Toward Optimized Practice

COLORECTAL CANCER SCREENING

Clinical Practice Guideline | November 2020

TARGET POPULATION
Asymptomatic adult population

EXCLUSIONS
Individuals with signs or symptoms suggesting colorectal cancer (CRC)

RECOMMENDATIONS

RISK ASSESSMENT

- ✓ Assess risk for colorectal cancer (CRC) to determine when to start screening, the appropriate screening test and frequency.
- ✓ An assessment of risk for CRC should occur earlier than age 50.
- ✓ Assess for indicators of increased risk including family and/or personal history of colorectal cancer, colonic adenomas or inflammatory bowel disease, and high risk CRC conditions, i.e., Lynch syndrome, Familial Adenomatous Polyposis (FAP).

AVERAGE RISK POPULATION

FECAL IMMUNOCHEMICAL TEST (FIT)

50 TO 74 YEARS OF AGE

- ✓ Screening is recommended with the Fecal Immunochemical Test (FIT).
- ✓ Screen with FIT every 1 to 2 years.
- ✓ If the FIT result is positive, promptly refer for a colonoscopy. Referrals should be sent to a local CRC screening program (see Appendix A) or endoscopist, depending on available resources.
- ✓ Wait 10 years after a normal colonoscopy to start or re-start screening with FIT. If the quality of the colonoscopy was uncertain, start or re-start screening with FIT five years after the colonoscopy.

PRACTICE POINT

FIT is the recommended screening test for the average risk population, aged 50 to 74 years.
Screen with FIT every 1 to 2 years.

75 YEARS OF AGE AND OLDER

- X As a general practice, DO NOT screen asymptomatic individuals with a life expectancy of less than 10 years and no personal or family history of colorectal neoplasia.
- ✓ The decision to screen individuals over 74 should be done on a case-by-case basis following a discussion between the client and healthcare provider regarding potential benefits and risks of screening, current medical status, and informed client preferences.
- ✓ Individuals in this age group are not eligible for screening at local CRC screening programs. Send colonoscopy referrals to the endoscopist.

WHEN NOT TO USE FIT

- X DO NOT use as a diagnostic test for CRC in SYMPTOMATIC patients (e.g., reported bloody stools or recent change in bowel habit).
- X DO NOT use to determine or exclude a cause for anemia.
- X DO NOT use when an average risk patient has had a high quality colonoscopy within the past 10 years.
- X DO NOT use as a CRC screening test when the patient has an acute gastrointestinal (GI) condition and/or where bleeding is occurring or highly likely:
  - Inflammatory bowel disease
  - Acute gastroenteritis or C. difficile colitis
  - Actively bleeding hemorrhoids or anal fissure

OTHER SCREENING TESTS

FIT is the recommended method of screening for the average risk population. Appendix B summarizes the evidence for other CRC screening tests, e.g., colonoscopy, flexible sigmoidoscopy, CT colonography, and others. Expertise and availability varies across the province.

INCREASED RISK POPULATIONS

Family history

Family history of colorectal cancer and/or high risk colonic adenomas are warning signs of increased risk (see Risk Assessment section for definition of high risk adenomas). Use clinical judgment.

One first degree relative > 60 years at diagnosis of colorectal cancer and/or high risk adenomas

- ✓ Screen with FIT every one to two years starting at age 40.
- ✓ If the FIT result is positive, promptly refer for a colonoscopy. Use local CRC screening program (see Appendix A) or endoscopist, depending on available resources.

One first degree relative ≤ 60 years at diagnosis of colorectal cancer and/or high risk adenomas or two or more affected relatives

- ✓ Refer for consideration of colonoscopy at age 40, or 10 years before the youngest index case, whichever is earliest. Use local CRC screening program (see Appendix A) or endoscopist.

- ✓ Assist individual with adherence to follow-up as recommended by local CRC screening program (see Appendix A) or endoscopist.

Personal history

Personal history of colorectal cancer, colonic adenomas or inflammatory bowel disease (e.g., ulcerative colitis or Crohn's colitis)

- ✓ Assist individual with ongoing follow-up by colonoscopy as recommended by local CRC screening program (see Appendix A) or endoscopist.
- ✓ Use Provincial Post Polypectomy Surveillance Guidelines available at https://screeningforlife.ca/wp-content/uploads/2019/12/ACRCSP-Post-Polypectomy-Surveillance-Guidelines-June-2013.pdf

✶ Be aware that not all polyps are considered high risk and require surveillance, e.g., small, single, hyperplastic polyps found in the distal colon.

