

# Understanding the Effects of Competition for Constrained Colonoscopy Services with the Introduction of Population-level Colorectal Cancer Screening: A Discrete Event Simulation Model

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**Background:** Median wait times for gastroenterology services in Canada exceed consensus-recommended targets and have worsened substantially over the past decade. Meanwhile, efforts to control colorectal cancer have shifted their focus to screening asymptomatic, average-risk individuals. Along with increasing prevalence of colorectal cancer due to an aging population, screening programs are expected to add substantially to the existing burden on colonoscopy services, and create competition for limited services among individuals of varying risk. Failure to understand the effects of operational programmatic screening decisions may cause unintended harm to both screening participants and higher-risk patients, make inefficient use of limited health care resources, and ultimately hinder a program's success. **Methods:** We present a new simulation model (Simulation of Cancer Outcomes for Planning Exercises, or SCOPE) for colorectal cancer screening which, unlike many other colorectal cancer screening models, reflects the effects of competition for

limited colonoscopy services between patient groups and can be used to guide planning to ensure adequate resource allocation. We include verification and validation results for the SCOPE model. **Results:** A discrete event simulation model was developed based on an epidemiological representation of colorectal cancer in a sample population. Colonoscopy service and screening modules were added to allow observation of screening scenarios and resource considerations. The model reproduces population-based data on prevalence of colorectal cancer by stage, and mortality by cause of death, age, and sex, and attendant demand and wait times for colonoscopy services. **Conclusions:** The study model differs from existing screening models in that it explicitly considers the colonoscopy resource implications of screening activities and the impact of constrained resources on screening effectiveness. **Key words:** Average-risk colorectal cancer screening; colonoscopy resources; resource competition; discrete event simulation. (*Med Decis Making* 2017;37:253–263)

Recent efforts to control colorectal cancer have shifted from screening higher-risk individuals, such as those with inflammatory bowel diseases, inherited syndromes, or a first-degree family history of colorectal cancer, to screening asymptomatic, average-risk individuals. The goal of average risk screening is twofold: (1) to interrupt the disease in earlier, more treatable stages, or (2) to prevent cancer by identifying and removing precancerous

polyps or adenomas.<sup>1,2</sup> To that end, many jurisdictions are implementing population-based, average-risk screening programs. While most programs follow the general guidance provided by published recommendations, such as the use of two-step screening (stool testing with colonoscopic follow-up of positive tests) to conserve limited colonoscopy resources, considerable variation exists in terms of choice of stool test, positivity threshold, frequency of testing, recruitment methods, and allocation of colonoscopy resources.<sup>3–8</sup> As these programs are recent initiatives, the effects of these decisions are largely unknown.<sup>9–11</sup> However, understanding the patient and health system effects of

screening programs are essential for their sustainability, for justification of the opportunity costs of their operation, and to avoid unintended harms.

Colonoscopy resources serve many populations and functions – average- and higher-risk cancer screening, diagnosis of symptomatic individuals with various etiologies, and surveillance of all requiring follow-up. Average-risk colorectal cancer screening increases the existing demand for colonoscopy services both in the short term, from either primary screening activities or positive stool tests requiring follow-up, and in the long term, due to the cumulative need for surveillance. Without adequate capacity, even two-step, average-risk screening has the potential to overwhelm colonoscopy services and impede access for higher-risk patient groups. A challenge for decision makers is to balance the needs of all, ensuring adequate resources to allow timely access for those likely to have serious underlying diseases, while enabling prevention and early identification efforts.

Determining the sufficiency of colonoscopy resources to support screening is not straightforward, and requires an understanding of the shifting influences of uptake rates, screening effectiveness, underlying population characteristics, and ongoing surveillance requirements. A systems-minded evaluation of the effects of health services decisions requires tools capable of handling these as well as

operational factors, such as resource constraints and competition, queuing, and stochasticity.<sup>12–14</sup> Discrete event simulation (DES) modeling provides such capacity while synthesizing available data, elucidating the interaction of system components, and allowing for the examination of “what if” questions.<sup>15–18</sup> Simulation modeling has been used to understand population and system implications of average-risk colorectal cancer screening; however, most models have not explicitly modeled colonoscopy resources or have assumed unlimited colonoscopy capacity.<sup>19–21</sup> While this is a reasonable assumption when resources are sufficient, constrained colonoscopy resources effectively create competition between patients, which must be considered to capture unintended harms both to screening participants and higher-risk individuals alike.

