



Using the Cancer Risk Management Model to evaluate colorectal cancer screening options for Canada

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ABSTRACT

Background

Several screening methods for colorectal cancer (CRC) are available, and some have been shown by randomized trials to be effective. In the present study, we used a well-developed population health simulation model to compare the risks and benefits of a variety of screening scenarios. Tests considered were the fecal occult blood test (FOBT), the fecal immunochemical test (FIT), flexible sigmoidoscopy, and colonoscopy. Outcomes considered included years of life gained, CRC cases and deaths prevented, and direct health system costs.

Methods

A natural history model of CRC was implemented and calibrated to specified targets within the framework of the Cancer Risk Management Model (CRMM) from the Canadian Partnership Against Cancer. The CRMM-CRC permits users to enter their own parameter values or to use program-specified base values. For each of 23 screening scenarios, we used the CRMM-CRC to run 10 million replicate simulations.

Results

Using base parameter values and some user-specified values in the CRMM-CRC, and comparing our screening scenarios with no screening, all screening scenarios were found to reduce the incidence of and mortality from CRC. The FOBT was the least effective test; it was not associated with lower net cost. Colonoscopy screening was the most effective test; it had net costs comparable to those for several other strategies considered, but required more than 3 times the colonoscopy resources needed by other approaches. After colonoscopy, strategies based on the FIT were predicted to be the most effective. In sensitivity analyses performed for the FOBT and FIT screening

strategies, FOBT parameter values associated with high-sensitivity formulations were associated with a substantial increase in test effectiveness. The FIT was more cost-effective at the 50 ng/mL threshold than at the 100 ng/mL threshold.

Conclusions

The CRMM-CRC provides a sophisticated and flexible environment in which to evaluate CRC control options. All screening scenarios considered in this study effectively reduced CRC mortality, although sensitivity analyses demonstrated some uncertainty in the magnitude of the improvements. Where possible, local data should be used to reduce uncertainty in the parameters.

KEY WORDS

Colorectal cancer, screening, outcomes, costs

1. INTRODUCTION

Colorectal cancer (CRC) is the 2nd most common cancer and cancer cause of death in Canada¹ and the 4th most common cancer worldwide². Screening has been shown to be effective in reducing the incidence of and mortality from the disease³⁻⁸. However, several alternative methods for CRC screening are available, not all of which have been evaluated by randomized clinical trials. All CRC screening methods ultimately require the use of colonoscopy for diagnosis, but they differ in their potential effectiveness and risks. Among the tests considered for primary screening, colonoscopy uniquely carries a risk of death by its application. Choice of screening method involves weighing the risks and benefits of the feasible options.

The Cancer Risk Management Model (CRMM) is an initiative from the Canadian Partnership Against Cancer, who developed a series of microsimulation models on a common platform to evaluate the effects of interventions aimed at reducing the impact

of cancer in Canada⁹. This ongoing project was undertaken to support advice on policy issues and to put sophisticated simulation tools into the hands of a broad user base so that individuals could evaluate user-driven scenarios¹⁰. Users are able to view and change the values of model parameters, but are provided with a suggested set (“base case”). Thus, users can evaluate new screening tests by specifying appropriate parameter values, and can also conduct sensitivity analyses of various parameter values on outcomes of interest. To guide the user, documentation about the source of the parameter estimates is provided. As part of the initial work, models for lung cancer and CRC were developed and implemented within the framework⁹. To permit examination of a richer variety of screening and follow-up approaches, the initial model for CRC was modified to incorporate a natural history model for CRC development based on the adenoma-to-carcinoma sequence¹¹. Here, we describe the development of the model, some of its capabilities, and examples of its results.

