

# Colorectal Cancer - Guideline Presentation

## Speaker deck

### OVERVIEW

We will review the following:

1. Background on Colorectal Cancer (CRC)
2. Methods of the CTFPHC
3. Recommendations and Key Findings
4. Implementation of Recommendations
5. Conclusions
6. Questions and Answers

### CTFPHC BACKGROUND

#### CTFPHC Working Group Members:

The Colorectal Cancer Working Group included members from the Canadian Task Force on Preventive Health Care (CTFPHC), the National Colorectal Cancer Screening Network, the Public Health Agency of Canada (PHAC) and the Evidence Review Synthesis Centre (ERSC) at McMaster University.

#### Task Force Members:

- Maria Bacchus (Chair)
- Rick Birtwhistle
- Jim Dickinson
- Gabriela Lewin
- Harminder Singh\*
- Scott Klarenbach
- Marcello Tonelli

#### National Colorectal Cancer Screening Network:

- Verna Mai\*

#### Public Health Agency of Canada:

- Lesley Dunfield\*
- Sarah Connor Gorber\*
- Nathalie Holmes\*

Evidence Review and Synthesis Centre:

- Donna Fitzpatrick-Lewis \*
- Ali Usman\*

\*non-voting member

## **SCREENING FOR COLORECTAL CANCER - BACKGROUND**

### **Background**

CRC is the second most common cause of cancer mortality in men and the third most common in women, with a current lifetime probability of dying of 3.5% and 3.1% respectively. It is estimated that 25,000 Canadians were diagnosed with CRC in 2015 (incidence of 49 per 100,000 Canadians) and 9,300 Canadians died from the disease (mortality of 17 per 100,000). Most CRCs appear to arise from colonic polyps that develop slowly, some of which transform to cancers. Currently, all Canadian programs recommend guaiac fecal occult blood testing (gFOBT) or fecal immunochemical testing (FIT), with colonoscopy for follow-up of positive screening results.

### **SCREENING TESTS FOR COLORECTAL CANCER**

Commonly used screening tests for colorectal cancer fall into two major categories. Fecal occult blood testing (FOBT), which includes both guaiac fecal occult blood testing (gFOBT) and fecal immunochemical testing (FIT), requires a patient to provide a stool sample that will be tested for blood that cannot be seen with the naked eye. Endoscopies, including sigmoidoscopy and colonoscopies, look for polyps by utilizing a long flexible tube with a light and camera inserted into the anus, rectum, and lower colon of the patient.

### **Screening for Colorectal Cancer**

### **METHODS OF THE CTFPHC**

The CTFPHC is an independent panel of clinicians and methodologists with expertise in prevention, primary care, literature synthesis, and critical appraisal. The mandate of the CTFPHC is to apply the latest evidence in preventive health care research to primary care practice and policy across Canada.

The Colorectal Cancer Working Group is composed of 7 CTFPHC members who received support from PHAC science officers to establish the guidelines research questions and analytical framework.

The Evidence Review and Synthesis Centre (ERSC) at McMaster University independently undertook a systematic review of literature based on this analytical framework and prepared a systematic review of the evidence with GRADE tables. The ERSC consulted with field experts during this process and participated in working group and CTFPHC meetings.

## CTFPHC Review Process

The CTFPHC review process is composed of an (i) internal review process and an (ii) external review process. The internal review process involves the guideline working group, the full CTFPHC, PHAC science officers and ERSC staff.