High risk conditions for CRC

High risk conditions for CRC such as Lynch syndrome or Familial Adenomatous Polyposis (FAP)

- ✓ Ensure individual has an established relationship with the local CRC screening program (see Appendix A) or an endoscopist for on-going care and monitoring.

> **PRACTICE POINT**
>
> *Lynch syndrome (HNPCC) is identified by personal and family history of multiple cancers, including endometrial, gastric, ovarian, hepatobiliary, urinary tract*

EVIDENCE-BASED IMPLEMENTATION CONSIDERATIONS

CRC screening is an important preventive health activity in which education and outreach are key components. Efforts to reduce CRC should include strategies that increase the number of individuals who present for screening. Health care providers can use opportunistic (screening when the individual presents for other reasons) and outreach (contacting individuals who are due for screening) interventions to promote screening. Relying on routine checkup appointments will likely miss many individuals. Patient contact for any reason can be used to discuss CRC screening. Studies have shown that the strongest stimulus for an individual's participation in CRC screening is the recommendation from a health care provider.

- ✓ Use preventive screening checklists, opportunistic screening, and outreach to increase the likelihood of engaging individuals to participate in CRC screening.

BACKGROUND

RISK

CRC is the second most common cause of cancer death for males and the third most common cause of cancer death for females.[1] The probability of developing CRC increases with age and varies with sex. In Alberta, approximately 1 in 13 men and 1 in 16 women will develop invasive CRC within their lifetime.[2] Males have a greater chance of dying from CRC than females, i.e., 1/32 males and 1/36 females will die of invasive CRC.[2] According to Alberta statistics, CRC mortality rates decreased over the period 1990 to 2010, for both males and females.[2] Declining rates may be attributed to screening's effect on early detection and management. CRC can be prevented by the detection and removal of precancerous polyps.

AGE

The incidence of CRC increases with age. Rates are low until about age 40, with the incidence increasing in older age groups.[2] In Alberta, the probability of developing cancer at ages 30-40 years is 1 in 1,613 for males and 1 in 1,355 for females.[2] For those 50-60 years of age, the rate is 1 in 161 for males and 1 in 158 for females.[2] According to the United States Preventive Services Task Force, more than 80% of diagnosed cases of CRC occur in those older than 55 years.[3] (See Table 1). For the majority of those with CRC, age is the only risk factor.

Age Group (Years)	Males	Females
Lifetime Risk (all ages)	1 in 13	1 in 16
0-20	Less than 1 in 10,000	Less than 1 in 10,000
20-30	1 in 5,428	1 in 4,506
30-40	1 in 1,613	1 in 1,355
40-50	1 in 450	1 in 410
50-60	1 in 161	1 in 158
60-70	1 in 77	1 in 77
70-80	1 in 45	1 in 46
80+	1 in 28	1 in 25

Table 1: Probability of Developing Colorectal Cancer by Age and Sex, Alberta 2006 – 2010. Reproduced with permission from Alberta Cancer Registry, Alberta Health.[1]

FAMILY HISTORY

Next to age, family history is the most common risk factor for CRC.[4] Risk of CRC increases as the number of affected relatives increases and the younger the age of the relative at diagnosis.[5,6,7] For example, having multiple family members diagnosed with CRC prior to age 60 carries a higher risk than one family member diagnosed with CRC at an advanced age. According to one meta-analysis, a population lifetime risk for a 50 year-old was 1.8% but increased to 3.4% with at least one affected first degree relative and 6.9% with two or more affected relatives.[6]

Lynch Syndrome

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC), accounts for 1% to 3% of all colorectal cancers.[8,9] It carries a lifetime risk for CRC estimated at 50-80%, and is higher for men than for women.[9,10] Besides being associated with CRC, Lynch syndrome carries a 40-60% lifetime risk of endometrial cancer.[10] To a lesser degree (<19%), other cancers associated with Lynch syndrome include: gastric (11-19%), ovarian (9-12%), hepatobiliary (2-7%), upper urinary tract (4-5%), pancreatic (3-4%), small bowel (1-4%), and CNS – glioblastoma (1-3%).[10]

Familial Adenomatous Polyposis (FAP)

FAP accounts for up to 1% of all CRC.[11] Almost all individuals with FAP will develop CRC if they are not identified and treated at an early stage.[11]

Inflammatory Bowel Disease (IBD)

IBD is associated with increased risk for CRC. For ulcerative colitis, the probability of developing CRC after 10 years of diagnosis is estimated at 2%, reaching 8% after 20 years and 18% after 30 years.[12]

Diabetes Mellitus

A recent meta-analysis found that diabetes is associated with an increased risk of colon cancer (relative risk 1.38 for both men and women) and rectal cancer (relative risk 1.20 for men).[13] The association remained when the authors controlled for smoking and obesity, or for smoking, obesity and physical exercise.