2. METHODS

2.1 Natural History Model

The existing literature on the natural history of CRC and on computer-based models of disease development was reviewed. To calibrate the model to the Canadian population experience, data about the incidence of and mortality rates for CRC were taken from the Canadian Cancer Registry. Data on stage distribution and stage-specific CRC survival were obtained from Canadian sources¹². Another review of the literature identified information about adenomatous polyp prevalence, incidence, growth rates, variation by sex, size, site distribution, and histology^{13–24}. Where possible, the literature was used to directly estimate parameters for the model; otherwise, it was used to inform parameter values for the model through calibration and provision of targets. Other published models of CRC^{25–28} were examined, and their parameter values were reviewed to provide insight into likely values or to identify potential discrepancies. Targets included polyp prevalence by age, sex, and site; colon and rectal cancer population incidence and mortality rates; and stage-specific survival rates. Interventional studies related to both screening and treatment were used to develop targets for the effects of specific interventions. Where such studies existed, priority was given to randomized trials to inform intervention targets. Deaths from other causes were simulated using age- and sex-specific rates for Canada.

The resulting model is illustrated schematically in Figure 1 and includes 6 anatomically defined subsites (rectum, sigmoid colon, descending colon, transverse colon, ascending colon, and cecum). The final model bore many similarities to models developed in the

United States and the Netherlands²⁹, which were previously used in the Cancer Intervention and Surveillance Modeling Network (<http://cisnet.cancer.gov>) consortium of models.

The CRMM-CRC model assumes that most CRCs develop from adenomas³⁰, whose growth is described by a 3-state Markov model based on polyp diameter (≤ 5 mm, 6–9 mm, ≥ 10 mm), with transitions controlled by parameter rates. Adenomas can grow in size, transform into stage 1 preclinical cancer, or regress. Preclinical cancers can either advance in preclinical stage or become clinical (diagnosed in the absence of screening). Within the general population, individuals have a varying propensity to develop adenomas (and thus CRC). Our propensity distribution was based on the analysis set out by Rutter *et al.*¹³. A detailed description of the model, including base-case parameter values, is available at the model Web site¹⁰.

2.2 Test Characteristics

Base-case colonoscopy sensitivity was estimated from published meta-analyses of “miss rates”^{26,31}. Colonoscopy specificity was assumed to be 100% for lesions that would be biopsied for pathology (for example, excluding mucosal tags, among others). Based on findings for cancer, colonoscopy sensitivity was lowered for proximal lesions^{32,33}. Colonoscopy complication rates were 0.00014 for death, 0.0012 for perforation, and 0.0003 for hemorrhage^{34–37}. Sigmoidoscopy parameters were assumed to be the same as those for colonoscopy in the distal colon and rectum. Sensitivities and specificities for fecal-based tests were taken from published comparative studies that included colonoscopy evaluation of all subjects^{38–47} and assumed that the fecal immunochemical test (FIT) uses a single sample. For other parameters, the model provides base-case values, but users can specify their own values. Sensitivity analyses for guaiac-based fecal occult blood tests (FOBT) and the quantitative FIT are obtained by including upper and lower range estimates of the test parameters (Appendix A) in the scenarios modelled. For the FOBT, the upper range (higher test positivity rate) corresponds to formulations of the screening test designed to provide high test sensitivity—for example, Hemoccult II SENS (Beckman Coulter, Mississauga, ON).

2.3 Follow-Up

In the CRMM-CRC model, for all methods of screening other than colonoscopy itself, a positive result is investigated by colonoscopy. Patient compliance to investigation is user-specified. After colonoscopy investigation, subjects are classified into four groups: adenoma-free, low risk, high risk, and cancer. Low-risk subjects have fewer than 3 small (<10 mm) non-villous adenomas and receive another colonoscopy