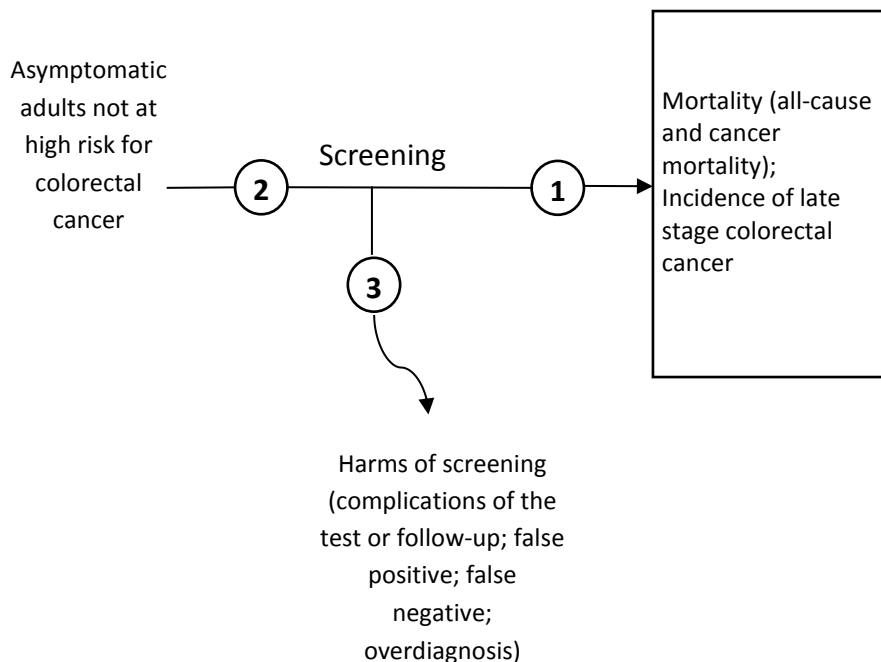
The external review process involves a review of the guidelines by key stakeholders from generalist and disease specific organizations, and federal, provincial and territorial stakeholder groups. The Canadian Medical Association Journal (CMAJ), where most of the CTFPHC guidelines are published, undertakes its own independent peer review journal process.

## Research Questions

The systematic review for screening for colorectal cancer included 3 key research questions (with 2 sub-questions) and 4 supplemental or contextual questions.

For more detailed information please access the systematic review [www.canadiantaskforce.ca](http://www.canadiantaskforce.ca)

## ANALYTICAL FRAMEWORK: SCREENING



The analytical framework outlines the scope of the evidence review and guideline recommendations. The purpose of the analytical framework is to show practicing physicians what the guideline includes and does not include and to visually display the relationship between the key concepts.

This guideline applies to asymptomatic adults 50 years and older who were not at high risk of colorectal cancer. As outlined in the analytical framework, this guideline looks at the sensitivity and specificity of different screening tests for CRC, the impact of screening on mortality and incidence of late stage colorectal cancer, as well as associated harms (e.g., complications of the test or follow-up; false positives; false negatives).

## ELIGIBLE STUDY TYPES

The primary population of interest for the colorectal cancer screening guideline are asymptomatic adults 18 years and older who were not at high risk of colorectal cancer. Excluded were adults who were at high risk, patients with symptoms suggesting underlying colorectal cancer, and those with genetic mutations associated with increased colorectal cancer risk.

Studies in both English and in French were included.

Studies on the screening of colorectal cancer were restricted to randomized control trials (RCTs), cohort (with comparison) and case control studies. Patient important outcomes and the scales used to measure such outcomes were based on those selected and prioritized by Canadian clinicians and policymakers.

## GRADE METHODOLOGY

### How is Evidence Graded?

The CTFPHC utilizes the GRADE system for providing clinical practice guideline recommendations based on a systematic review of the available evidence. The **GRADE** acronym stands for: **G**rading of **R**ecommendations, **A**ssessment, **D**evelopment and **E**valuation.

The GRADE system is composed of two main components:

1. **The quality of the evidence:** The quality of the evidence measures the degree of confidence that the available evidence correctly reflects the theoretical true effect of the intervention or service. It is graded as high, moderate, low or very low based on how likely further research is to change our confidence in the estimate of effect.

2. **The strength of recommendation:** The strength of the recommendation (strong/weak) is based on the quality of supporting evidence, the degree of uncertainty about the balance between desirable and undesirable effects, the degree of uncertainty or variability in values and preferences, and the degree of uncertainty about whether an intervention represents a wide use of resources.