Obesity

Body mass index (BMI) and waist circumference (WC) are positively associated with risk for CRC. In one meta-analysis the relative risks for the obese versus normal category of BMI were 1.334 and the relative risk for the highest versus lowest category of waist circumference were 1.455.[14] There was less heterogeneity among studies of waist circumference.

Lifestyle

Physical activity: There is consistent evidence supporting an inverse relationship between physical activity and risk of CRC. The overall relative risk for those who are physically active is 0.76 with the relative risk at 0.76 for men and 0.79 for women.[15] The impact of physical activity in reducing CRC risk is supported by biological mechanisms, including: "decreased inflammation, reduced intestinal transit time, decreased insulin-like growth factor levels, reduced hyperinsulinemia and modulated immune function."[15]

Alcohol consumption: There is a strong link between alcohol consumption and CRC evident for those who drink 2 or more alcoholic beverages a day. A higher relative risk is observed when comparing moderate drinkers (2-3 drinks a day) to heavy drinkers (4 or more drinks a day), and there may be a stronger risk for men.[16]

Smoking: Smoking is strongly associated with increased risk for colorectal cancer and mortality, including a significant dose-response relationship.[17]

Diet: There is evidence that higher intake of processed and red meat are positively associated with CRC.[18]

RECOMMENDATIONS

RISK ASSESSMENT

To determine the appropriate approach to CRC screening, it is important to assess an individual's risk considering age, family history, personal history and presence of high risk conditions. These factors will determine when screening should be initiated, and the appropriate tests and frequency. Individuals considered at increased risk include:

- Family history of CRC or high risk colonic adenomas in a first degree relative or two or more affected relatives.
    - A high risk colonic adenoma is defined as having one or more of the following:
        - Size greater or equal to 1 cm
        - Villous elements
        - High grade dysplasia
        - More than 3 adenomas found at one colonoscopy

  For further information, please see Post Polypectomy Surveillance Guidelines: https://screeningforlife.ca/wp-content/uploads/2019/12/ACRCSP-Post-Polypectomy-Surveillance-Guidelines-June-2013.pdf
- Personal history of CRC, colonic adenomas, or inflammatory bowel disease (i.e., ulcerative colitis or Crohn's colitis)
- High risk conditions, such as Lynch syndrome or Familial Adenomatous Polyposis (FAP)

Based on risk stratification, follow the recommendations for either the Average Risk Population or Increased Risk Population.

AVERAGE RISK POPULATION

The average risk population includes individuals' ages 50 to 74 years with no signs or symptoms suggesting CRC, and the absence of family history, personal history or other high risk CRC conditions as described in the section on Increased Risk Population.

Screening test: The Fecal Immunochemical Test (FIT) is the recommended method for screening those at average risk. This stool-based test relies on the detection of blood from adenomas or carcinomas.[3] The FIT uses an antibody against human globin – the protein part of hemoglobin.[19] In comparison to the guaiac fecal occult blood test (gFOBT), the FIT has higher sensitivity, specificity and test adherences rates.[19] A systematic review of randomized control trials (RCTs) comparing diagnostic accuracy of the gFOBT versus FIT, found better performance by the FIT, with positivity rates and sensitivities both higher than gFOBT.[19] One RCT reported the FIT to be twice as likely to find colorectal cancers and five times more likely to find advanced polyps.[20] The FIT does not have dietary restrictions and thus is not subject to false negative results in the presence of Vitamin C supplements.[20]

RCTs have studied the likelihood of completing screening with FIT as compared to the gFOBT[20,21] and colonoscopy.[21] In both cases, compliance with the FIT is superior, i.e., 24.6% for colonoscopy versus 34.2% for FIT;[21] and 12% more favourable participation rate for FIT vs. gFOBT.[20]

There are no RCTs available evaluating the outcomes of FIT screening to mortality from CRC. A 2007 Cochrane review[22] pooling RCT results of the gFOBT found that a CRC screening program with biennial gFOBT can lead to a 16% reduction in CRC mortality after 12 to 18 years of periodic screening and a 25% CRC mortality reduction for those attending at least one round of gFOBT screening. Given the increased test performance and adherence rates for FIT compared to the gFOBT, the effect of screening with the FIT is anticipated to produce even better outcomes.

