Appendix 5 (as supplied by the authors): Economic implications of screening

The CTFPHC examined the cost-effectiveness of screening for CRC, which was one of its contextual questions.[1] The systematic review[1] found two Canadian modeling studies[2, 3] and the Canadian Partnership Against Cancer (CPAC) used the Cancer Risk Management Model (CRMM)[4] to run specific CRC screening scenarios on behalf of the CTFPHC, as ancillary evidence.

Economic evaluations from systematic review

The systematic review[1] identified two Canadian economic evaluations which both used Markov models.

The first economic evaluation[2] compared 10 different screening strategies to estimate costs and quality adjusted life expectancy of 50 year old average risk Canadians. The cost information was provided by a third-party payer in 2007 Canadian dollars. It is unclear from the study if this included any non-physician costs related to colonoscopy (e.g. capital, nursing, drugs and cleaning costs). The analysis focused on three screening strategies compared with no screening: low-sensitivity gFOBT and FIT performed annually as well as colonoscopy performed every 10 years. According to the study designers, these three strategies were chosen as they were being used for population screening in some Canadian provinces. The study concluded that both incidence and mortality from CRC were greatly reduced using these three screening strategies (44%, 65% and 81% respectively for incidence and 55%, 74% and 83% respectively for mortality). In addition, it was found that all screening is cost-effective but that low-sensitivity FIT performed annually or colonoscopy performed every ten years offered the best value in Canada. Incremental cost-utility ratios (ICUR) were $9,159 for FIT, $611 for gFOBT and $6,133 for colonoscopy.

The second economic evaluation[3] examined CRC screening in two average-risk age-stratified patient cohorts (people aged 50–64 and 65–75). The screening strategies applied were gFOBT or FIT (annually), fecal DNA (3 years), colonoscopy (10 years), flexible sigmoidoscopy or computed tomographic colonography (CTC) (5 years). Costs were derived from the Calgary Health Region costing database for flexible sigmoidoscopy and colonoscopy and included the non-physician costs (capital, nursing, drugs, and cleaning costs) and the physician fees for the procedure. CTC costs were conservatively assumed to be the same as that of a CT abdomen/pelvis and stool-based screening was assumed to be part of a patient's regular visit to their general practitioner so only included the cost of the screening kit and related laboratory/processing costs.

The study concluded that screening with FIT with high test performance characteristics (sensitivity 0.94; specificity 0.91) reduces incidence and mortality due to CRC and was the most cost-effective strategy in comparison to no screening and to the other screening strategies. For FIT with mid-test performance characteristics (sensitivity 0.81; specificity 0.96), the number of cancers could be reduced in the lifetimes of average-risk patients by 71% and the number of CRC deaths by 74% while saving $68 (CAN) per person. Of note, the median accuracy for CRC screening tests identified in the systematic review

supporting these guidelines (sensitivity 0.81%; specificity of 0.95%) is in line with the mid-test performance characteristics identified in this economic evaluation.

It is important to note that both studies modeled higher CRC incidence and mortality than were found in the trials in the systematic review[1] and they acknowledged that the actual time for adenoma progression to carcinoma is not well known.

CPAC's Cancer Risk Management Model simulation

In addition to studies identified in the systematic review[1], computer simulation of various CRC screening scenarios was undertaken using the Canadian Partnership Against Cancer's Cancer Risk Management Model (CRMM). Prior to commencement of the work, the CTFPHC had the model evaluated by the Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Institute (VCHI) via the Canadian Agency for Drugs and Technologies in Health (Available at canadiantaskforce.ca/files/crmm-crc.reportmay2015.pdf).

VCHI's evaluation determined that CPAC's model had a high level of internal validity in terms of overall model structure and assumptions. However, the evaluators noted the model is more focused on model-based projections in epidemiology, and is not fully developed as a health economic model (mainly due to a lack of capacity for probabilistic sensitivity analysis). Further, deterministic sensitivity analysis was not conducted. For example, the lack of certainty on the true benefit of colonoscopy (given the lack of RCT data), or plausible range of efficacy of any of the other screening tests were not examined. Further, the cost of screening and diagnostic tests may not include all overhead costs (such as the costs of scaling up delivery of a resource intensive test such as flexible sigmoidoscopy or colonoscopy), and true costs may be underestimated particularly for more resource intensive strategies such as colonoscopy which requires more than 3 times the human resources needed than the other screening tests[5] and would require dramatic increase in numbers if used as a screening test. A breakdown of the costs used in the model can be found in Table S1.

Despite these limitations, including the lack of sensitivity analysis, the results of the reference case simulations were congruent with the CTTPHC's recommendations and studies identified in the review.