## How is the Strength of the Recommendations Determined?

The strength of the recommendations (strong or weak) is based on four factors:

1. The quality of the supporting evidence
2. The certainty about the balance between desirable and undesirable effects
3. The certainty or variability in the values and preferences of individuals
4. The certainty about whether the intervention represents a wise use of resources

## Interpretation of Recommendations

Implications	Strong Recommendation	Weak Recommendation
For patients	Most individuals would want the recommended course of action; Only a small proportion would not.	The majority of individuals in this, situation would want the suggested course of action but many would not.
For clinicians	Most individuals should receive the intervention.	Recognize that different choices will be appropriate for individual patients; Clinicians must help patients make management decisions consistent with values and preferences.
For policy makers	The recommendation can be adapted as, policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

This is a standard GRADE table which outlines how weak or strong recommendations should be interpreted and implemented by different groups or stakeholders. It is

important to consider the strength of the recommendations when interpreting the CTFPHC guidelines for implementation in clinical practice, for policy, or for patients in decision making.

## Screening for Colorectal Cancer RECOMMENDATIONS & KEY FINDINGS

### SUMMARY OF KEY FINDINGS

Screening tool	Age	Risk Ratio			
		CRC Mortality	95% CI	Incidence of late stage CRC	95% CI
FOBT ( 4 RCT meta analysis)	45-80	0.82	0.73-0.92	0.92	0.85-0.99
Flexible Sigmoidoscopy (pooled analysis, 4 RCTs)	55-74	0.72	0.65-0.81	0.75	0.66–0.86

This table summarizes the evidence found for screening tools that decreased CRC mortality (3<sup>rd</sup> column) and incidence of late stage CRC (5<sup>th</sup> column). Evidence from high quality RCTs showed that both FOBT and flexible sigmoidoscopy decreased both of these outcomes, as indicated in the bottom two rows. For CRC mortality, a Meta-analysis of 4 RCTs using FOBT as a screening test showed a risk ratio of 0.82 (CI 0.73-0.92). A pooled analysis of 4 RCTs showed a risk ratio of 0.72 (CI 0.65-0.81) for flexible sigmoidoscopy. For the incidence of late stage CRC, using FOBT screening resulted in a reduced risk ratio of 0.92 (CI 0.85-0.99) and 0.75 (CI 0.66-0.86) for flexible sigmoidoscopy. Note that the CTFPHC found no RCTs that showed a mortality benefit with colonoscopy screening, CT colongraphy, barium enema, DRE, or fecal DNA testing. Further, no screening test was found to reduce all-cause mortality.

## COLORECTAL CANCER 2015 GUIDELINES

This guideline provides recommendations for practitioners on preventive health screening in a primary care setting. The recommendations apply to adults aged 50 years and older and who are not at high risk for colorectal cancer. These recommendations do not apply to adults with previous CRC or polyps; inflammatory bowel disease; signs or symptoms of CRC; history of CRC in one or more first degree relatives; or hereditary syndromes predisposing to CRC, such as familial adenomatous polyposis or Lynch Syndrome.

## FOBT OR FLEXSIG SCREENING

1. We recommend screening adults aged 60 to 74 years of age for colorectal cancer (CRC) with FOBT (either gFOBT or FIT) every two years OR flexible sigmoidoscopy every 10 years (*strong recommendation; moderate quality evidence*).
2. We recommend screening adults aged 50-59 for CRC with FOBT (gFOBT or FIT) every two years OR flexible sigmoidoscopy every 10 years (*weak recommendation; moderate quality evidence*).