A DES model (Simulating Cancer Outcomes for Planning Exercises (SCOPE)) was constructed to evaluate the effects of average-risk colorectal cancer screening on patient and system outcomes, with particular attention paid to the competition for limited colonoscopy resources between different patient groups, namely, average-risk screening program participants and higher-risk screening and diagnostic patients. This paper presents the SCOPE model, delineates its assumptions, and reports validation and calibration results. Results of experiments conducted using the SCOPE model are reported elsewhere.<sup>22</sup>

## METHODS

A DES model (SCOPE) based on a colorectal cancer natural history foundation module with screening and colonoscopy service modules was constructed using Arena.<sup>23</sup> A basic model was constructed initially, with increasing complexity introduced as needed. The research questions, performance measures and availability of data guided the level of detail specified in the model. Integration of all modules was necessary for observing the interaction between system components, screening program and service delivery strategies, and outcomes for the different patient populations (Figure 1).

### Natural History Module

The natural history module simulated the development of colorectal cancer based on the adenoma-carcinoma sequence.<sup>24–26</sup> Briefly, the adenoma-carcinoma (or polyp-cancer) sequence is an approximately 10-year process in which the normal

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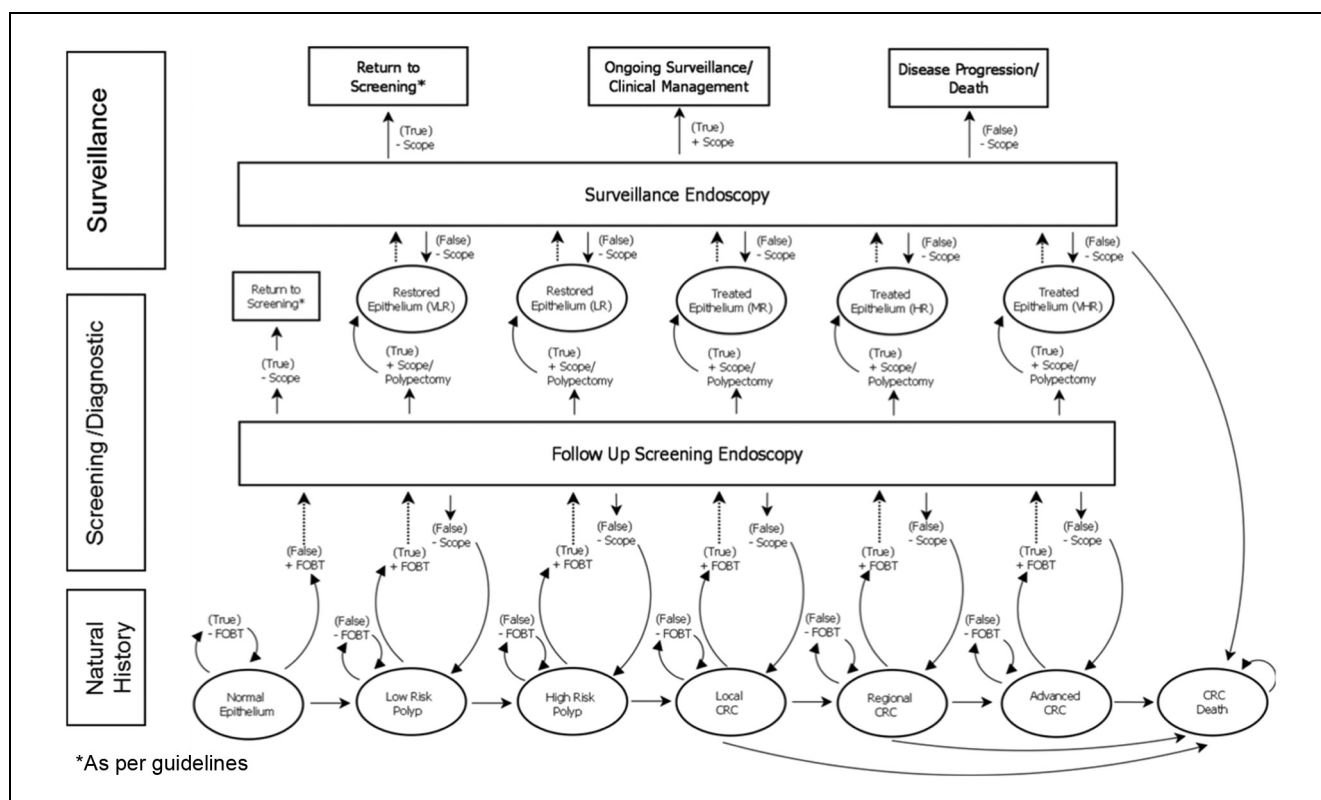


