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Colorectal Screening for Cancer Prevention in Asymptomatic Patients

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Scope

This guideline provides recommendations for the detection of colorectal cancer and adenomas in asymptomatic patients, aged ≥ 19 years. It does not apply to patients with previous colorectal adenomas or cancer, anemia, or bowel related symptoms. Any symptoms need to be investigated promptly. Recommendations following removal of colorectal adenomas or cancer can be found at BCGuidelines.ca – *Follow-up of Colorectal Polyps or Cancer.*

Key Recommendations

- Screening for colorectal cancer should occur after risk stratification which determines the appropriate screening test and interval.
- FIT every 2 years for average-risk individuals aged 50 – 74 years.*
- Follow-up of ANY positive FOBT with colonoscopy.
- Use of FOBT is not appropriate when frank blood is present.
- Colonoscopy every 10 years is an acceptable alternative to FOBT for screening.
- Patients followed by colonoscopy do not require other screening modalities (i.e., FOBT).

Epidemiology

Colorectal cancer (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 1100 people die each year from CRC in British Columbia (BC).[1] The age-standardized incidence rate of CRC in BC in 2012 was 53/100,000 men and 35/100,000 women.[1]

Table 1. Lifetime Probability of Developing or Dying from Colorectal Cancer in BC.[1]

	Lifetime Probability		Probability (%) of Developing Cancer in Next 10 Years by Age					
	Developing CRC %	Dying CRC %	30-39	40-49	50-59	60-69	70-79	80-89
Men	7.5	3.6	0.1	0.2	0.8	2.0	3.4	3.3
Women	6.4	3.1	0.1	0.2	0.6	1.3	2.3	2.7

In patients who are 50 years and older, more than 25% will have at least one adenoma. The majority of CRCs arise from pre-existing adenomas, the 'adenoma–carcinoma sequence'. Two major types of polyps are found in the colon and rectum: adenomas and hyperplastic polyps. Hyperplastic polyps are considered to have **no** malignant potential.

* *This has been revised from 1 – 2 years (March 2013) to 2 years (June 2016).*

The risk of an adenoma becoming malignant is greatest for "advanced" adenomas.

- tubular adenomas ≥ 1 cm,
- villous adenomas,
- adenoma with high grade dysplasia (HGD),
- sessile serrated polyps ≥ than 1 cm,
- sessile serrated polyps with dysplasia,
- or traditional serrated adenoma.

Individuals with multiple adenomas of any size are also at increased risk.[2] Because it generally takes 5–10 years for a small adenoma to develop into a malignancy, cancer may be prevented by adenoma removal.[3]

Risk Factors

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

Additional risk factors for CRC include:[2, 4]

- Personal history of adenoma(s)
- Family history
    - o Single first degree relative[†] with CRC under age 60[5]
    - o Two or more first degree relatives with CRC at any age
    - o Familial adenomatous polyposis (FAP) or hereditary non-polyposis colon cancer (HNPCC) see *Appendix A: Family History and Other Influences on Colorectal Cancer Risk*
- Long standing (at least 8 years) inflammatory bowel disease involving the colon.

Approximately 75% of all CRC occurs in patients of average risk with no family history.[4] In general, having a single affected second degree relative with CRC does not significantly increase one's risk of CRC. At the present time there is no evidence that people with other sporadic cancers (e.g., breast, prostate) are at increased risk of developing CRC.

Other risk factors for CRC may include diet, smoking, sedentary lifestyle and obesity. These risk factors are newly recognized but there is currently insufficient evidence to modify screening recommendations.

Screening

Indications for Screening

Individuals who are asymptomatic can be classified as having average or increased risk for CRC.

Average risk patients:

- Meet none of the criteria below for increased risk

Increased risk patients:

- Personal history of adenomas, particularly advanced or multiple adenomas – see BCGuidelines.ca – *Follow-up of Colorectal Polyps or Cancer*
- 1st degree relative age < 60 with CRC or advanced or multiple adenomas – see Appendix A
- Two or more 1st degree relatives with CRC at any age
- Longstanding inflammatory bowel disease[2]
- Family history of familial FAP or HNPCC – see Appendix A

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

Average Risk Asymptomatic Patients, Aged 50 to 74 years[6]

Fecal immunochemical test (FIT) every 2 years is recommended[‡] (see Table 2),[7,8] with any positive FIT to be followed by a colonoscopy. There is direct evidence from several population-based prospective randomized trials that FOBT, with follow-up of any positive result with colonoscopy, can reduce mortality from CRC.[8]

A colonoscopy is also an acceptable screening option every 10 years. For an average risk individual with a negative colonoscopy, further screening of any type is not required for 10 years. After a 10 year interval, the choice of subsequent screening modality can be determined.