Detailed information on the CRMM methods can be found elsewhere.[4-6]

The CRMM simulation was based on various configurations of the screening tests included in this guideline with additional intervals: low sensitivity and mid-point gFOBT & FIT+ (biennial & annual), flexible sigmoidoscopy (5 years, 10 years, once per lifetime) and colonoscopy (10 years, once per lifetime). We also looked at three age cohorts (50-59, 60-74, 50-74) and assumed 100% screening participation.

The reference scenario chosen for calculating the ICUR was gFOBT or FIT biennially for individuals aged 50-74, consistent with most screening programs. Tables S2 and S3 present total and incremental costs, QALYs, and incremental cost-effectiveness of alternate screening strategies compared with biennial gFOBT and biennial FIT respectively, assuming 100% population participation with screening.

The overall results of the simulation found that all screening scenarios reduced incidence and mortality of CRC as compared to no screening. Unless the comparator screening strategy is found to be more effective (QALY > 0), it is not discussed below.

Comparator: Biennial gFOBT ages 50-74 (Table S2)

Annual gFOBT (ages 50-74) was found to be more effective, but also more costly (Incremental Cost-Utility Ratio (ICUR=$7,611)) than biennial gFOBT (50-74).

Biennial FIT (50-74) was both more effective and less costly than biennial gFOBT (50-74). Annual FIT (50-74) was found to be more effective, but also more costly (ICUR=$3,084) than biennial gFOBT (50-74).

Flexible sigmoidoscopy every 10 years for ages 50-74 was found to be more effective and less costly, compared with biennial gFOBT (50-74). Flexible sigmoidoscopy every 5 years for ages 50-74 were found to be more effective, but also more costly ($10,628 respectively) than biennial gFOBT (50-74). Flexible sigmoidoscopy once per lifetime was both less effective and less costly than biennial FOBT.

Colonoscopy was found to be the more effective and less costly for all scenarios: 10 years or lifetime, as compared with biennial gFOBT (50-74).

Comparator: Biennial FIT ages 50-74 (Table S3)

Biennial gFOBT is less effective and more costly than biennial FIT. Annual gFOBT (ages 50-74) was found to be more effective, but also more costly (ICUR=$28,699) than biennial FIT (50-74). Annual FIT (50-74) was found to be more effective, but also more costly (ICUR=$7,807) than biennial FIT (50-74).

Flexible sigmoidoscopy every 5 years for ages 50-74 and every 10 years for ages 50-74 were found to be more effective, but also more costly (ICUR $18,324 and $1,688 respectively) than biennial FIT (50-74).

Colonoscopy was found to be more effective and cost saving for all scenarios: 10 years or lifetime and as compared with biennial FIT (50-74).

There was lack of confidence in the results of colonoscopy given the lack of RCT data to definitely establish greater efficacy, as well as the potential for underestimation of true cost of provision. Further, among screening tests colonoscopy has the greatest harms, has health equity concerns given the lack of availability of colonoscopy in remote areas, and is its use is associated with the greatest consumption of finite health care resources – considerable expansion of health care infrastructure and resources would be required if colonoscopy were a frequently used screening strategy.

A table representing the cost of colorectal screening strategies per patient over time (5, 10, 15 and 20 years) is also presented in Table S4.

The CTFPHC also examined incremental cost-utility of expanding screening from ages 60-74 to 50-74. The simulation found that all screening modalities resulted in increased costs and QALYs when expanding to the younger cohort except for flexible sigmoidoscopy and colonoscopy when offered once per lifetime. See Table S5.

Table S1 - Screening and Diagnostic Follow-up Costs used in CPAC's CRMM*

Screening and Diagnostic Follow-up Costs (cost per screen)	
Physician extra visits	$28.55
gFOBT kit	$2.76
gFOBT processing	$13.00
FIT kit	$18.00
FIT processing	$6.00
Flexible sigmoidoscopy (includes practitioner fee $57.70 and institution fees of $438)	$495.70**
Colonoscopy cost (includes physician fee: $185.20 and institution fees of $438)	$632.20**

*Note that in the CRMM model, the cost of screening and diagnostic tests may not include all overhead costs (such as the costs of scaling up delivery of a resource intensive test such as flexible sigmoidoscopy or colonoscopy).

**Total costs include practitioner and institutional costs which consists of direct and indirect costs defined as:

Direct costs - are costs that are directly related to the provision of care to the patient and include Nursing (incl. Operating Room, ICU), Diagnostic Imaging, Pharmacy and Labs.

Indirect costs - are overhead expense relating to the running of hospitals and include administration, finance, human resources, plant operations etc.