Figure 1 Process map of the full SCOPE model

epithelial tissue lining of the large intestine transitions through dysplastic (precancerous) changes in cells to cancer.<sup>24–26</sup> The majority of colorectal cancers develop from polyps; however, only a small proportion of polyps go on to become cancer.<sup>26</sup> Due to the lack of direct evidence of the rate of development of de novo cancers, all colorectal cancers in the model were assumed to develop from pre-existing adenomas. Potential for malignancy varies by polyp size, histological type, and the grade of epithelial abnormality.<sup>24</sup> Polyps were categorized in the sequence as low (<1 cm, tubular histology) or high ( $\geq 1$  cm, high-grade dysplasia, villous histology) risk.<sup>2,24–26</sup> Cancer was broadly classified as either early (localized), regional, or advanced (metastasized) disease.

The population was stratified into two risk groups: average and higher risk. For the average-risk group, the onset of and progression to any stage in the adenoma-carcinoma sequence was assigned based upon transition probabilities derived from age-specific incidence rates in average-risk Western populations.<sup>27–31</sup> The higher-risk group captured the proportion of the population with a history of

colorectal cancer among first-degree relatives or with predisposing conditions, such as inflammatory bowel disease or inherited disorders,<sup>32–34</sup> and individuals were considered twice as likely to develop polyps as those of average risk.<sup>6</sup> Annual transition probabilities and initial stages for higher-risk individuals were adjusted based on this assumption.<sup>22</sup>

The natural history model included background mortality. For each individual in the model, age- and sex-specific background mortality rates (deaths from all causes) were applied annually based on Statistics Canada Life Tables (2007 to 2009).<sup>35</sup> Individuals were subject to competing risks of background and colorectal cancer mortality, assuming conditional independence of the risks. Using standard approaches to handling competing risks widely used in multi-decrement life tables, individuals were exposed to the risk of both background and colorectal cancer mortality each year, and the attribution of cause was stochastic and proportional to the force of mortality for each cause.<sup>36</sup>

Adenoma-carcinoma stages were updated yearly for individuals who survived the year; individuals

**Table 1** Sensitivity and Specificity: Stool Tests

Stage	Stage-specific FIT (sensitivity analyses) <sup>a</sup>	Stage-specific sensitive g-FOBT (sensitivity analyses) <sup>a</sup>
1. Normal epithelium	0.05 (0.02, 0.08)	0.12 (0.09, 0.15)
2. Low-risk polyp	0.104 (0.07, 0.135)	0.075 (0.05, 0.1)
3. High-risk polyp	0.271 (0.23, 0.31)	0.185 (0.15, 0.22)
4. Local colorectal cancer	0.565 (0.51, 0.62)	0.5 (0.45, 0.55)
5. Regional colorectal cancer	0.75 (0.7, 0.8)	0.7 (0.65, 0.75)
6. Advanced colorectal cancer	0.80 (0.75, 0.85)	0.87 (0.8, 0.92)

<sup>a</sup>At stage 1 (normal epithelium), specificity is expressed as false positives. At stages 2–6 (presence of pathology), sensitivity is expressed as true positives.

remained in the current stage or progressed to the next stage. Colorectal cancer mortality risk depended on stage, increasing with advancing cancer stages.

### Screening Module

The purpose of the screening module was to simulate the uptake and outcomes of colorectal cancer screening for asymptomatic, average-risk, 50- to 74-year-olds and to examine changes in case capture due to variations in participation rates, test sensitivity and specificity, demographic factors and disease prevalence. Higher-risk individuals were screened using primary colonoscopy.

