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Part 1: Screening for the Purposes of Colorectal Cancer Prevention and Detection in Asymptomatic Adults

Effective Date: April 13, 2022

Scope

This guideline provides recommendations for the detection of colorectal cancer (CRC) and precancerous lesions in asymptomatic adults, including identifying those whose family history suggest hereditary syndromes (see Appendix A: Hereditary Colorectal Cancer [CRC] Syndromes). This guideline does not apply to individuals with anemia, or bowel-related signs or symptoms. These individuals should be evaluated directly via diagnostic tests, rather than via the fecal immunochemical test (FIT) screening test. It also does not apply to individuals with inflammatory bowel disease whose CRC prevention should be individualized. Recommendations following removal of colorectal precancerous lesions or cancer can be found at **BCGuidelines.ca:** *Follow-up of Colorectal Cancer and Precancerous Lesions (Polyps)*.

Key Recommendations

- Screening for colorectal cancer (CRC) should be based on risk stratification that determines appropriate screening test and interval.
- Wherever possible, individuals should be encouraged to have their initial screening and follow-up conducted through the British Columbia (BC) Colon Screening Program (CSP), even if they have previously been screened outside of the program.
- Fecal immunochemical test (FIT) every 2 years is the preferred screening strategy for average-risk individuals aged 50 – 74 years.
- Since a positive FIT is specific for the presence of human blood, any positive FIT should be followed up with colonoscopy. Do not repeat the FIT.
- FIT is not necessary when frank blood is present. Those individuals should be directly investigated via diagnostic tests rather than the FIT screening test.
- Individuals at average risk for CRC, who have had a colonoscopy or flexible sigmoidoscopy within the last 10 years with no precancerous lesions identified do not require additional screening.
- Individuals with a family history of CRC should follow different age and frequency screening criteria:
  - **2 or more first-degree relatives (FDRs) with CRC diagnosed at *any* age:** colonoscopy every 5 years starting at age 40 or starting 10 years younger than the age of diagnosis of the earliest affected relative.
  - **1 FDR with CRC diagnosed *before* age 60 years:** colonoscopy every 5 years starting at age 40 or starting 10 years younger than the age of diagnosis of the affected relative.
  - **1 FDR with CRC diagnosed *after* age 60 years:** FIT every 2 years starting at age 50.
  - **1 or more second-degree relatives with CRC at *any* age:** FIT every 2 years starting at age 50.
  - Hereditary CRC syndromes and recommended screening are addressed in Appendix A: Hereditary Colorectal Cancer (CRC) Syndromes.

Epidemiology

CRC ranks as the third most common malignancy in Canada and the second most frequent cause of cancer death.[1] The incidence of CRC rises steadily after the age of 50. More than 1300 people die each year from CRC in BC.[1] The age-standardized incidence rate of CRC in BC in 2019 was 72.3/100,000 men and 51.3/100,000 women.[1]

Table 1: Lifetime Probability of Developing or Dying from Colorectal Cancer (CRC) in Canada.[1]

	Lifetime Probability		Probability (%) of Developing Cancer in Next 10 Years by Age					
	Developing CRC	Dying from CRC	30-39	40-49	50-59	60-69	70-79	80+
Males	1 in 14	1 in 32	0.1	0.2	0.8	2.0	3.4	3.3
Females	1 in 18	1 in 37	0.1	0.2	0.6	1.3	2.3	2.7

Most CRCs arise from precancerous lesions (previously known as polyps); as it generally takes 5 to 10 years for a small precancerous lesion to develop into a malignancy, cancer may be prevented by removal of such a lesion.[3] Two major types of precancerous lesions are found in the colon and rectum: adenomas and serrated lesions. Amongst the serrated lesions, sessile serrated lesions (SSLs) and traditional serrated adenomas (TSAs) are considered to have the potential for malignant transformation while hyperplastic polyps (HPs) do not. Individuals with multiple precancerous lesions of any size are at increased risk of CRC.[2]

The risk of a precancerous lesion becoming malignant is greatest for 'high risk' lesions (also known as advanced adenomas), which are defined as having any of the following:

a) adenomas with villous features
b) adenomas with high grade dysplasia
c) adenomas or sessile serrated lesion (SSL) ≥ 10 mm (as measured by the colonoscopist at the time of excision)
d) SSLs with cytologic dysplasia
e) traditional serrated adenomas (TSAs)
f) hyperplastic polyps ≥ 10 mm (as measured by the colonoscopist at the time of excision).

