

### Detection of Colorectal Neoplasms in Asymptomatic Patients

#### Scope

This guideline provides recommendations for the detection of colorectal cancer and adenomas in asymptomatic patients. These recommendations are intended to rationalize screening for various patient groups. They do not apply to patients with previous colorectal cancer, anemia, or bowel related symptoms.

Screening should not be offered to an individual where the findings would not alter the patient's management due to age or co-morbidity.

Recommendations for asymptomatic patients following curative resection of colorectal cancer are specified in the guideline, *Follow-up of Patients after Curative Resection of Colorectal Cancer*.

#### Risk Classification

Individuals can be classified as having average, moderate and high risk for colorectal cancer (CRC). Approximately 75 per cent of all colorectal cancer occurs in patients of average risk with no family history.<sup>1</sup> At the present time there is no evidence that people with other sporadic cancers (e.g. breast) are at increased risk of developing CRC.

##### High risk patients:

- Previous colorectal cancer
- Family history of:
  - familial adenomatous polyposis (FAP) – see below
  - hereditary nonpolyposis colon cancer syndrome (HNPCC) – see below

##### Moderate risk patients:

- Previous adenomas
- Longstanding inflammatory bowel disease<sup>2</sup>
- CRC in first degree relatives (see Recommendation 3)

##### Average risk patients:

- Meet none of the above criteria

For complete description of tests for the detection of colorectal neoplasms, see pages 4 & 5.

## FAP

FAP is a rare autosomal dominant condition in which affected individuals develop countless colorectal adenomas. Polyp formation begins between puberty and age 40. These polyps will inevitably progress to CRC if therapeutic intervention is not undertaken. Genetic counselling and testing should be offered to all 1<sup>st</sup> degree relatives\*. Currently genetic testing for FAP is not covered by MSP in British Columbia. Genetic counselling and testing for FAP can be obtained by referral to the Hereditary Cancer Program at the BC Cancer Agency.

Hereditary Cancer Program:

In Vancouver call: 604 877-6000 ext. 2325

Other areas call toll free: 1 800 663-3333 ext. 2325.

- Family members with negative genetic tests should be treated as average-risk individuals, see Recommendation 2.
- In the absence of clearly negative genetic test results, see Recommendation 4.

Note: \***1<sup>st</sup> degree relatives** who have a blood relationship to the patient include: parents, brothers, sisters and children. **2<sup>nd</sup> degree relatives** who have a blood relationship to the patient include: aunts, uncles, nieces, nephews, grandparents and grandchildren.

## HNPCC

HNPCC is a rare familial condition defined by the Amsterdam Criteria II<sup>†3,4</sup>:

- a) Three or more family members with CRC, or any Lynch Syndrome malignancy (see below), 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.

Two subtypes of HNPCC have been identified: one with CRC only (Lynch Syndrome I), the other is associated with cancer of the endometrium, small bowel, ureter or renal pelvis (Lynch Syndrome II). For patients with small families or incomplete family histories, some leeway in the above criteria may be applied in determining the patient's risk classification for CRC.

Individuals with a family history of HNPCC should be screened by colonoscopy beginning ten years less than the age at presentation of the youngest family member who had colorectal cancer;<sup>5, 6</sup> or at age 25. Colonoscopy should be performed every 2 years until age 40, then annually thereafter.<sup>3, 7</sup>

It is important to note that HNPCC adenomas progress rapidly to carcinoma and that many HNPCC neoplasms are in the proximal colon. When HNPCC is suspected in a family, genetic testing and counselling should be offered. Currently genetic testing for HNPCC is not covered by MSP in British Columbia. Genetic counselling and testing for HNPCC can be obtained by referral to the Hereditary Cancer Program at the BC Cancer Agency

Hereditary Cancer Program:

In Vancouver call: 604 877-6000 ext. 2325

Other areas call toll free: 1 800 663-3333 ext. 2325.

**†This list has been expanded in the Bethesda Criteria – see reference.**

### **RECOMMENDATION 1: All Patients 50 Years Of Age And Over**

Annual digital rectal examination (DRE).

