that 1 year OC was a cost-effective practice. Renehan and colleagues⁴⁸ found intensive follow-up to be economically justified compared with conventional (less intensive) follow-up after curative resection for CRC.⁴⁸

One key limitation to our study was the lack of well-described studies to inform estimates of disease progression in patients with postresection CRC. Several studies have been conducted in patients with postresected CRC⁴⁹ with variable results, particularly in terms of the diagnosis of adenomas over time. This is likely due to inconsistent (and often not well reported) scheduling of OC over time. Not all subjects in the studies underwent OC or do so with consistent frequency. The incidence of metachronous cancers would be affected by the degree to which the study cohort was evaluated by OC. For example, more frequent OC would increase the likelihood of detecting an underlying metachronous cancer but would also reduce that chance that the cancer developed in the first place by removing adenomas. We found only one study that we felt provided data sufficiently detailed to use for our calibrations.²⁷ Thus, to model disease progression, we used studies among persons found with a high-risk adenoma.^{22–26} In sensitivity analysis, we found that the results were sensitive to assumptions about the transition probabilities associated with disease progression (ie, slower progression favoured the CTC-based strategy).

CONCLUSION

We conducted a simulation study and found that the standard of care for surveillance after resection for CRC was considered cost-effective by most well-accepted metrics with greater benefits at a greater cost than a CTC-based approach that replaced the first-year CT and OC with a single test, CTC. However, our analysis was sensitive to some key parameters such as the sensitivity of CTC for detecting adenomas 10 mm or larger. With a sensitivity greater than 91%, greater adherence with CTC compared with OC (eg, 99% vs 75%) and greater patient age (69 years and older), the CTC-based strategy became cost-effective.

Contributors DW is the principal investigator of the study. All authors contributed to the design of the analysis. KMK and JP developed the model and JRB and DW analysed trial data used to inform the model. All authors participated in the discussion and interpretation of results. KMK drafted the manuscript. All authors critically revised the manuscript for intellectual content and approved the final version.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All data used to inform the model were derived from the medical literature or summary data from an institutional review board-approved trial.

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Data availability statement No data are available.

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