In a two-step, average-risk screening program, such as recommended by Canadian guidelines, stool testing could be simulated using either guaiac (g-FOBT) or immunochemical (FIT) test parameters, and follow-up of positive tests modeled using colonoscopy, flexible sigmoidoscopy, or repeat stool tests (g-FOBT or FIT) as the modality of choice. In many jurisdictions, primary screening with colonoscopy is limited to higher-risk individuals due to resource constraints. However, the SCOPE model can also accommodate primary colonoscopy screening for the average-risk population.

As individuals progressed through the model, random draws from probability scores determined the uptake and outcome of stool testing and colonoscopy (positive or negative, and in the case of colonoscopy, stage of findings), based on the sensitivity and specificity of the exams as reported in the literature for each stage in the adenoma-carcinoma sequence (Table 1). Individuals' screening outcomes (whether true or false positive/negative) depended upon their true stage in the adenoma-carcinoma sequence as assigned by the natural history module and the sensitivity and specificity of the test. There is substantial uncertainty around the estimates of sensitivity and specificity of stool tests reported in the

literature,<sup>22,37</sup> which was captured using sensitivity testing of the range of values reported in studies of average-risk populations (Table 1).<sup>38,19,39,40</sup>

The identification of adenomas or cancer led to follow-up investigation and treatment sequelae (e.g., removal of adenomas or effective treatments) that altered the underlying adenoma-carcinoma sequence provided by the natural history module. Thus, the model measured screening effectiveness as aggregate differences in outcomes between screening and no screening scenarios. As such, screening strategies could be compared both with the status quo, and with each other.

In the event of nonparticipation in screening, or in the case of participation in screening with false-negative results, individuals could progress through disease stages in the natural history module, with increasing likelihood of detection through symptomatic presentation, diagnosis, or future screening participation.

### Colonoscopy Services Module

Individuals presented to colonoscopy services by one of three pathways: 1) following a positive screening test, 2) by becoming symptomatic or undergoing higher-risk screening by colonoscopy, and 3) by requiring ongoing surveillance colonoscopy following a positive colonoscopy. Colonoscopy resources were modeled as available colonoscopy "slots" and apportioned to average-risk screening follow-up, diagnostic or high-risk screening, or surveillance activities, allowing for the representation of competition for services. Factors influencing their availability, such as human resource requirements, equipment availability, or funding decisions were considered exogenous to the model; although, the model could be extended to explicitly represent these factors.

Following colonoscopy, colorectal epithelium was assumed to be either: 1) restored following removal of

low-risk polyps, or 2) treated following removal of high-risk polyps. Colonoscopy findings assumed increasing likelihood of detection with increasing stage in the adenoma-carcinoma sequence.

### Surveillance Activities

Surveillance activities, whereby patients with adenomas or carcinomas detected by colonoscopy underwent subsequent surveillance with colonoscopy, were also modeled within the colonoscopy services module. This enabled representation of the demand for colonoscopy services resulting from surveillance. Individuals from any of the average-risk follow-up screening, high-risk screening/diagnostic colonoscopy, or surveillance arms could be directed to surveillance services based on the findings of their index or subsequent surveillance colonoscopies. The frequency of surveillance was based upon North American guidelines for follow-up.<sup>7,8,41</sup>

### INPUT DATA

Data for the SCOPE model parameters and transition probabilities were collected from a variety of sources, including publicly available administrative and survey data sources, published controlled trials and observational studies, and expert opinion.<sup>3–5,7,8,19,22,27–31,34,35,38–40,42–53</sup> Where possible, parameter values represented those observed in community settings rather than RCTs to more accurately reflect observations outside of strict study protocols. Observations derived from average-risk populations were selected over higher-risk clinical subpopulations, and were refined by age- and sex-specific rates where available. The model consisted of a combination of deterministic and stochastic variables. For example, the number of colonoscopy slots are not random and were specified to reflect the availability of services. Conversely, patient arrival rates to colonoscopy services or transition probabilities between states were represented as stochastic variables to more accurately reflect uncertainty in the system.