Average Risk Asymptomatic Patients, Aged Over 74 years

For patients over the age of 75 years, the value of screening should be individually assessed taking into account a balance of the risks, benefits and patient comorbidities. Screening is not recommended after 85 years of age.[13]

Increased Risk Asymptomatic Patients, of Any Age[5]

With single 1st degree relative younger than age 60 with CRC or advanced adenoma(s) or two or more 1st degree relatives of any age with CRC, the recommended screening is:

- Colonoscopy every 5 years starting at age 40, or 10 years earlier than the age of youngest affected relative at diagnosis.
- Use FOBT, FS and CT colonography only when patients decline colonoscopy or have an incomplete colonoscopy.

With inflammatory bowel disease involving the majority of the colon for over 8 years or the left colon for over 15 years,[14] the recommended screening is:

- Colonoscopy every 1 to 2 years with multiple biopsies to detect occult neoplasia (dysplasia).

For information on increased risk due to family history of FAP or HNPCC, see Appendix A.

Surveillance of Patients with Prior History

The following patients should undergo a surveillance program as outlined in BCGuidelines.ca – *Follow-up of Colorectal Cancers and Polyps:*

- Personal history of CRC
- Personal history of an advanced adenoma (see definition on page 2)
- Personal history of 1 or 2 non-advanced adenomas

Controversies in Care

Other methods for CRC screening are available. There is no single infallible technique for detection, but an effective screening technique for CRC should be feasible, accurate, safe, acceptable, and cost-effective.

- Flexible sigmoidoscopy (FS) has been used as a once only screening tool in the UK for individuals 55 – 64 years.[9] The prevalence of adenomas in the proximal colon markedly increases with age, while prevalence of adenomas in the rectum and sigmoid colon plateau after age 59 years.[10] This can limit the utility of FS.
- CT colonography every 5 years from age 50 has been recommended in some US guidelines[11] but other guidelines, including those from Canadian Association of Gastroenterology, do not recommend a CT colonography for average risk screening.[12, 13]

Test Options

The following are test options that are available for screening and diagnosis. Pros and cons for each test are listed as well as the tests that are no longer recommended. For patients who test positive on any non-colonoscopy screening test, a full colonoscopy is advised.

Fecal Occult Blood Test (FOBT)

As discussed above in Screening, FOBT (FIT preferred) is a cost effective method[15] and the most convenient first line screening modality in BC. Any positive test should be investigated with a colonoscopy. Patients undergoing regular colonoscopic

[‡] *This has been revised from 1 – 2 years (March 2013) to 2 years (June 2016).*

screening do not require FOBT. It is recommended that patients who report frank blood in the stool not have FOBT but instead be referred for possible endoscopic investigation. Digitally obtained stool should not be used for FOBT; testing is performed on spontaneously evacuated stool.[16] FIT is preferable to guaiac FOBT (Table 2).[17]

Pro: non-invasive; inexpensive; widely available.

Con: lower sensitivity and specificity than direct visualization for neoplasia; variable patient compliance; frequency of testing.

Table 2. Test Performance of gFOBT Versus FIT (≥100 ng/mL).

	FIT*	Guaiac**
Interaction with diet or medications	No	Yes
PPV† for all advanced adenomas and cancer	52%[18]	55%[18]
NPV‡ for all advanced adenomas and cancer	96%[19]	84%[20]
Specificity for human hemoglobin	Yes – antibody directed against human globin	No – reacts with any source of heme
Patient Participation	60%[18]	47%[18]

* *Auto-OC Micro*

** *Hemoccult II*

† *Positive predictive value (PPV) – The percentage of patients with a positive test who actually have the disease.*

‡ *Negative predictive value (NPV) – The percentage of patients with a negative test who do not have the disease.*

Colonoscopy

Colonoscopy is the gold standard for adenoma detection and removal to prevent CRC.[2, 3, 23] Colonoscopy allows for direct inspection of the entire colon, and allows for biopsy and polypectomy. It requires a thorough bowel preparation. Complications can arise from the bowel preparation as well as the procedure.

Pro: high sensitivity and specificity; allows for immediate biopsy and polypectomy; examines entire colon; longer interval between screening.

Con: usually requires sedation to minimize discomfort; risk of serious complications (perforations 3.8 per 10,000);[13, 22] accuracy and complication rate of the colonoscopy depends on the expertise of the endoscopist and adequacy of preparation; access and cost.