Source: The Ontario Case Costing Initiative

Table S2 – Costs, QALYs and Incremental Cost-Utility of various CRC screening programs compared to biennial gFOBT (50-74) assuming a 100% population participation with screening*

Screening Strategy	Total Cost ($millions)	Cost of Screening	Cost of Treatment	QALYs (100,000s)	Compared with 'Biennial FOBT 50-74'		
					Incremental Cost ($millions)	Incremental QALY (100,000s)	ICUR (3%)
Biennial FOBT 50-74	$104,803	$19,382	$85,421	9,980			
Annual FOBT 50-74	$107,613	$28,450	$79,163	9,984	$2,810	3.7	$7,611
Biennial FIT 50-74	$103,752	$21,901	$81,851	9,983	-$1,051	2.3	Dominant
Annual FIT 50-74	$106,685	$31,453	$75,232	9,987	$1,882	6.1	$3,084
FS x 5 yrs-50-74	$112,191	$40,358	$71,834	9,987	$7,389	7.0	$10,628
FS x 10 yrs-50-74	$104,230	$29,091	$75,139	9,986	-$573	5.2	Dominant

FS x once/life-50-74	$100,037	$15,659	$84,378	9,980	-$4,766	-0.5	$95,245**
COL x 10 yrs-50-74	$96,446	$33,191	$63,255	9,992	-$8,357	11.9	Dominant
COL x once/life-50-74	$91,374	$19,152	$72,222	9,989	-$13,429	8.7	Dominant

**All values discounted using 3% discount rate.*

*** These strategies are less effective and less costly than biennial FOBT (50-74). The ICUR reflects the incremental cost-utility of biennial FOBT (50-74) compared with each of these strategies, rather than the ICUR of each strategy compared with biennial FOBT (50-74) which is used for the remainder of the results.*

Table S3 – Costs, QALYs and Incremental Cost-Utility of various CRC screening programs compared to biennial FIT(50-74) assuming a 100% population participation with screening*

					Compared with 'Biennial FIT 50-74'		
Screening Strategy	Total Cost ($millions)	Cost of Screening	Cost of Treatment	QALYs (100,000s)	Incremental Cost ($millions)	Incremental QALY (100,000s)	ICUR (3%)
Biennial FIT 50-74	$103,752	$21,901	$81,851	9,983			
Biennial FOBT 50-74	$104,803	$19,382	$85,421	9,980	$1,051	-2.3	Dominated
Annual FOBT 50-74	$107,613	$28,450	$79,163	9,984	$3,861	1.3	$28,699
Annual FIT 50-74	$106,685	$31,453	$75,232	9,987	$2,934	3.8	$7,807
FS x 5 yrs-50-74	$112,191	$40,358	$71,834	9,987	$8,440	4.6	$18,325
FS x 10 yrs-50-74	$104,230	$29,091	$75,139	9,986	$479	2.8	$1,688
FS x once/life-50-74	$100,037	$15,659	$84,378	9,980	-$3,715	-2.8	$13,050**
COL x 10 yrs-50-74	$96,446	$33,191	$63,255	9,992	-$7,306	9.6	Dominant
COL x once/life-50-74	$91,374	$19,152	$72,222	9,989	-$12,377	6.4	Dominant

**All values discounted using 3% discount rate.*

*** These strategies are less effective and less costly than biennial FIT (50-74). The ICUR reflects the incremental cost-utility of biennial FIT (50-74) compared with each of these strategies, rather than the ICUR of each strategy compared with biennial FIT (50-74) which is used for the remainder of the results.*

Table S4 - Cost of colorectal screening strategies over time ($ per patient) based on costs identified in Table S1

	5 years	10 years	15 years	20 years
Annual gFOBT*	$221.55	$443.10	$664.65	$886.20
Biennial gFOBT*	$110.78	$221.55	$332.33	$443.10
Annual FIT*	$262.75	$525.50	$788.25	$1,051.00
Biennial FIT*	$131.38	$262.75	$394.13	$525.50
FS once only**	$524.25	$524.25	$524.25	$524.25
FS every 10 yrs**	$524.25	$1,048.50	$1,048.50	$1,572.75
FS every 5 yrs**	$524.25	$1,048.50	$1,572.75	$2,097.00
COL once only**	$660.75	$660.75	$660.75	$660.75
COL every 10 yrs**	$660.75	$1,321.50	$1,321.50	$1,982.25

* Includes extra physician visit, kit and processing

** Includes direct and indirect costs as defined in Table S1

Table S5 – Incremental cost-utility of expanding from 60-74 to 50-75*

Biennial FOBT	$3,374
Annual FOBT	$6,881
Biennial FIT	$2,801
Annual FIT	$6,536
FS x 5 years	$14,106
FS x 10 years	$5,478
FS x once/life	Dominant (more effective and cost-saving)
COL x 10 years	$1,583
COL x once/life	Dominant (more effective and cost-saving)

** All values discounted using 3% discount rate.*

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