Sensitivity analyses were used to determine if uncertainty in input parameters had a significant impact on performance measures.<sup>54</sup> If system performance measures were highly sensitive to changes to an input parameter, close attention was paid to calibration of those parameters against other outcomes. For example, model output was not sensitive to changes in background mortality or age, but

was very sensitive to transition probabilities between stages in the adenoma-carcinoma sequence. Therefore, much of the calibration of the model concentrated on refinement of these transition probabilities so that the model reflected population-based data on prevalence of cancer by stage, and mortality by cause of death, age, and sex.

### VALIDATION AND VERIFICATION

Validation and verification of simulation models aimed to determine whether models and their outputs were “correct”. Validation confirms an accurate representation of the system under study (i.e., “Did I build the right thing?”), while verification ensures that the programming and implementation are correct (i.e., “Did I build the thing right?”).<sup>55</sup> Every opportunity was taken to validate and verify the SCOPE model during the development process. Validation and verification is an iterative process, and is outlined in detail below.<sup>12</sup> Briefly, the conceptual model was validated initially for the accuracy of its representation of the system. Construction of the model using Arena software afforded visual representations of the model to aid with communication to stakeholders.<sup>23</sup> Once built, the simulation model was verified to determine whether the assumptions in the conceptual model had been accurately programmed through debugging, testing of extreme input values, tracing the paths of individuals through the program, and review by team members. Finally, output data were validated through comparison with existing performance measures and other models, where available.

### Conceptual Model Validation

Standard practices were followed for the initial validation of DES models,<sup>12</sup> including consultation with those familiar with colorectal cancer development and progression, screening activities, and colonoscopy service provision to ensure accurate representation of the system and processes. Assumptions were acknowledged in a written document and validated for accuracy through interviews with gastroenterologists, oncologists, colorectal cancer screening nurses, and colonoscopy booking clerks.<sup>22</sup> A time study was conducted in an active colonoscopy suite to confirm assumptions regarding process and capacity, including throughput, exam time, and the availability of colonoscopists and suites for screening and other activities.

**Simulation Verification**

The model was run initially for debugging, which involved systematically reviewing the computer programming to detect and correct errors. The model was constructed in stages, beginning with moderate levels of detail and adding increasing detail and subprograms as necessary, which were debugged successively before they were built upon. The model was debugged in its entirety once completely constructed. Coding and processes were reviewed by team members.

Extreme values were tested and probabilistic input data replaced with deterministic values to test whether the output was reasonable. Deterministic Markov models were used for comparison, when appropriate, such as when verifying the outcomes of the natural history process to ensure the accuracy of the Monte Carlo processes employed in the probabilistic aspects of the DES model. The point estimates generated by Markov models of the natural history were included within the ranges produced by the SCOPE model. The model's behaviour was observed graphically as the simulation clock ran, and individuals were traced as they progressed through the model to ensure flow was as expected. Counters were placed at several intervals and checked using hand calculations to ensure the model operated as envisioned.<sup>12</sup>

**Output Validation**

Key to validation of a DES model is validation of the output.<sup>12</sup> The model was calibrated deterministically by comparing model and patient outcomes and system performance measures with real world observations where possible. The model was run over a 15-year horizon with populations of individuals of ages 50 to 99 years, distributed by age and sex based on the 2006 Canadian Census.<sup>52</sup> This permitted comparison of the proportion of colorectal cancer deaths in the synthetic populations with those observed in the Canadian population in 2006.<sup>45</sup> While the main purpose of the SCOPE model was not to simulate death rates for the population, the Canadian rates provided a useful comparison for the observed patterns of colorectal cancer mortality by age, sex and risk category. Proportions were compared for average and higher-risk individuals, and for males, females and both sexes (Figures 2–4).

The proportions of colorectal cancer deaths in the simulated populations mirrored those observed

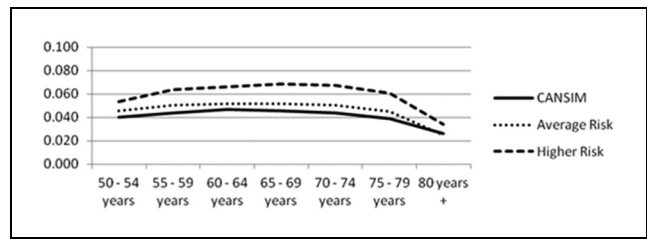


Figure 2 Proportion of colorectal cancer deaths/all deaths – males.