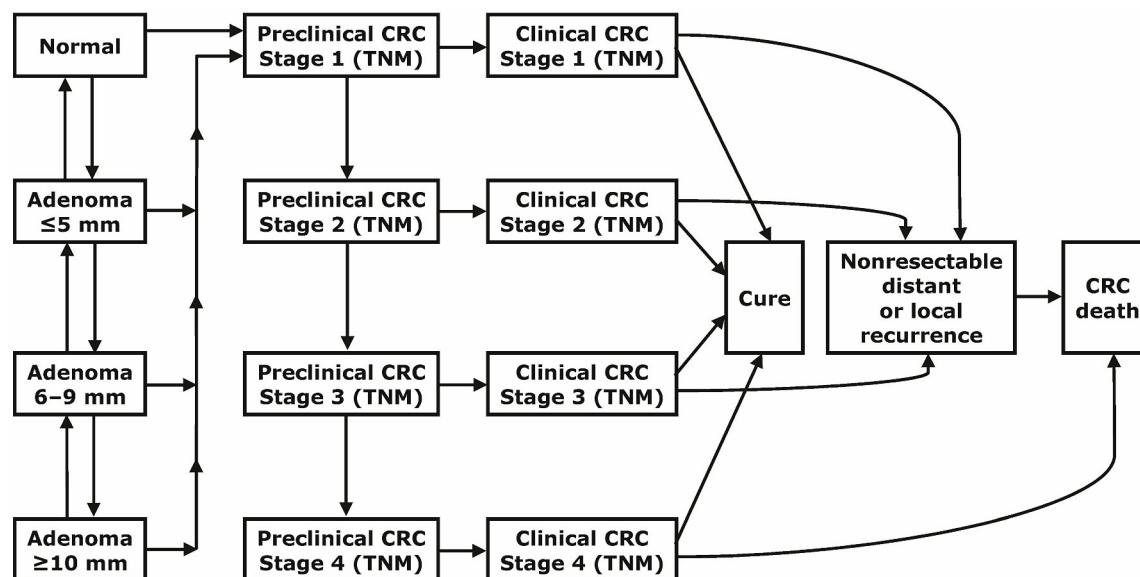


FIGURE 1 Schematic of the cancer risk management model for colorectal cancer (CRC) from the Canadian Partnership Against Cancer.

in 5 years; if clear, they then return to screening. High-risk subjects, defined as having 3 or more small adenomas, 1 or more large adenomas (≥ 10 mm) or an adenoma with a villous or tubulovillous component, receive colonoscopies at 3 and 5 years. Subjects with cancer receive a colonoscopy the next year and every 3 years thereafter. All adenomas identified at colonoscopy are assumed to be successfully treated.

2.4 Survival

Survival was modelled using a two-piece Weibull distribution that had been fitted to Kaplan–Meier survival curves based on data from Canadian centres. A hazard multiplier parameter was used to “calibrate” the survival curve such that the number of deaths generated from the curves matched the numbers expected from the Canadian Mortality Database as performed in an earlier version of the model¹². Stage-specific cancer survival in screen-detected cancers was assumed superior to that for incident cancers⁴⁹ and was reflected by applying a hazard rate multiplier.

2.5 Cost Information

Cost data were obtained from a variety of sources. Physician fees relating to diagnosis, treatment, and palliative care were obtained from billing sources for family practitioners and specialists in Ontario⁵⁰. Diagnostic costs—including laboratory tests, radiology tests, and biopsies—were obtained from provincial formularies and professional fees as required⁵⁰. Practice patterns of evaluation and follow-up of abnormal findings were based on expert opinion^{51–54}. Treatment data were obtained from the Ontario

Case Costing Initiative⁵⁵ and in consultation with Cancer Care Ontario. Cost estimates were adjusted to the year 2012, assuming inflation of 3% when the estimates were derived from earlier years. Further detail can be found at the CRMM-CRC Web site¹⁰ and in earlier publications^{9,12}.

2.6 Validation of Screening Effectiveness

Model predictions were compared with results from randomized trials available at the time of model development. For the FOBT, published results from a meta-analysis were used⁵⁶. For sigmoidoscopy, individual trial results were used^{6–8,57,58}.

3. RESULTS

The CRMM-CRC is available for examination and use on a publicly available Web site hosted by the Canadian Partnership Against Cancer¹⁰. To illustrate some of the capabilities of the model, we provide some examples of the evaluation of various screening interventions. Parameter values came from the scenarios presented here; where they differ from base-case values on the model Web site, they are presented in Appendix A.