**Basis of the recommendation:** In the judgement of the CTFPHC, FOBT and flexible sigmoidoscopy are both reasonable screening tests for patients aged 50-74 years of age based on high quality (RCT) evidence. The CTFPHC based the splitting of this recommendation for screening into two age groups by placing a relatively higher value on the different balance of benefits to harms, and a relatively lower value on the added complexity of two recommendations rather than one. This recommendation also places a relatively higher value on the potential for additional years of life saved in younger patients and a relatively lower value on the lack of statistical significance for mortality benefit in subgroup analyses of younger participants. Although the relative benefits are similar for older (60-74 years) and younger (50-59 years) age groups, the absolute benefits are smaller in those aged 50-59 years due to lower incidence. This warrants a weak recommendation to screen in those aged 50-59 years as compared to the strong recommendation for people aged 60-74 years.

## NOT SCREENING ADULTS AGED 75+

3. We recommend not screening adults aged 75 years and over for CRC (*weak recommendation; low quality evidence*)

**Basis of the recommendation:** The CTFPHC based this recommendation on the lack of high quality studies (RCTs) evaluating the benefits and harms of screening for colorectal cancer over the age of 75 and reduced life expectancy in older age groups. A weak recommendation means that adults over 75 years who are interested in screening and less concerned with the lack of reported benefits or potential harms, may choose to be screened and should discuss screening

options with their primary care provider to help them reach a decision based on their quality of life, values, and preferences.

## NOT SCREENING USING COLONOSCOPY

4. We recommend not using colonoscopy as a primary screening test for colorectal cancer (CRC) (*weak recommendation; low quality evidence*)

**Basis of the recommendation:** The CTFPHC recognizes that although colonoscopy may offer clinical benefits that are similar to or greater than those associated with flexible sigmoidoscopy, direct RCT evidence of its efficacy in comparison to the other screening tests (in particular, FIT) is currently lacking. In addition to a lack of evidence, considerations regarding wait lists, resource constraints and greater potential for harms also informed the CTFPHC recommendation. This is a weak recommendation and patients who are less concerned about the potential harms of colonoscopy and/or who are more interested in a test that allows a longer screening interval may still request screening with colonoscopy.

### NNS for CRC Mortality by Age-Groups with Varying Underlying Baseline Risk

Outcome	Screening test	Age Group (years)	ARR	NNS	NNS (95% CI)
CRC Mortality	Biennial gFOBT	< 60 (45 to 59)	0.0377%	2655	1757 - 6244
CRC Mortality	Biennial gFOBT	≥ 60 (60 to 80)	0.2032%	492	326-1157
CRC Mortality	Flexible Sigmoidoscopy	< 60 (45 to 59)	0.0540%	1853	1441-2713
CRC Mortality	Flexible Sigmoidoscopy	≥ 60 (60 to 80)	0.2912%	343	267-503



This table presents data on the outcomes (CRC mortality) of different types of screening tests for colorectal cancer (CRC) by age group. The estimates of absolute risk reduction (ARR) in CRC mortality for screening as compared to control and number-needed to screen (NNS) to prevent one death from colorectal cancer are based on age-specific baseline risks of dying from CRC (obtained from SEER Cancer Statistics Review, 1975-2012). As indicated by NNS data (5<sup>th</sup> column), for those less than 60 years of age, you need to screen many more people (2655) to save one life than those greater than 60 years of age (492) due to lower incidence of CRC in the younger age group (i.e., less than 60 years). A similar pattern is present for flexible sigmoidoscopy, whereby a larger NNS is needed in the less than 60 year age group due to lower incidence of CRC.

## Harms of Screening

The CTFPHC found no high quality studies evaluating the harms and benefits of screening for colorectal cancer. Some possible harms related to screening could include the death; perforation; bleeding (with or without hospitalization); false-positive or false-negative test results; and over-diagnosis. Possible harms will vary depending on the screening test and cut-off points used.

## Comparison of Screening for Colorectal Cancer Recommendations

Our recommendations on screening are consistent with the previous 2001 CTFPHC guideline with additional supporting evidence found. Provincial screening programs also recommend screening with FOBT (the majority recommend FIT) every 1-2 years, which is consistent with the current CTFPHC recommendation. No province currently recommends screening with flexible sigmoidoscopy.