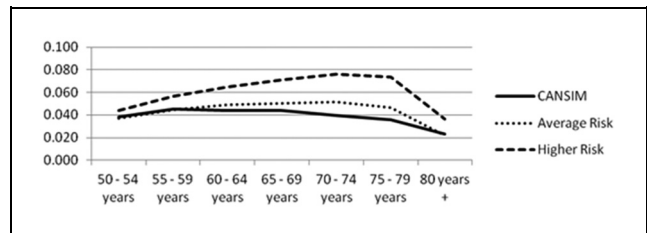


Figure 3 Proportion of colorectal cancer deaths/all deaths – females.

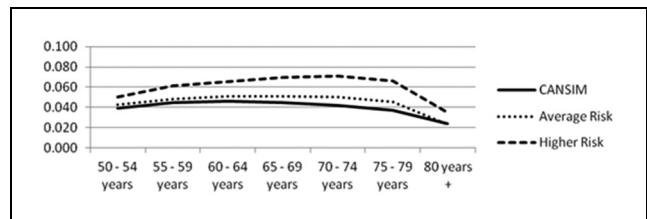


Figure 4 Proportion of colorectal cancer deaths/all deaths – both sexes.

in the Canadian population. The minor differences are likely due to the assumption of independence between colorectal cancer death and all-cause mortality in the SCOPE model. Due to shared risk factors, those at risk of colorectal cancer mortality are also at higher risk of other related causes of mortality, such as other cancers, cardiovascular disease and diabetes.<sup>56</sup> This phenomenon is reflected in the Canadian population figures. However, this relationship is highly complex, with little supporting data to elucidate a clear picture of the nature of the relationship and, as such, we chose not to adjust mortality by introducing dependence into death probabilities. The consequence is that the model may slightly overestimate the proportion of deaths due to colorectal cancer.

As expected, colorectal cancer deaths accounted for consistently greater proportions of deaths among

**Table 2** Simulated Demand for Colonoscopies per 10,000 Population

Year	Colonoscopies/10,000 without Average Risk Screening (95% CI)	Colonoscopies/10,000 with Average Risk FIT Screening <sup>a</sup> (95% CI)	Colonoscopies/10,000 with Average Risk g-FOBT Screening <sup>a</sup> (95% CI)
1	155.7 (154.9-156.5)	237.2 (236.3-238.1)	283.5 (282.6-284.5)
2	156.4 (155.6-157.2)	235.7 (234.7-236.7)	280.8 (279.7-281.9)
3	156.0 (155.2-156.7)	231.5 (230.7-232.3)	279.2 (278.1-280.3)
4	163.7 (162.8-164.6)	240.1 (239.2-241.0)	287.0 (285.9-288.2)
5	165.4 (164.6-166.3)	240.0 (238.9-241.0)	287.0 (285.8-288.2)
6	175.6 (174.8-176.5)	252.5 (251.4-253.5)	299.1 (297.9-300.2)
7	180.9 (180.0-181.9)	257.7 (256.7-258.7)	304.0 (302.8-305.1)
8	182.3 (181.4-183.3)	258.6 (257.5-259.6)	304.6 (303.5-305.6)
9	183.1 (182.2-183.9)	258.8 (257.8-259.7)	304.4 (303.3-305.4)
10	184.4 (183.4-185.4)	260.5 (259.4-261.5)	304.6 (303.6-305.7)
11	188.6 (187.8-189.4)	264.9 (263.8-266.0)	308.3 (307.2-309.4)
12	191.0 (190.1-191.9)	263.8 (262.9-264.8)	307.4 (306.3-308.4)
13	193.4 (192.5-194.3)	264.4 (263.4-265.4)	307.1 (305.9-308.4)
14	195.8 (194.9-196.6)	265.4 (264.3-266.5)	307.5 (306.4-308.6)
15	197.9 (197.2-198.7)	263.9 (262.8-264.9)	305.8 (304.6-307.0)

<sup>a</sup>Assumes average-risk population ages 50–74 years, biannual administration, 30% uptake rate.