A conventional way to express the overall results of screening interventions is to evaluate the effect of the intervention in a cohort of individuals exposed throughout their lifetime. We therefore longitudinally followed a simulated cohort of Canadian residents 44 years of age in 2014, consisting of approximately equal numbers of men and women, who were exposed to 23 screening scenarios or to no screening. The screening tests considered were the FOBT, the FIT, flexible sigmoidoscopy, and

colonoscopy (results for colonography are not presented, but are available within the model) given at varying frequencies and various ages. Table 1 describes the screening strategies considered. The scenarios presented assumed 100% compliance to screening, which allows for easier comparison of the effects of the different scenarios; however, the outcomes are not considered realistic for policy purposes. Results for each screening scenario were based on 10 million replications each.

Table 2 summarizes the effects of several screening strategies in terms of additional years of life gained, additional colonoscopies required, cases of and deaths from CRC prevented, and additional health system costs for CRC compared with no screening. The values in Table 2 can be used to calculate the

incremental effects of changing screening tests, changing screening frequency, or changing the age range for screening.

For example, using base-case parameter values (scenarios 1–17), the number of CRC deaths prevented per 100 screened ranged from 1.33 for biennial FOBT in individuals 50–74 years of age (scenario 1) to 2.45 for colonoscopy every 10 years (scenario 16). Thus, changing from FOBT to colonoscopy screening would prevent a further 1.12 CRC deaths and require an additional 259 colonoscopies per 100 screened, which translates to 231 additional colonoscopies per CRC death prevented (Table 2). Using upper-range values for the FOBT (scenario 19) increases the predicted number of deaths prevented to 2.09 per 100 screened. Using

TABLE 1 The screening strategies modelled

<i>ID</i>	<i>Scenario</i> <i>Short form</i>	<i>Age range (years)</i>	<i>Screening interval</i> <i>(years)</i>	<i>Screening test</i>
1	50–74_2_FOBT	50–74	2	Fecal occult blood (guaiac)
2	50–74_1_FOBT	50–74	1	
3	45–74_2_FOBT	45–74	2	
4	50–79_2_FOBT	50–79	2	
5	50–74_2_FIT50	50–74	2	Fecal immunochemical test (abnormal: ≥ 50 ng/mL)
6	50–74_1_FIT50	50–74	1	
7	45–74_2_FIT50	45–74	2	
8	50–79_2_FIT50	50–79	2	
9	50–74_2_FIT100	50–74	2	Fecal immunochemical test (abnormal: ≥ 100 ng/mL)
10	50–74_1_FIT100	50–74	1	
11	45–74_2_FIT100	45–74	2	
12	50–79_2_FIT100	50–79	2	
13	50–74_3_FIT50	50–74	3	Fecal immunochemical test (abnormal: ≥ 50 ng/mL)
14	50–74_5_FSIG	50,55,60,65,70	5	Flexible sigmoidoscopy
15	60_onetime_COL	60	N/A	Colonoscopy
16	50–74_10_COL	50,60,70	10	Colonoscopy
17	50–74_2_FIT100	50–74	2	Fecal immunochemical test (abnormal: ≥ 100 ng/mL)
	60_onetime_FSIG	60	N/A	Flexible sigmoidoscopy
18	50–74_2_FOBT_L ^a	50–74	2	Fecal occult blood (guaiac)
19	50–74_2_FOBT_H ^a	50–74	2	
20	50–74_2_FIT50_L ^a	50–74	2	Fecal immunochemical test (abnormal: ≥ 50 ng/mL)
21	50–74_2_FIT50_H ^a	50–74	2	
22	50–74_2_FIT100_L ^a	50–74	2	Fecal immunochemical test (abnormal: ≥ 100 ng/mL)
23	50–74_2_FIT100_H ^a	50–74	2	

^a L and H refer to the low and high estimates for the parameter ranges (sensitivity and specificity) for the FOBT and FIT tests as given in the table found in Appendix A.