### **RECOMMENDATION 2: Average Risk Asymptomatic Patients**

No known risk factors

- a) Fecal occult blood test (FOBT) – yearly, between age 50 and 75 (recommended)
- b) Flexible Sigmoidoscopy – every 5 years, between age 50 and 75 (optional, in addition to FOBT)

Colorectal cancer in 2<sup>nd</sup> degree relatives of any age

- a) Colonoscopy – every 10 years between age 50 and 75, or
- b) Double contrast barium enema (DCBE) and flexible sigmoidoscopy – every 5 -10 years, between age 50 and 75.

Adenomatous polyp in a 1<sup>st</sup> degree relative younger than age 60

- a) Colonoscopy – every 10 years between age 50 and 75, or
- b) DCBE and flexible sigmoidoscopy – every 5 -10 years, between age 50 and 75.

### **RECOMMENDATION 3: Moderate Risk Asymptomatic Patients**

Colorectal cancer in 1<sup>st</sup> degree relative, age 55 or younger; or two or more 1<sup>st</sup> degree relatives of any age

- Colonoscopy – every 5 years beginning at age 40 or 10 years before the age of presentation of the youngest case in the family, whichever is lower.

Colorectal cancer in 1<sup>st</sup> degree relative over age 55

- Colonoscopy – every 10 years beginning at age 40.

Personal history of polyp >1cm, or multiple colorectal adenomas of any size

- Colonoscopy – 3 years after polypectomy and every 5 years thereafter if recurrent adenomas are present; if no further adenomas then every 10 years thereafter.

Personal history of 1 or 2 colorectal adenomas <1cm

- Colonoscopy – 5 years after polypectomy and every 5 years thereafter if recurrent adenomas are present; if no further adenomas then every 10 years thereafter.

Inflammatory Bowel Disease involving entire colon for over eight years or the left colon for over 15 years

- Colonoscopy every 1-2 years in patients without dysplasia.

### **RECOMMENDATION 4: High Risk Asymptomatic Patients – Family History of FAP**

These patients should be referred to a specialist for evaluation, ongoing monitoring, genetic counselling and testing. Flexible sigmoidoscopy should start annually at age 12, then every 2 years from age 25, then every three years from age 35, then as per the guidelines for average-risk individuals starting at age 50 years.

### **RECOMMENDATION 5: High Risk Asymptomatic Patients – Family History of HNPCC**

These patients should be referred to a specialist for evaluation, ongoing monitoring, genetic counselling and testing. Colonoscopy every two years starting at age 25 or ten years before the age of presentation of the youngest case of CRC in the family, and annually after age 40.

## Tests for the Detection of Colorectal Neoplasms

### 1. Fecal Occult Blood Test (FOBT)

FOBT detects the presence of hemoglobin in the stool and therefore is an indirect method of detection of neoplasia. FOBT is pointless and unnecessary in patients who report frank blood in the stool. FOBT is a sensitive test for hemoglobin from any source, including dietary intake. Neoplasms in the colon bleed intermittently, therefore the sensitivity of a single FOBT for the detection of neoplasia is low.<sup>8</sup>

FECAL OCCULT BLOOD TEST	
Number of positive FOBT cards	Percent of subjects* with advanced neoplasia
0 of 3	9%
1 of 3	23%
2 of 3	33%
3 of 3	53%

A strong association exists between the number of positive test cards and the likelihood of advanced neoplasia. The standard recommendation is to test separate stool samples from three days annually. A single positive test warrants evaluation of the whole colon (see colonoscopy).<sup>9</sup>

\*Lieberman and Weiss, NEJM 2001;345:557

Sensitivity of FOBT has been shown to range from 12% (any neoplasia) to 36% (high grade neoplasia). The positive predictive value (probability that a person with a positive test has neoplasia) was 54% for any neoplasia, and 40% for advanced neoplasia; the negative predictive value (probability that a person with a negative test does not have neoplasia) was 64% and 88% respectively.<sup>9</sup>

Despite its shortcomings, FOBT is suitable for general population screening because it is widely available, inexpensive and simple to use. Patient compliance is a problem with FOBT as only about half of patients submit all three samples.<sup>10</sup>

*Pro: non-invasive; inexpensive; widely available*

*Con: low specificity and sensitivity for neoplasia; poor patient compliance*

### 2. Flexible Sigmoidoscopy

Flexible sigmoidoscopy examines the distal colon and rectum and therefore misses the 40% of cancers and polyps that are beyond its reach.<sup>11</sup> Biopsies and polypectomies can be performed during this procedure. The bowel must be cleansed with an oral laxative or an enema for adequate visualisation. The test takes approximately 5 to 10 minutes to perform.