the higher-risk populations. Adjusting the transition probabilities between normal epithelium to low-risk polyps to twice that of the average-risk population allowed for calibration of the model to reflect the higher observed rates of disease and disease-related mortality among the population at higher risk of colorectal cancer. Higher-risk individuals, such as those with IBD or first-degree relatives with colorectal cancer, are approximately twice as likely to develop the disease as average-risk individuals.<sup>33</sup>

Colonoscopy demand generated by the model was compared to available data for colonoscopy volumes. Participation was assumed to be 30% for programmatic screening, based on observed rates in community (i.e., non-trial) settings in Canada.<sup>57</sup> Sensitivity analyses of higher participation resulted in increased demand for surveillance colonoscopies that was not offset by improved case-finding.<sup>22</sup> Total demand for colonoscopies (Table 2) was comparable to the number of colonoscopies performed among Ontario residents 50 to 74 years in the absence of organized population screening, in which regional colonoscopy rates ranged from 286.8 to 463.1 colonoscopies per 10,000 population.<sup>58</sup> The demand estimated by the model is conservative in initial years, as the demand for surveillance colonoscopy reflects only that generated onward from time zero. The model also does not account for opportunistic screening, which would have contributed to the rates observed by Schultz and others.<sup>58</sup>

Opportunistic screening rates vary significantly by region, with some having very little to no capacity to offer it.

### Between-Model Validation

Independent development of simulation models provides an opportunity to test corroboration.<sup>59</sup> The SCOPE model's outputs were compared to published results of other simulation models employing a natural history perspective, particularly the Canadian Cancer Risk Management Model (CRMM), as it incorporates Canadian demographic data and assumes a publicly funded health care system.<sup>60</sup> While the SCOPE model differed from the CRMM in terms of assumptions and the consideration of competition for limited colonoscopy resources, both models similarly reproduced observed Canadian colorectal cancer incidence and all-cause mortality rates.<sup>60</sup> System outcomes, such as demand for colonoscopy, could not be compared, as these are not modeled by the CRMM.

### DISCUSSION

The SCOPE model was specifically constructed to study the effects of average-risk screening decisions in the presence of limited colonoscopy resources for both screening participants and other, higher-risk, patient groups. Simulation modeling is

an increasingly popular tool in health services research, as it provides a powerful means for studying health care decisions in complex, dynamic environments. It lends itself well to studying the implications of the execution of programmatic colorectal cancer screening. However, its application to date in most average-risk colorectal cancer screening research assumes unlimited colonoscopy resources, which does not reflect the reality of the competing demands of a constrained health care system and does not consider outcomes for higher-risk individuals requiring colonoscopy services.<sup>19,60–66</sup> For example, the widely validated MISCAN, CRC-SPIN, and SimCRC colorectal cancer screening models do not capture colonoscopy resources.<sup>19,20,39,67</sup> Wilschut and colleagues<sup>68</sup> employed the MISCAN-Colon model to estimate the number of colonoscopies, costs, and health effects of different screening strategies, varying the stool tests, cutoff levels, surveillance strategies, and age ranges for participation. However, they included only those colonoscopies performed for follow-up of a positive FOBT, surveillance colonoscopies, and those that preceded the diagnosis of cancer outside the screening program. They did not include individuals requiring colonoscopy services outside of programmatic screening, including high-risk screening, diagnostic evaluation of non-neoplastic etiologies, and subsequent ongoing surveillance for those populations.

Average-risk colorectal cancer screening requires substantial colonoscopy resources, even with two-step screening.<sup>68,69</sup> While a key rationale for two-step screening is to reduce the additional demand for colonoscopies, stool tests have high false-positive rates. Depending on the test and the positivity threshold used, as many as 40% of those presenting for colonoscopic confirmation may have had false-positive stool tests.<sup>70,71</sup> Those with positive (either true or false) stool tests are referred for follow-up colonoscopic examinations with nontrivial risk profiles and ensuing anxiety. In the event of inadequate colonoscopy resources, a potentially serious diagnosis may not be confirmed or ruled out in a timely fashion. Further, ensuing prolonged wait times could serve as a general disincentive to participation in screening, which would in turn reduce the programs' effectiveness.