Other guidelines support FIT over gFOBT because FIT has both superior test characteristics and adherence rates for the detection of CRC.[23,24,25]

Screening interval: One and two year screening intervals are recommended in other CRC screening guidelines and are primarily based on modelling studies.[2,20,22] There is, however, strong evidence to support that the effectiveness of screening, for all screening modalities, will decrease substantially if adherence to the screening regimen declines.[3,26] This committee recommends a 1-2 year interval since it allows family physicians some flexibility to realistically meet this standard.

Screening following a normal colonoscopy: For individuals with a normal colonoscopy result, wait 10 years to start or re-start screening with FIT. This recommendation is based on the recommendations from other guidelines[24,27] and observational and case control studies suggesting that patients with colonoscopy have reduced CRC incidence or mortality for duration of effect of 10 years or more.[27] This recommendation is valid for good quality colonoscopy only. The quality of the colonoscopy depends on its completeness (reaching and inspecting the cecum), the quality of bowel preparation, and the degree of attention paid to mucosal details during the examination.

Positive FIT results: All individuals with a positive FIT result should be referred promptly for a colonoscopy. A repeat FIT test, just to be certain, is not recommended. One cancer is detected for every 20 positive FITs.[21]

Increased Risk Population

Family history: Mortality reduction studies directed at screening persons with a family history of CRC or adenomatous polyps are not yet available. However, we do know that family history is the second most common risk factor for CRC after age. As stated above, this risk increases as the number of affected relatives increases and the younger the age of the relative at diagnosis. The evidence for a precise cut-off age is not strong so clinical judgment is called for.

A first degree relative or two or more affected relatives with CRC or adenomatous polyps are warning signs of increased risk. Studies are increasingly showing that first degree relatives of individuals diagnosed with CRC had a risk of CRC at age 40 that was similar to the risk of CRC in average risk individuals at the age of 50.[6]

Individuals with a first degree relative ≤60 years at diagnosis or two or more affected relatives should be referred for consideration of colonoscopy at age 40 or 10 years before the youngest index case, whichever comes first. Colonoscopy is the recommended screening modality as it affords opportunity for therapeutic intervention and biopsy.[4] Family history of a first degree relative > 60 years at diagnosis makes very little contribution to risk. A recent RCT illustrates FIT used for CRC screening (annual FIT for 3 years) detected all CRCs and was equivalent to colonoscopy for detecting advanced neoplasia in first-degree relatives of individuals diagnosed with CRC.[28] Therefore screening with FIT starting at age 40 is recommended.

In certain cases, an individuals' anxiety and "need to know" may influence a referral.

Personal history: For individuals with a personal history of CRC, colonic adenomatous polyps or inflammatory bowel disease, regular surveillance colonoscopy is required. The recommended surveillance interval will depend on the number, type and size of colonic adenomas. Post-polypectomy surveillance recommendations are best made by the program or endoscopist that performed the colonoscopy, upon review of the pathology report. Provincial Post Polypectomy Surveillance guidelines are available at: https://screeningforlife.ca/wp-content/uploads/2019/12/ACRCSP-Post-Polypectomy-Surveillance-Guidelines-June-2013.pdf Not all polyps require surveillance. For example, no follow up is required for small, single, hyperplastic polyps found in the distal colon. A personal history of ulcerative colitis or Crohn's colitis also necessitates an on- going relationship with a specialist for surveillance.

High risk conditions for CRC: It is important to identify individuals with high risk conditions for developing CRC, and ensure they have an established relationship with an endoscopist or surveillance program. These conditions include: Lynch syndrome (HNPCC) and Familial Adenomatous Polyposis (FAP). Consider Lynch syndrome in those with a personal or family history of multiple cancers, some of which include colorectal, endometrial, gastric, ovarian, hepatobiliary, upper urinary tract, pancreatic, small bowel and CNS – glioblastoma.[9] Consider FAP in those presenting with multiple colon polyps at young age.

CRC SCREENING 75 YEARS OF AGE AND OLDER

CRC Screening on Asymptomatic Patients with a Life Expectancy of Less than 10 Years and No Family or Personal History of Colorectal Neoplasia

CRC screening and surveillance testing may not be appropriate for individuals over 74 years old when risk is greater than benefit. The risk from the colonoscopy procedure increases for patients of older ages and especially with comorbidities. In addition, patients greater than 74 years of age are more likely to bleed, have a positive FIT and require a colonoscopy follow-up.