*Pro: greater specificity than FOBT; usually does not require sedation; biopsy for diagnosis permits concomitant biopsy*

*Con: limited examination of the colon; discomfort; accuracy is dependent upon operator expertise and patient preparation; rare bowel perforation (0.014%)<sup>10</sup>; may not be readily available; no advantage over colonoscopy*

### 3. Flexible Sigmoidoscopy and FOBT

This combination has been used to offset the limitations of FOBT and flexible sigmoidoscopy when used alone. Unfortunately this combination fails to identify about 25% of patients with advanced neoplasia and about 50% of patients with advanced neoplasia in the proximal colon.<sup>9</sup>

*Pro: combined approach has a higher sensitivity than a non-combined approach; direct visualisation of left sided lesions*

*Con: fails to identify approximately 25% of patients with advanced neoplasia and about 50% of patients with advanced proximal neoplasia*

#### 4. Colonoscopy

---

Colonoscopy is currently the gold standard because it allows for direct inspection of the entire colon, and it allows for biopsy and polypectomy which are not possible with diagnostic imaging studies. Recent studies indicate that advanced neoplasia is more uniformly distributed throughout the colon than was previously believed and therefore justifies colonoscopy.<sup>12</sup> Colonoscopy takes approximately 15-30 minutes to perform. The bowel must be completely cleansed with an oral laxative for adequate visualisation. Colonoscopy usually requires sedation.

Colonoscopy is an expensive but effective test.<sup>8</sup> Complications can arise from the bowel preparation as well as the procedure (including electrolyte disturbance, bowel perforation (0.05%)<sup>13</sup>, bleeding (0.19%).<sup>14</sup>

*Pro: high sensitivity and specificity; allows for immediate biopsy and polypectomy; examines entire colon*

*Con: requires sedation; time needed for preparation, procedure and recovery; risk of bleeding and perforation; accuracy of the colonoscopy depends on the expertise of the endoscopist*

#### 5. Barium Enema

---

A barium enema examination can be performed as either a single contrast procedure or a double contrast procedure. Single contrast barium enema outlines the colon with barium alone. Double contrast barium enema (DCBE), also known as Air Contrast Barium Enema (ACBE), utilizes a combination of air and barium resulting in better visualisation of mucosal detail. Single contrast examinations are generally not recommended because of low sensitivity.

DCBE enables total colonic imaging, but overall is less accurate than colonoscopy.<sup>15</sup> DCBE has similar detection rates for clinically significant lesions (greater than 1 cm in diameter). For lesions less than 1 cm in diameter, DCBE is less sensitive than colonoscopy, especially in the rectum. DCBE is highly dependent on several factors, particularly meticulous bowel preparation. DCBE takes approximately 30-45 minutes to perform.

*Pro: widely available*

*Con: less accurate than colonoscopy; does not permit concomitant biopsy or polyp removal*

#### 6. CT Colonography (CTC)

---

CTC (also known as Virtual Colonoscopy) is a total colonic imaging tool utilizing a specialised multi-slice CT scanner. It is a relatively brief procedure that does require bowel preparation and insufflation of carbon dioxide gas.<sup>16</sup> The examination occurs during a single breath hold of 10 seconds or less.<sup>17</sup> At the present time the role of this technique is under study.

*Pro: minimally invasive; low radiation exposure*

*Con: high cost procedure; lack of availability; at the present time limited data regarding accuracy; does not permit concomitant biopsy or polyp removal*

#### 7. Fecal DNA Analysis

---

This test detects abnormal DNA in CRC cells shed in the stool. This test shows promise but is not currently available.