Major Risk Factors

The most important risk factor for CRC is increasing age over 50.[3,4]

Other major risk factors for CRC include:[2,4]

- Personal history of high-risk precancerous lesions (advanced adenoma, see above).
- Family history of CRC:
  - Single FDR* with CRC under age 60.[5]
  - Two or more FDRs with CRC at any age.
  - Hereditary CRC syndrome such as familial adenomatous polyposis (FAP), Lynch Syndrome or hereditary non-polyposis colon cancer (HNPCC). See Appendix A: Hereditary Colorectal Cancer (CRC) Syndromes.
- Individuals with long-standing and extensive inflammatory bowel disease. These individuals require an individualized approach to dysplasia detection, distinct from the recommendations in this guideline, guided by an inflammatory bowel disease specialist.

Approximately 75% of all CRC occurs in individuals of average risk with no family history.[4] A second degree relative with CRC does not significantly increase one's risk of CRC. There is no evidence that individuals with other sporadic cancers (e.g., breast, prostate, lung) are at increased risk of developing CRC.

* **1st degree relatives** have a blood relationship to the individual: parents, brothers, sisters and children. **2nd degree relatives** have a blood relationship to the individual: aunts, uncles, nieces, nephews, grandparents & grandchildren.

Additional risk factors for CRC include a diet rich in red and processed meat and low in fruits and vegetables, smoking, sedentary lifestyle and obesity, diabetes, and alcohol consumption. However, there is currently insufficient evidence to modify screening recommendations based on these modest risk factors.

Certain populations are less likely to have been screened and are therefore indirectly at higher risk for CRC, i.e., First Nations, Inuit and Métis, low-income individuals, rural and remote communities, and new immigrants.[2]

Primary Prevention

Other than individuals who are already taking Acetylsalicylic Acid (ASA) for cardiovascular disease up to age 70, there is currently no value in ASA intake for prevention of CRC.[3] However, higher dose ASA (600 mg per day) is associated with decreased risk of CRC in Lynch Syndrome individuals.[4]

Several other medications, vitamins, supplements, and dietary factors have been evaluated as chemoprotective agents for CRC but have not been shown to be effective with any degree of certainty.[5]

Screening Strategies

BC Colon Screening Program (CSP)

Wherever possible, individuals should be referred by their primary care practitioner to have their initial screening and follow-up conducted through the BC Colon Screening Program (CSP), even if they have previously been screened outside of the program. To learn more, see associated documents. The intention is that these individuals will be recalled by the CSP at the appropriate interval.

It is estimated that up to 60% of individuals who qualify for screening are not registered in the CSP and may therefore run some risk of being lost to follow-up. Issues contributing to loss of follow-up include orphaned patients, patient and practitioner mobility, and significant time intervals between re-screening and surveillance. These issues underscore the importance of patient education and patients being engaged in their care plans.

Maintaining an up-to-date registration with the CSP will assure individuals receive their mailed follow-up reminders. The program offers patient navigator services when colonoscopy is required.

These guidelines and approach to patient care need to be balanced against individual factors and clinical judgement of the practitioners involved.

Individuals with significant family history of CRC

Significant family history includes those with 2 or more FDRs with CRC diagnosed at any age or 1 FDR with CRC diagnosed before age 60 years.

These individuals should be offered a colonoscopy every 5 years at age 40 years, or 10 years younger than the age of diagnosis of the affected relative. There is no need for FIT testing in this population.

Hereditary CRC syndromes and recommended screening are addressed in Appendix A: Hereditary Colorectal Cancer (CRC) Syndromes. Referrals can be made to the Hereditary Cancer Program at the BC Cancer Agency, see www.bccancer.bc.ca.

Average risk asymptomatic individuals, aged 50 to 74 years[6]

For most individuals in this group, the primarily recommended strategy is FIT every 2 years,[7,8] with any positive FIT to be followed by a colonoscopy.[7] After a negative colonoscopy, screening with FIT can be delayed for a 10 year interval.