The US Preventive Services Task Force (USPSTF) published recommendations for colorectal cancer screening in 2008 and an update of the guideline is currently underway. The CTFPHC and USPSTF recommendations for age groups are fairly consistent. The USPSTF differs from the CTFPHC and recommends screening with either FOBT (gFOBT or FIT) every year, flexible sigmoidoscopy every 10 years plus FIT every year, or colonoscopy every 10 years. The CTFPHC only included RCTs and found no evidence to support screening with colonoscopy. In comparison, the USPSTF included modelling studies and observational data and concluded that colonoscopy is an option for screening. The CTFPHC also recommended screening with FOBT every two years, whereas the USPSTF recommends yearly screening. The CTFPHC chose two year intervals as this was the interval used more commonly in gFOBT RCTs. No difference between annual and biennial screening on CRC specific mortality was found.

## Screening for colorectal cancer

### **IMPLEMENTATION OF RECOMMENDATIONS**

## Resources

The CTFPHC expects that most Canadians will be screened with either FIT or gFOBT due to limited access to and availability of flexible sigmoidoscopy. Although flexible sigmoidoscopy is not frequently performed for screening in many jurisdictions, it may warrant further consideration as it can be completed in the same facilities as colonoscopy and using similar equipment, but without the requirement of a specialist (such as a gastroenterologist). Screening programs would need to consider the implications of establishing screening facilities, such as training of providers, the bowel preparation required by patients, and the resources needed for flexible sigmoidoscopy as compared to FOBT.

## Values and Preferences

The CTFPHC found evidence on the values and preferences of patients related to screening for colorectal cancer. Overall, factors that influence patients' willingness to be screened include sedation needs, perceived test accuracy, confidence in completing the test, bowel preparation, and frequency of tests. Specifically, Canadian patient screening test preferences were based upon invasiveness of screening test, level of preparation required for the screening test, and pain from the screening test. American patient priorities for screening included preventing cancer (55%), avoiding test side effects (17%), minimizing false positives (15%), and the combination of frequency, test preparation, and test procedures (14%).

## KT TOOLS

The CTFPHC creates KT tools to support the implementation of guidelines into clinical practice. A clinician recommendation table and patient FAQ have been developed for the colorectal cancer guideline. After the public release, these tools will be freely available for download in both French and English on the website: [www.canadiantaskforce.ca](http://www.canadiantaskforce.ca).

## CONCLUSIONS

The CTFPHC recommends that starting at age 50, primary care providers should discuss the most appropriate choice of test with patients who are interested in screening. Screening for colorectal cancer (CRC) with FOBT or flexible sigmoidoscopy reduces CRC mortality in those aged 50-74 years and the direct harms associated with these tests are minimal.

The strong recommendation to screen adults aged 60-74 years with gFOBT, FIT or flexible sigmoidoscopy indicates that primary care providers should offer this service to

all individuals in this age group. The weak recommendation to screen adults aged 50-59 years with gFOBT, FIT or flexible sigmoidoscopy indicates that a more nuanced discussion of the harms and benefits with patients will be required. Starting at age 75, primary care providers should discuss individual screening preferences. Patient values and preferences, test availability and life expectancy should all be considered in determining the best screening options for individuals.

The CTFPHC recommends not using colonoscopy as a screening tool at this time. Four trials are currently underway investigating the mortality benefit of screening with colonoscopy. These will be considered by the CTFPHC as the results become available.

## CTFPHC Mobile App Now Available

The app contains guideline and recommendation summaries, knowledge translation tools, and links to additional resources.

Key features include the ability to bookmark sections for easy access, display content in either English or French, and change the font size of text.

## More information

For more information on the details of this guideline or to access the KT tools please refer to the evidence review in the resources section of the website

[www.canadiantaskforce.ca](http://www.canadiantaskforce.ca).