The decision to screen should be based on individual assessment of the risk/benefit ratio of colorectal cancer screening or surveillance for each patient. This includes results of previous screening tests, family history, any possible risks from the test, life expectancy and the individual's preferences. This risk/benefit ratio of screening should be discussed with and understood by the individual and the decision to screen is between the individual and provider.[2, 29,30,31]

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For more information see: actt.albertadoctors.org

Guideline Committee

The committee consisted of representatives from family medicine, internal medicine, gastroenterology, general surgery and diagnostic radiology.

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Minor revision – January 2020 (web links)

Minor revision – November 2020 (inclusive language)

* Formal CPG update planned in 2021

APPENDIX A

CRC SCREENING PROGRAMS

Edmonton Zone

SCOPE Program: Edmonton AB T5K 0C0

Phone 780-342-0180
Fax 780-342-0311
Email scope@albertahealthservices.ca,
Website https://www.albertahealthservices.ca/findhealth/service.aspx?Id=1011952

Calgary Zone

Forzani and MacPhail Colon Cancer Screening Centre: Teaching, Research and Wellness Building (TRW)

6th Floor, 3280 Hospital Drive NW
Calgary AB T2N 4N1,

Phone (403) 944-3800
https://www.albertahealthservices.ca/info/ccsc.aspx

South Zone

Medicine Hat Colorectal Cancer Screening Clinic
666 5th Street S.W., Medicine Hat, AB, T1A 4H6
Phone (403) 529-8016, Fax (403) 528-5644

Lethbridge and Area Colorectal Cancer Screening Program:
2100 11 Street
Coaldale AB T1M 1L2
Phone (403) 345-7009, Fax (403) 345-2698

GENERAL RESOURCES

Colorectal Cancer Screening: https://screeningforlife.ca/colorectal/

Cancer Care Alberta:

https://www.albertahealthservices.ca/cancer/cancer.aspx

APPENDIX B

OTHER COLORECTAL CANCER SCREENING TESTS

Note: Availability and expertise of the following tests may vary across the province

Flexible sigmoidoscopy: A Canadian expert panel on the evidence for the efficacy of flexible sigmoidoscopy in CRC screening concluded that the recently published results from four very large RCTs[32,33,34,35] provide clear evidence that screening with flexible sigmoidoscopy reduces CRC incidence by about 20% and mortality by about 25% in average risk individuals. Authors of a recent meta-analysis of RCTs of sigmoidoscopy for CRC screening also came to the same conclusion based on the fact that, by intention to screen, sigmoidoscopy reduces incidence of CRC by 18% and mortality due to CRC by 28%, respectively, and by 32% and 50% respectively in those who actually received screening.[36] Limitations of flexible sigmoidoscopy include: it views only about a third of the colon and can miss small polyps.[37] The risks of complications are very low (.0018% for perforation and .0082% for bleeding).[20] Considerations that may affect compliance include: required bowel preparation, time away from work and the test may be uncomfortable.

Colonoscopy: Based on prospective observational studies and case-control studies, the reduction in CRC incidence and mortality in individuals undergoing colonoscopy compared to the general population, ranged from 0.45 to 0.77 for CRC[38,39,40,41,42] incidence and from 0.31 to 0.65 for CRC mortality[38,43,44]. There are concerns that colonoscopy might not be as effective in the right colon as in other segments of the colorectum.[40,43] Advantages of colonoscopy include: testing is done every 10 years, ability to biopsy and remove polyps, opportunity to diagnose other disease of the colon. The risk of complications reported is approximately 0.5%,[21] including bleeding, perforation, and cardiopulmonary complications. Considerations that may affect compliance include: required bowel preparation, sedation, time away from work, and the test may be uncomfortable.

CT Colonography: Evidence suggests CT Colonography has comparable sensitivity and specificity to colonoscopy for detecting large polyps but is less accurate than colonoscopy for detecting smaller (<1 cm) polyps according to one meta-analysis.[45] Considerations that may affect compliance include: exposure to radiation, required bowel preparation, time away from work, and the test may be uncomfortable. A colonoscopy is required if the CT colonoscopy is abnormal.

Double contrast barium enema (DCBE): The effectiveness of DCBE for polyp detection is less than CT colonography. Guidelines and publications reviewed do not support DCBE as a CRC screening test.[3,23,46]

gFOBT: The gFOBT has lower sensitivity, specificity and test adherence rates when compared to the FIT.[19] As of 2014, the gFOBT will be discontinued for screening in Alberta.

Carcinoembryonic antigen (CEA): The specificity of CEA for detecting colorectal cancer is high but the sensitivity is very low. Overall evidence does not support CEA as a screening test.[47,48,49,50]