More invasive alternatives to regular FIT screening include, flexible sigmoidoscopy (every 10 years), colonoscopy (every 10 years) or computed tomography (CT) colonography (every 5 years). Of these options, only FIT every 2 years and flexible sigmoidoscopy every 10 years are recommended by the Canadian Task Force on Preventative Health.[6]

It should be noted that those with 1 FDR with CRC diagnosed after 60 years or 1 or more second-degree relatives with CRC at any age are not at increased risk.

Average risk asymptomatic individuals, age 75 years and older

Recognizing the generally long time course for development of cancer from precancerous lesions (previously referred to as polyps) in individuals who have been regularly screened up to age 75 years, screening by FIT or other modalities is not recommended after age 75.[12,13] However, the value of screening should be individually assessed in the older individual, taking into account a balance of all risks, benefits, individual comorbidities, frailty[7,8] and anticipated life expectancy. A previously unscreened individual may benefit from a one time screening test over 75 years.[9]

Screening is not recommended after 85 years of age.[13]

Controversies in care

Average risk asymptomatic individuals, under age 50 years and with no family history

For reasons not yet fully understood, the incidence of early onset CRC is increasing in Canada and other countries.[10] Early onset CRC is defined as CRC diagnosed under the age of 50 years. Preliminary research suggests an association with lower income, obesity, and a more sedentary lifestyle.[11] American CRC screening guidelines have recommended initiating screening at 45 years of age, acknowledging that this recommendation is based on low quality evidence.[12,13] However, to our knowledge all other countries with screening guidelines, have continued to commence screening at age 50 years.[14,15] While relative rates of early onset CRC have been increasing, the absolute number diagnosed in the 45 – 49 year age group remains low (1 in 18,000 in 2012 to 2016 versus 1 in 19,000 in 1992 to 1996).[11] **At this time, screening average risk asymptomatic individuals under the age of 50 years is not recommended**.

Physicians should be mindful of the increasing incidence of CRC in younger adults when evaluating *symptomatic* individuals.

Risks and Benefits of Screening Modalities

All screening modalities have associated benefits and harms, including the risk of missing a precancerous lesion (previously referred to as polyp) or CRC, but an effective screening technique for CRC should be feasible, accurate, safe, acceptable, and cost-effective.

The following CRC screening modalities are available with the pros and cons of each outlined in Table 2: Summary of CRC screening modality risks and benefits. Tests that are not recommended for screening are listed. For individuals who test positive on any non-colonoscopy screening test, a full colonoscopy is advised.

Fecal immunochemical test (FIT)

FIT is recommended every 2 years. Performing the test through the BC Colon Screening program (CSP) is the preferred method for CRC screening in BC where it is coordinated by a nurse navigator and a patient recall system with quality assurance initiatives. When used in the appropriate population, FIT is the most cost-effective strategy.[15] Any individual with a positive FIT should be referred for colonoscopy. **Individuals at higher risk for CRC who are undergoing regular colonoscopy screening should not have a FIT**. Individuals who report frank blood in the stool or have other symptoms concerning for CRC should not have a FIT. FIT's sensitivity for cancer as performed in BC is approximately 90%.[16] When used repeatedly every 2 years it becomes an increasingly sensitive strategy for detecting precancerous lesions (polyps).

Colonoscopy

Colonoscopy is the recommended test following a positive FIT, a flexible sigmoidoscopy in which CRC or precancerous lesions (polyps) are identified, or a CT colonography in which CRC or precancerous lesions are identified. During colonoscopy, precancerous lesions (polyps) are removed to prevent the development of CRC.[2,3,23] Colonoscopy examines the entire colon and requires an oral bowel preparation. The recommended screening interval following a colonoscopy in which no precancerous lesions or CRC are identified is 10 years for average risk individuals. Complications can arise from the bowel preparation as well as the procedure.

Flexible Sigmoidoscopy

Flexible sigmoidoscopy examines the rectum and sigmoid colon. It can usually be done without intravenous sedation but does require colon preparation, which may be given orally or via enema.[9] The recommended screening interval after a flexible sigmoidoscopy with no pre-cancerous lesions identified is 10 years.