TABLE II Comparison of outcomes for possible screening scenarios compared with no screening for a cohort of 45-year-olds followed until death

Scenario ID	Outcome					
	Additional years of life per person ^a	Additional colonoscopies (per 100 screened)	CRC cases prevented (per 100 screened)	CRC deaths prevented (per 100 screened)	Additional cost ^a (000s) (per 100 screened)	Colonoscopies (per death prevented)
1	0.18	43.14	1.97	1.33	114.31	32.49
2	0.25	69.99	3.00	1.80	195.11	38.85
3	0.20	47.40	2.01	1.31	129.97	36.19
4	0.20	49.01	2.19	1.50	128.97	32.75
5	0.28	77.56	3.92	2.07	142.46	37.41
6	0.31	114.39	4.62	2.30	221.48	49.71
7	0.30	85.51	3.93	2.03	161.36	42.03
8	0.30	87.83	4.31	2.29	160.67	38.41
9	0.27	60.84	3.67	1.99	133.44	30.63
10	0.31	91.10	4.45	2.25	216.21	40.53
11	0.29	66.33	3.66	1.95	151.12	34.02
12	0.28	69.04	4.04	2.19	150.58	31.59
13	0.26	60.29	3.41	1.86	106.98	32.33
14	0.25	72.47	3.98	1.84	292.13	39.29
15	0.23	122.70	4.00	1.88	90.08	65.31
16	0.32	302.12	5.27	2.45	218.52	123.10
17	0.28	71.69	4.03	2.08	181.86	34.47
18	0.16	23.47	1.48	1.15	103.02	20.34
19	0.28	91.88	4.13	2.09	142.17	44.03
20	0.27	68.55	3.75	1.99	137.53	34.50
21	0.29	92.99	4.15	2.16	150.75	43.01
22	0.25	58.66	3.29	1.83	132.17	32.03
23	0.29	77.78	3.97	2.10	142.60	37.10

^a No discounting.

base-case parameter values, screening scenarios based on the FOBT (scenarios 1–4) were inferior to other strategies with lower effectiveness, but with no increased net costs (Table II, Figure 2). Compared with most other scenarios, flexible sigmoidoscopy every 5 years from 50 to 74 years of age had higher net costs without increased effectiveness (Table II, Figure 2). Colonoscopy at 50, 60, and 70 years of age was the most effective scenario considered. Strategies using the FIT with a 50 ng/mL cut-point approached colonoscopy in effectiveness, with comparable net costs (scenarios 6 and 7). As might be anticipated, colonoscopy screening, compared with other scenarios, placed far greater demands on colonoscopy resources (Table I, Figure 3). Despite the comparable effectiveness of colonoscopy screening and some FIT-based approaches, the requirement for colonoscopy services is quite different (Table II).

Figure 2 provides a more conventional economic analysis for the same 23 screening scenarios relative to no screening, plotting years of life gained against cost differences, and discounting both at a rate of 3% per year. In discounted analyses, later

benefits and costs have less weight than earlier ones, such that the ranking of the various scenarios in Table II and Figure 2 varies.

Figure 4 illustrates a different aspect of the findings by examining the predicted impact of implementing selected screening approaches on the predicted pattern of CRC in the Canadian population for a 20-year projection period. Unlike the preceding figures, which assumed 100% compliance with screening, the projection in Figure 4 assumes 60% compliance with each protocol. It can be seen that even at those levels of compliance, the more effective screening approaches substantially modify demographically driven increases in the population burden of CRC over the 20-year period.

4. DISCUSSION AND CONCLUSIONS

The CRMM-CRC model provides results calibrated to Canadian risks of CRC incidence and death, and reproduces the general findings of models from other jurisdictions of the effectiveness of several approaches in preventing development of and death

from CRC. It provides projections of the effects of screening measures on the Canadian population so that clinical and administrative stakeholders can assess the value of such measures in several dimensions. Results from the CRMM-CRC model (Table II)