Of particular concern with the adoption of average-risk colorectal cancer screening in the absence of adequate colonoscopy capacity is the potential for the creation of competition for resources between average- and higher-risk individuals. Without additional resources, efforts to minimize wait times for screening follow-up colonoscopies are likely to hinder

access for higher-risk individuals and negatively impact outcomes. As colonoscopy resources are shared, measures to manage the competition for resources must be evaluated for their effects on access, demand for downstream services, and outcomes for all patient groups. While it is generally possible to estimate the number of initial colonoscopies required to follow-up positive tests for any given stool test or positivity threshold in the first round of screening, the stochastic influences of disease prevalence, demographic characteristics, screening effectiveness and uptake rates over time quickly complicate the picture. In the presence of constrained colonoscopy resources, limiting the evaluation of average-risk colorectal cancer screening programs to screening participants overlooks the potential for unintended harms to others in the system.

Population-based screening decisions have been founded largely upon results extrapolated from clinical trials with higher participation rates, and are to be further informed by the opportunity for the naturalistic observation of programs under way.<sup>11</sup> While it is clearly sensible to compare experiences, the dangers in relying on this approach include an inadequate period of observation for long-term outcomes as well as an inability to differentiate among the dynamic interrelationships of population, patient and system factors, particularly with a limited number of screening programs creating insufficient naturalistic variation in many variables of interest.

Failure to understand the effects of operational decisions in light of resource constraints may hinder screening programs' success, cause unintended harm, and make inefficient use of limited health care resources. Unlike many previous colorectal cancer screening models, the SCOPE model specifically considers the effects of competition for resources among patient groups of differing risk. This can be observed for a variety of scenarios, such as at the start-up of a screening program or following successive screening rounds, by selection of different screening tests, or using alternative positivity thresholds. The model has been used to construct such experiments, which are reported elsewhere.<sup>22</sup>

As in all models, there are many sources of uncertainty. As such, careful attention was paid to the validation and verification of the SCOPE model. It is usual to compare different modeling approaches to the same problem; however, existing models do not consider competition between patient groups. Comparison with deterministic Markov models was limited to the verification



of the outcomes of the natural history process due to the complexity of the conceptual model. Nevertheless, this was useful for ensuring the accuracy of the stochastic processes employed in the SCOPE model. Comparison with another Canadian model demonstrated similar results for the natural history module.<sup>60</sup>

There are also limitations to consider. The SCOPE model assumes the independence of colorectal cancer mortality and all-cause mortality, which is not the case. In actual fact, individuals at higher risk of colorectal cancer mortality are also at higher risk of other causes of mortality through shared risk factors. For example, physical inactivity and obesity increase the risk of developing colorectal cancer, cardiovascular disease and diabetes.<sup>56</sup> However, colorectal cancer mortality was not subtracted from of all-cause mortality, as this would require dependence assumptions, and mortality rates from colorectal cancer are very small relative to all-cause mortality. Modeling and forecasting colorectal cancer mortality was not a primary purpose of SCOPE, and this limitation has minimal effects on the comparison of outcomes between the synthetic average and higher-risk populations, or the demand or competition for colonoscopies, which were the main outcomes of interest. Opportunistic screening was not modeled, as it varies considerably between jurisdictions and relies upon availability of colonoscopy resources. This is unlikely to alter the study findings, as it would be provided only if resources were available beyond the demand of programmatic or higher-risk screening, diagnostic and surveillance activities.

The main strengths of the SCOPE model reside in its recognition and representation of the competition for limited colonoscopy services between patient groups of varying risk for colorectal cancer, integration of the most currently available information, and the inclusion of observations from average-risk populations in community settings where available. This approach is essential for an accurate understanding of the effect of the introduction of lower-risk individuals into a health care system already struggling to meet the needs of higher-risk patient populations, and has applications to other population-level screening endeavours. The model is flexible in that it permits study of various screening scenarios, including two-step screening with a stool test followed by colonoscopy as well as primary screening with colonoscopy, as in use in other jurisdictions, such as the United States.

The introduction of new populations into a constrained health care system, such as occurs with the

advent of average-risk colorectal cancer screening, requires the careful consideration of the short- and long-term consequences of the screening yield and cumulative surveillance requirements amid the fluctuating effects of demographic factors and disease prevalence for both screening participants and higher-risk patients requiring care.

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