Computed tomography (CT) Colonography

CT colonography images the entire colon utilizing a CT scanner. It requires a thorough bowel preparation, pre-procedure ingestion of fecal and fluid tagging agents, and spasmolytic (e.g., Buscopan®). The colon and rectum are insufflated with carbon dioxide gas through a retention tube inserted into the rectum. The individual is positioned in the scanner in supine and prone or decubitus positions and scans acquired. CT colonography imaging of extraluminal structures is limited because intravenous contrast is not administered. Complications such as abdominal cramping or diarrhea can arise from the bowel preparation or CO_2 insufflation, but typically resolve within a short period of time. The usual interval for CT Colonography is 5 years if no precancerous lesions (previously referred to as polyps) are identified, if the individual chooses not to use FIT.

Table 2: Summary of CRC screening modality risks and benefits

Modality	Pros	Cons
FIT	• Non-invasive. • Inexpensive. • Widely available. • Can be done at home. • Only requires one sample. • No medication or diet restrictions. • Highest participation rate compared to other modalities. • Reduction in CRC mortality and incidence.[6]	• Lower sensitivity and specificity than direct visualization for precancerous lesions on a single test but improves with repeated testing over time. • Variable individual compliance with follow-up colonoscopy. • Testing every 2 years.
Colonoscopy	• High sensitivity and specificity. • Allows for immediate biopsy and polypectomy. • Examines entire colon. • Longer interval between screening.	• Sedation requires a minimum of one day off work and another adult accompany the individual. • Full bowel cleansing required. • Risk of serious complications in the BC context (overall 47 per 10,000, perforation 6 per 10,000; bleeding 27 per 10,000; death 3 per 100,000).[13,22] • Accuracy and safety rate varies. • High-cost procedure. • Access (including long waits), cost of bowel preparation, hospital attendance, and healthcare costs. • No randomized trials demonstrating a decrease in CRC mortality or incidence.
Flexible Sigmoidoscopy	• Can usually be done without sedation. • Allows for immediate biopsy and polypectomy. • Reduction of CRC incidence and mortality protective beyond 10 years.[17,18]	• Proximal colon is not examined.[20] • Discomfort. • Accuracy and complication rate varies. • Distal lesions require further full colonoscopy due to risk of proximal lesions. • Risk of complications (perforations 0.46 per 10,000).[13]
CT Colonography	• Minimally invasive. • Low complication rate (perforations 0.46 per 10,000).[24] • No sedation used. • Usually effective where colonoscopy is technically incomplete or contraindicated.	• Full bowel cleansing required. • Discomfort. • Radiation exposure.* • Cost implications i.e., time off work. • Bowel preparation. • High-cost procedure. • Reduced sensitivity for detection of flat polyps and polyps < 6 mm.[25] • Does not permit biopsy or polyp removal. • Diagnosis of CRC or precancerous lesions requires a further full colonoscopy. • Accuracy varies. • No studies demonstrating a decrease in CRC mortality or incidence.

* Radiation dose for CTC is difficult to determine precisely as it is dependent on multiple factors including individuals' body habitus and how many scans/views are needed. Protocols used are based on individual size and composition and aim to reduce dose as much as possible. Average radiation doses are approximately 7mSv (equivalent to 70 CXRs or 2 years background radiation).[19,20]

Tests Not Recommended for Screening

Evidence does not support the use of the following as primary screening tools for CRC in asymptomatic individuals:

- Barium enemas
- Carcinoembryonic Antigen (CEA) tests
- Combined use of FIT with flexible sigmoidoscopy for primary screening

Resources

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Abbreviations

- ASA Acetylsalicylic Acid
- CEA Carcinoembryonic Antigen
- CRC Colorectal cancer
- CT Computed tomography
- FAP Familial adenomatous polyposis
- FDR First-degree relative
- FIT Fecal immunochemical test
- FOBT Fecal Occult Blood Test
- FS Flexible sigmoidoscopy
- HNPCC Hereditary non-polyposis colon cancer
- HP Hyperplastic polyps
- MAP MUTYH Associated Polyposis
- SSL Sessile serrated lesions
- TSA Traditional serrated adenomas