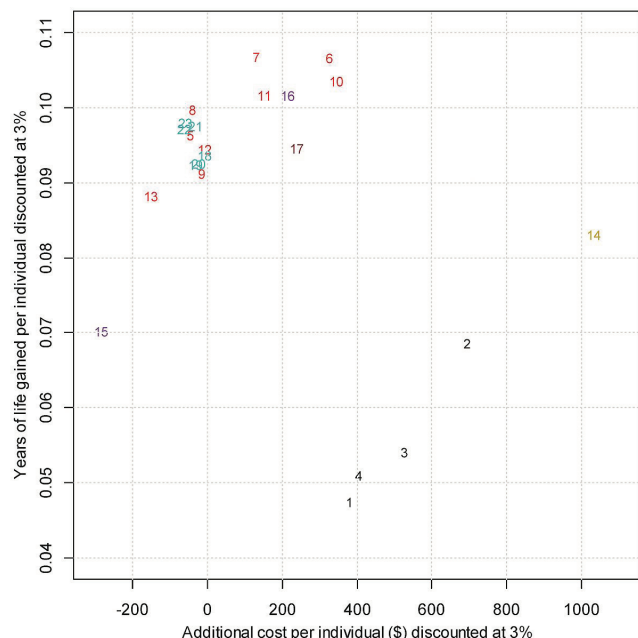


FIGURE 2 Plot of discounted life-years gained versus lifetime medical care costs for colorectal cancer (CRC) screening and treatment. The plot presents 23 screening scenarios (see Table I) compared with no screening for a cohort of 45-year-olds followed until death.

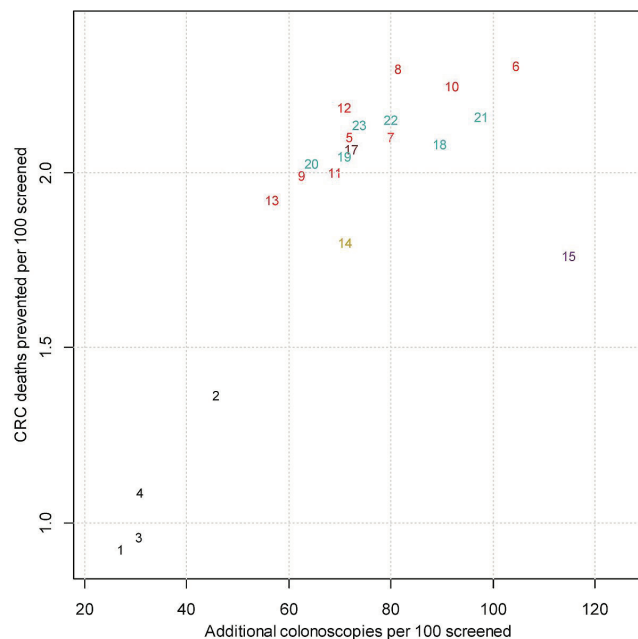


FIGURE 3 Plot of colorectal cancer (CRC) deaths prevented versus increased colonoscopies required per 100 screened. The plot presents 23 screening scenarios (see Table I) compared with no screening for a cohort of 45-year-olds followed until death.

using the assumed parameter values indicate that FIT-based testing provides an effective alternative to colonoscopy-based primary screening and makes considerably less use of colonoscopy resources over the long term. Figure 4 demonstrated that, even with 60% compliance, adoption of either FIT- or colonoscopy-based screening strategies could largely prevent anticipated increases in the burden of CRC over the next 20 years caused by the growth of the Canadian population in the age groups at greatest risk of CRC. Other analyses have also shown screening for CRC to be cost-effective^{27,28,30}. Many of the screening scenarios under consideration will result in financial savings⁵⁹ where results are influenced by the discount rate, which affects the relative value of the short-term and long-term costs and benefits. We have highlighted the colonoscopy requirement because of the high demand for colonoscopy required by some screening scenarios. Unnecessary colonoscopies and colonoscopies of low net return should be avoided because of the associated risks. Screening scenario choice hinges on feasibility with respect to colonoscopy capacity and the trade-off between colonoscopy risks and benefits. The CRMM-CRC model is a micro-simulation model, and so repeat analyses with the same parameters do not yield identical results: each is a unique simulation, and consequently,