*Pro: highly specific (100%); cost disadvantage is counterbalanced by high specificity thereby precluding the need for follow-up colonoscopy which would have been needed by many patients with a false-positive FOBT*

*Con: expensive; poor sensitivity (37%); not currently available*

---

**See: Detection of Colorectal Neoplasms in Asymptomatic Patients – Flow Chart.**

## Rationale

Colorectal cancer (CRC) ranks as the third most common malignancy in Canada and the second most frequent cause of cancer death.<sup>18</sup> The incidence of CRC rises steadily after the age of 50. More than 700 people die each year from CRC in British Columbia.<sup>19</sup>

The majority of colon cancers arise in pre-existing adenomas (the so-called 'adenoma–carcinoma sequence'). Generally adenomas are polypoid lesions of the bowel mucosa. They may be readily identified and removed during endoscopic examination. All adenomas have malignant potential and the risk is proportional to the size; the risk becomes significant with adenomas 1cm or greater, and the risk dramatically increases with adenomas greater than 2 cm in diameter. It has been estimated that the time taken for a small adenoma to develop into a carcinoma is rarely less than three years and in most cases considerably longer. Removal of adenomas has been demonstrated to reduce colon cancer mortality.<sup>2</sup>

Detection of neoplasms is facilitated by history, physical examination, including digital rectal examination (DRE), fecal occult blood testing (FOBT), endoscopy and diagnostic imaging. The current debate among professional organizations centres on the particular type of test to use, the appropriate age to begin testing, and test frequency.<sup>20, 21</sup>

First degree relatives of CRC patients have an increased risk for developing this disease. The risk increases with the number of relatives affected and with younger age at diagnosis. Rarely, families have a CRC syndrome such as familial adenomatous polyposis (FAP) or hereditary nonpolyposis colon cancer (HNPCC). Patients with these syndromes typically present in early adulthood. Patients with FAP develop hundreds of colorectal adenomas; multi-focal cancer is inevitable unless prophylactic therapy is provided. HNPCC patients have fewer adenomas, but the malignant potential is higher than for sporadic adenomas.

Non-genetic factors that may increase the risk of developing CRC include a high animal fat diet, physical inactivity, and obesity.

Two major types of polyps are found in the large bowel: adenomas and hyperplastic polyps. Hyperplastic polyps are considered to have no malignant potential. Adenomas may be rounded polyps usually on a stalk (tubular adenomas), broad based papillary growths (villous adenomas) or coin shaped flat lesions with a central depression (flat adenomas); tubular adenomas are the commonest type of adenoma. Most, but not all colon cancers develop in pre-existing adenomas. The risk of an adenoma becoming malignant is related to its histological type and size. The risk is greatest for villous adenomas, flat adenomas and for adenomas of all types greater than 2 cm in diameter. Generally it takes three to five years for a small adenoma to develop into a malignancy. Recently, some of the molecular abnormalities underlying the polyp–cancer sequence have been discovered. The three to five year interval between growth of a small adenoma and the development of invasive cancer permits cancer prevention by endoscopic removal of this precursor lesion. Colon cancer and polyps can occur in any area of the colon and rectum but 60 per cent are found distal to the splenic flexure.

For patients who test positive for occult blood or whose sigmoidoscopy reveals a neoplastic lesion (carcinoma or adenoma), full colonoscopy is advised. Under exceptional circumstances, when colonoscopy is not readily available or feasible, double-contrast barium enema plus flexible sigmoidoscopy may be used as an alternative.<sup>15</sup>

Colon cancer screening represents an evolving field. A multiplicity of guidelines exist. This guideline represents an amalgamation of various published recommendations.<sup>22</sup>