Practitioner resources

- **BC Colon Screening Program:** http://www.bccancer.bc.ca/screening/colon
- **Hereditary Cancer Program at the BC Cancer Agency:** www.bccancer.bc.ca
- **Pathways:** https://pathwaysbc.ca/login
- **UBC CPD BC Cancer Primary Care Learning Sessions - Colorectal Cancer:** https://elearning.ubccpd.ca/
- **Canadian Cancer Society:** www.cancer.ca
- **Colon Cancer Canada:** www.coloncancercanada.ca
- **Public Health Agency of Canada:** Cancer

Patient, Family and Caregiver resources

- **BC Colon Screening Program:** http://www.bccancer.bc.ca/screening/colon
- **BC Colon Screening:** Facts and Myths
- **BC Cancer:** Hereditary Cancer Program
- **HealthlinkBC:** Health information, translation services, Health Service Navigators and dieticians, www.healthlinkbc.ca or by telephone at 811.
- **Canadian Cancer Society:** www.cancer.ca
- **Colon Cancer Canada:** www.coloncancercanada.ca
- **Public Health Agency of Canada:** Cancer

Appendices

- Appendix A: Hereditary Colorectal Cancer (CRC) Syndromes

Associated Documents

- **BCGuidelines.ca:** *Follow-up of Colorectal Cancer and Precancerous Lesions (Polyps)*
- **BC Cancer:** Colon Screening Program: Colonoscopy Referral Form
- **BC Cancer:** Standard Out-Patient Laboratory Requisition Form

This guideline is based on scientific evidence current as of the effective date.

This guideline was developed by the Guidelines and Protocols Advisory Committee in collaboration with the Provincial Laboratory Medicine Services, and adopted under the *Medical Services Act* and the *Laboratory Services Act*.

For more information about how BC Guidelines are developed, refer to the GPAC Handbook available at BCGuidelines.ca: GPAC Handbook.

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Appendix A: Hereditary Colorectal Cancer (CRC) Syndromes

Hereditary CRC implies a strong predisposition to an inherited CRC due to a genetic mutation. The hallmarks of hereditary CRC syndromes are pre-cancerous lesions and CRC diagnosed at a younger age, metachronous and synchronous CRC, multiple affected relatives, and, often, other associated cancer diagnoses.[21,22]

Genetic counselling and testing are available through the Hereditary Cancer Program at BC Cancer. Individuals affected with hereditary cancer predispositions to colon cancer, and their family members, should be followed by a gastroenterologist who, in conjunction with the Hereditary Cancer Program at the BC Cancer Agency will determine ongoing medical care.

1. Lynch Syndrome

Lynch syndrome (LS) is an autosomal dominant condition caused by a germline mutation in a mismatch repair gene (MLH1, MSH2, MSH6, PMS2) or by deletions in the EPCAM gene. LS is characterized by an increased risk for cancers of the colon, endometrium, ovary, stomach, small intestine, hepatobiliary tract, urinary tract, brain, and skin. LS accounts for 2-4% of all CRCs. While usually associated with CRC, it is important to understand that endometrial cancer is often the first cancer diagnosed in women with LS.

Muir-Torre syndrome is a subset of LS with an associated predisposition to sebaceous neoplasms and is primarily associated with MSH2 gene mutations.

Confirmation of LS is important both for people with cancer, because of the associated risk for another LS cancer, and to inform appropriate cancer risk management for their adult family members.

2. Polyposis syndromes

Inherited risk for CRC is associated with a number of polyposis syndromes (genes), some of which are well-defined and others are less common. Identification of an unusual number of polyps and/or unusual polyps should prompt consideration of Hereditary Cancer Program referral for polyposis assessment.

Polyposis syndromes/genes include: Familial Adenomatous Polyposis/Attenuated Familial Adenomatous Polyposis (APC), Juvenile Polyposis (*SMAD4*, *BRMP1A*), MUTYH-Associated Polyposis (*MUTYH*), Polymerase Proofreading-associated syndrome (*POLE/POLD1*), Serrated Polyposis syndrome (formerly Hyperplastic Polyposis), and Mixed Polyposis. Peutz-Jeghers syndrome (*STK11*) and Cowden syndrome (*PTEN*) are also associated with specific types of polyps.

3. Other Hereditary Cancer Syndromes

A number of other hereditary cancer syndromes are associated with an increased risk for CRC. These may be associated with a moderate to high risk for CRC and require increased CRC screening recommendations.