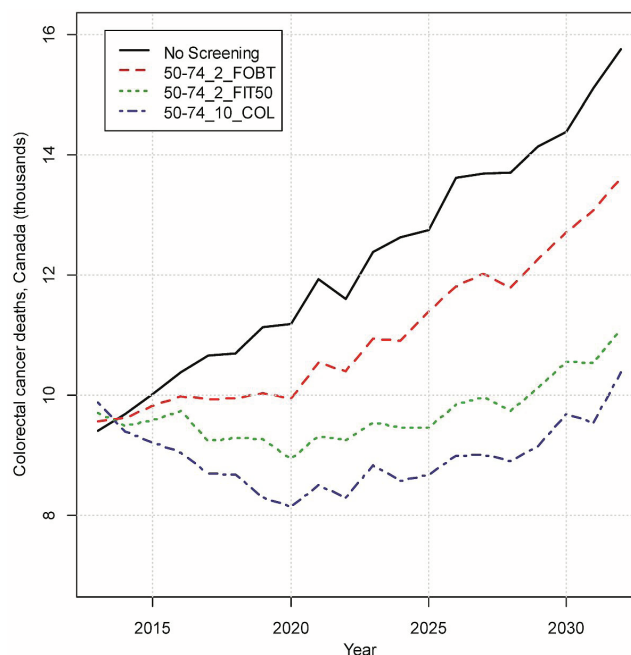


FIGURE 4 Predicted effect of 4 screening strategies on colorectal cancer deaths in Canada for 2013–2033, assuming 60% population compliance: no screening, screening every 2 years in individuals 50–74 years of age either by fecal occult blood testing (50–74_2_FOBT) or by fecal immunochemical testing [50–74_2_FIT50 (abnormal: ≥ 50 ng/mL)], and screening at 50, 60, and 70 years by colonoscopy (50–74_10_COL).

stochastic variation occurs in the findings. Care must therefore be taken in attaching significance to small differences in predicted outcome between the individual scenarios.

Many mathematical models of CRC have been published worldwide, and a recent review⁶⁰ has considered them from an econometric perspective. Models drawing on Canadian data have previously been published^{27,28,61}. Although detailed findings vary, all models concluded that screening for CRC was effective and provided good value for money. Models that have been produced using more recent data^{27,28,59} have found that some screening strategies result in net cost savings; older analyses generally did not predict savings³⁰. This improved assessment of screening is likely related to recognition of the increased costs of managing advanced CRC and improved estimates of the effectiveness of screening from recently published trials of sigmoidoscopy.

The approach presented here has several strengths. It draws on a body of work in which microsimulation tools for evaluating cancer control interventions were developed⁶², providing connections to tools developed for the analysis of social policy⁶³. It utilizes Canadian data sources for disease incidence and general mortality, and data derived from Canadian studies of patient outcomes. The microsimulation framework is powerful and permits the simulation of strategies in a wide range of user-defined Canadian subpopulations (cohorts and so on). Users are able to provide their own estimates of clinical parameters and to specify their scenarios of interest rather than rely on available analyses from the model developers. Nevertheless, this power and flexibility comes with some limitations. If choosing to vary clinical parameters (especially those associated with the natural history component), users must have a working understanding of the structure of the model, because changes might cause the model to lose its ability to predict findings based on the literature to which it was calibrated. The reported values of key parameters, such as the sensitivities and specificities of screening tests, show considerable variation in the literature. Microsimulation models require millions of calculations and thus take time to complete. Sensitivity analyses—in which the influence on model predictions of the uncertainty related to model inputs is assessed—are an important part of model evaluation⁶⁴. It is not feasible for the general user to perform probabilistic sensitivity analyses⁶⁵ in the model, although specified sensitivity analyses in which the user specifies alternative parameter values, can easily be undertaken. The anticipated future demand for colonoscopy services (when colonoscopy is not the primary screening method) is greatly influenced by the estimation of false-positive results for the primary screening test. Consequently, we would recommend the use of extensive sensitivity analyses for screening options under active consideration. No observation of false-positive rates after several

rounds of negative FIT results is currently available. Observations from Europe⁶⁶ indicate that positivity rates fall by approximately one third between the 1st and 2nd rounds of screening, apparently because of earlier removal of bleeding polyps and because of a lower false-positive rate for subjects who were negative at round 1. It is therefore likely that false-positive rates for the FIT will decline the longer that screening continues. Model estimates, which are largely based on the results from early screens, could therefore prove to be too high.