Flexible Sigmoidoscopy

Flexible sigmoidoscopy examines the rectum and sigmoid colon. It can usually be done without sedation but does require some colon preparation.[9]

Pro: usually does not require sedation; allows for immediate biopsy and polypectomy; has random controlled trial evidence for reduction of CRC incidence and mortality.[9]

Con: proximal colon is not examined;[20] discomfort; accuracy and complication rate of the sigmoidoscopy depends on the expertise of the endoscopist and adequacy of preparation; distal lesions require further full colonoscopy due to risk of proximal lesions; risk of complications (perforations 0.46 per 10,000).[13]

CT Colonography

CT Colonography images the entire colon utilizing a CT scanner. It requires a thorough bowel preparation and insufflation of carbon dioxide gas through the rectum. This test also images extraluminal structures. Complications can arise from the bowel preparation.

Pro: minimally invasive; low complication rate (perforations 0.46 per 10,000) compared to colonoscopy;[24] no sedation used; usually effective where colonoscopy is technically incomplete.

Con: discomfort; radiation exposure; high cost procedure; reduced sensitivity for detection of flat polyps and polyps <6 mm;[25] does not permit biopsy or polyp removal; the accuracy depends on expertise of the radiologist and adequacy of preparation; there are currently no outcome studies regarding CRC mortality prevention.

Test Not Recommended for Screening

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

- Digital rectal exams (DRE)
- Barium enemas
- Carcinoembryonic Antigen (CEA) tests
- Combined use of FOBT with flexible sigmoidoscopy for primary screening

Resources

References

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Resources

- BC Cancer Agency, Colon Screening, www.bccancer.bc.ca/screening/colon/
- HealthlinkBC – Health information, translation services and dietitians, www.healthlinkbc.ca or by telephone 811.
- Hereditary Cancer Program at the BC Cancer Agency www.bccancer.bc.ca or Toll Free: 1 800 663-3333 ext. 2325, in Vancouver call: 604 877-6000 ext. 2325
- Canadian Cancer Society, www.cancer.ca
- Colorectal Cancer Association of Canada, www.colorectal-cancer.ca
- Colon Cancer Canada, www.coloncancercanada.ca

Appendices

- Appendix A: Family History and Other Influences on Colorectal Cancer Risk

Associated Documents

The following documents accompany this guideline:

- Patient guide
- Guideline summary
- BCGuidelines.ca: *Follow-up of Colorectal Cancers and Polyps*

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

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- permit exceptions when justified by clinical circumstances

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Appendix A: Factors Influencing Colorectal Cancer Risk

Family History of a single relative presenting over age 60 with CRC or advanced adenomas does not significantly increase patient risk.

Risk Factors

1. Family History of Familial Adenomatous Polyposis (FAP)

FAP is a rare autosomal dominant condition in which affected individuals develop countless colorectal adenomas usually beginning in puberty. These adenomas will inevitably progress to multi-focal colon cancer if colectomy is not undertaken. Genetic counselling and testing should be offered to all 1st degree relatives as soon as possible through the Hereditary Cancer Program at the BC Cancer Agency (www.bccancer.bc.ca). Individuals affected with FAP and their first degree relatives should be followed by a gastroenterologist who, in conjunction with the Hereditary Cancer Program, will determine ongoing medical care.

Attenuated FAP – tends to present at an older age and results in fewer adenomas, often right sided, compared to traditional FAP. Attenuated FAP should be suspected in individuals that have developed > 10 adenomas during their lifetime. These patients should be referred to the Hereditary Cancer Program at the BC Cancer Agency.

2. Family History of Hereditary Nonpolyposis Colon Cancer (HNPCC)

HNPCC is an uncommon familial condition defined by the Amsterdam Criteria II:[1]

a) Three or more family members with CRC, or any Lynch Syndrome malignancy (small bowel, ureter, renal pelvis, endometrium), one of whom must be a first degree relative of the other two.

b) At least two generations must be affected by CRC or Lynch Syndrome malignancy.

c) At least one CRC must be diagnosed before age 50 years.

Individuals with a family history of HNPCC should undergo colonoscopy beginning ten years earlier than the youngest age at which a family member was diagnosed with colorectal cancer; or at age 25. Colonoscopy should be performed every 2 years until age 40, then annually thereafter. Individuals should be referred to the Hereditary Cancer Program at the BC Cancer Agency for assessment, counselling and, if appropriate, genetic testing.

3. Advanced Adenomas

Known to carry a higher cancer risk:

- tubular adenomas ≥ 1 cm,
- villous adenomas,
- adenoma with high grade dysplasia (HGD),
- greater than 1 sessile serrated polyps ≥ 1 cm,
- sessile serrated polyps with dysplasia, or
- traditional serrated adenoma.

[1] *Cruz-Correa M, Giardiello FM. Diagnosis and management of hereditary colon cancer. Gastroenterol Clin North Am 2002;31:537-49.*