A limitation of the model as presented is that it is based on the assumption that an improved reduction in the incidence of CRC will result because of the superior sensitivity of the FIT for polyp and cancer detection, as demonstrated in studies comparing those parameters for the FIT and the FOBT. No randomized trial establishing the veracity of that assumption has been published or is currently under way, although future results from a trial comparing FIT with colonoscopy⁶⁷ can be expected to be informative. It is therefore critical that jurisdictions opting to use FIT for CRC screening should establish evaluation and monitoring mechanisms to verify that the anticipated outcomes are achieved.

The CRMM provides a well-developed framework for the evaluation of cancer control measures in the Canadian population. Models will continue to be developed and updated, providing a wide-range of users with access to a powerful suite of tools for evaluating cancer control policy.

5. CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

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APPENDIX A: CANCER RISK MANAGEMENT PLATFORM, COLORECTAL CANCER MODEL: NON-BASE CASE PARAMETERS USED IN SCREENING SIMULATIONS

This appendix documents the parameter estimates used in the simulations presented in the main paper. The simulations were run using the Colorectal (CRC) model of the Cancer Risk Management Model (CRMM) in November 2014. Most parameters in the model were not changed. Parameters in the natural history component of the model were unchanged. Treatment and cost parameters were not changed. These specifications were used:

- Demographic parameters
 - Special tabulation parameters: User-defined cohort age filter was 44, and year filter was 2014.
 - Demographic parameters: Immigration start year was 2222 (turns immigration off).
 - Population health parameters: Average health utility of population by age was set to 1 for all ages.
 - Economic parameters: Economic annual growth rate was 0.
- Screening test specifications
 - The table that follows shows the screening test characteristics used in the model. Parameters were estimated using values from the literature, except in two areas. Specificity was related to a finding, by colonoscopy, of no adenomas when none were present. That approach seems to have been used in several other models, although it leads to specificities of unity for colonoscopy. Sensitivity for colonoscopy was set to be slightly lower in the proximal colon⁴⁸ than in the distal colon, reflecting observations of reduced effectiveness for the proximal colon, although studies have not consistently found a difference.
 - Recruitment and participation: Age and 2 years of first screen (cohort 44 years of age in 2014, born in 1969–1970); participation was 100%; phase-in period was 0.
 - Modality selection: Modality, start and end age, adherence was 100%, screen interval, maximum screens.

Test sensitivities and specificities^a

State	Fecal tests									Investigations		
	Occult blood			Immunochemical						Flexible sigmoidoscopy	Colonoscopy	
	Low ^b	Base	High	≥50 ng/mL			≥100 ng/mL				Distal colon	Proximal Colon
				Low	Base	High	Low	Base	High			
1–5 mm	1.1	3.0	8.0	5.0	6.0	8.0	4.0	4.0	6.0	75.0	75.0	65.0
6–9 mm	2.4	4.0	13.0	10.0	12.0	14.0	8.0	10.0	12.0	85.0	85.0	85.0
10 mm+	7.6	10.0	41.0	32.0	35.0	41.0	24.0	30.0	37.0	95.0	95.0	87.5
Cancer	50.0	50.0	64.0	70.0	82.0	90.0	65.0	75.0	85.0	95.0	95.0	95.0
Normal	1.1	3.0	8.0	5.0	6.0	8.0	4.0	4.0	6.0	0.0	0.0	0.0

^a Expressed as test positivity rates within each disease state. When used in the model, they are hierarchically applied. For example, when multiple polyps are present, the rate is based on the largest polyp.

^b Abstracted from Wilschut *et al.*⁴⁷.