## References

- <sup>1</sup> Stoffel EM, Syngal S. Colon cancer screening strategies. *Curr Op Gastroenterol* 2002;18:595-601.
- <sup>2</sup> Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, et al. Colorectal Cancer Screening and Surveillance: Clinical Guidelines and Rationale – Update Based on New Evidence. *Gastroenterol* 2003;124:544-60.
- <sup>3</sup> Cruz-Correa M, Giardiello FM. Diagnosis and management of hereditary colon cancer. *Gastroenterol Clin North Am* 2002;31:537-49.
- <sup>4</sup> Raedle J, Trojan J, Brieger A, Weber N, Schäfer D, Plotz G, et al. Bethesda Guidelines: Relation to Microsatellite Instability and *MLH1* Promoter Methylation in Patients with Colorectal Cancer. *Ann Intern Med* 2001;135:566-76.
- <sup>5</sup> Burke W, Petersen G, Lynch P, Botkin J, Daly M, Garber J, et al. Cancer Genetics Studies Consortium. Recommendations for follow-up care of individuals with an inherited predisposition to cancer. I Hereditary nonpolyposis colon cancer. *JAMA* 1997;277:915-9.
- <sup>6</sup> Vasen HF, den Hartog Jager FC, Menko FH, Nagengast FM. Screening for hereditary nonpolyposis colorectal cancer: a study of 22 kindreds in The Netherlands. *Am J Med* 1989;86:278-81.
- <sup>7</sup> Vasen HF, Mecklin JP, Watson P, Utsunomiya J, Bertario L, Lynch P, et al. Surveillance in hereditary nonpolyposis colorectal cancer: an international cooperative study of 165 families. *Dis Colon Rectum* 1993;36:1-4.
- <sup>8</sup> Wolf SH. The best screening test for colorectal cancer- a personal choice. *N Engl J Med* 2000;343:1643.
- <sup>9</sup> Lieberman DA, Weiss DG. One-time screening for colorectal cancer with combined fecal occult-blood testing and examination of the distal colon. *N Engl J Med* 2001;345:555.
- <sup>10</sup> McLeod RS. Screening strategies for colorectal cancer: A systematic review of the evidence. *Can J Gastroenterol* 2001;15:647-60.
- <sup>11</sup> Bond JH. Colorectal cancer update: prevention, screening, treatment and surveillance for high-risk groups. *Med Clin North Am* 2000;85:1163-82.
- <sup>12</sup> Podolsky DK. Going the distance-the case for true colorectal cancer screening. *N Engl J Med* 2000;343:207-8.
- <sup>13</sup> Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med* 2000;344:169-74.
- <sup>14</sup> Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. *N Engl J Med* 2000;343:162-8.
- <sup>15</sup> Ransohoff DF, Lang CA. Screening for colorectal cancer with the fecal occult blood test: a background paper. *Ann Intern Med.* 1997;126:811-22.
- <sup>16</sup> Rubin DT, Dachman AH. Virtual colonoscopy: a novel imaging modality for colorectal cancer. *Curr Oncol Rep* 2001;3:88-93.
- <sup>17</sup> Hara AK, Johnson CD, MacCarty RL, Welch TJ, McCollough CH, Harmsen WS. CT colography: single- versus multi-detector row imaging. *Radiology* 2001;219:461-5.
- <sup>18</sup> National Cancer Institute of Canada: Canadian Cancer Statistics 2001, Toronto, Canada, 2001.
- <sup>19</sup> British Columbia Vital Statistics Agency, Ministry of Health Services. Annual Report: Death-Related Statistics 2000 and 2001.
- <sup>20</sup> Bond JH. Rectal bleeding: is it always an indication for colonoscopy? *Am J Gastroenterol* 2002;97:223-5.
- <sup>21</sup> Mulcahy HE, Patel RS, Postic G, Eloubeidi MA, Vaughan JA, Wallace M, et al. Yield of colonoscopy in patients with nonacute rectal bleeding: a multicenter database study of 1766 patients. *Am J Gastroenterol* 2002;97: 328-33.
- <sup>22</sup> Health Canada. National Committee on Colorectal Cancer Screening: Recommendations for Population-based Colorectal Screening. Ottawa; 2002.

## Sponsors

This guideline was developed by the Guidelines and Protocols Advisory Committee under the auspices of the British Columbia Medical Association, the Medical Services Commission, and the Government of British Columbia.

Funding for this guideline was provided in full or part through the Primary Health Care Transition Fund.

**Effective Date:** March 1, 2004

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

## Contact

Guidelines and Protocols Advisory Committee  
1515 Blanshard Street 2-3  
Victoria BC V8W 3C8

Fax: (250) 952-1417

Phone: (250) 952-1347

E-mail: [hlth.guidelines@gems6.gov.bc.ca](mailto:hlth.guidelines@gems6.gov.bc.ca)

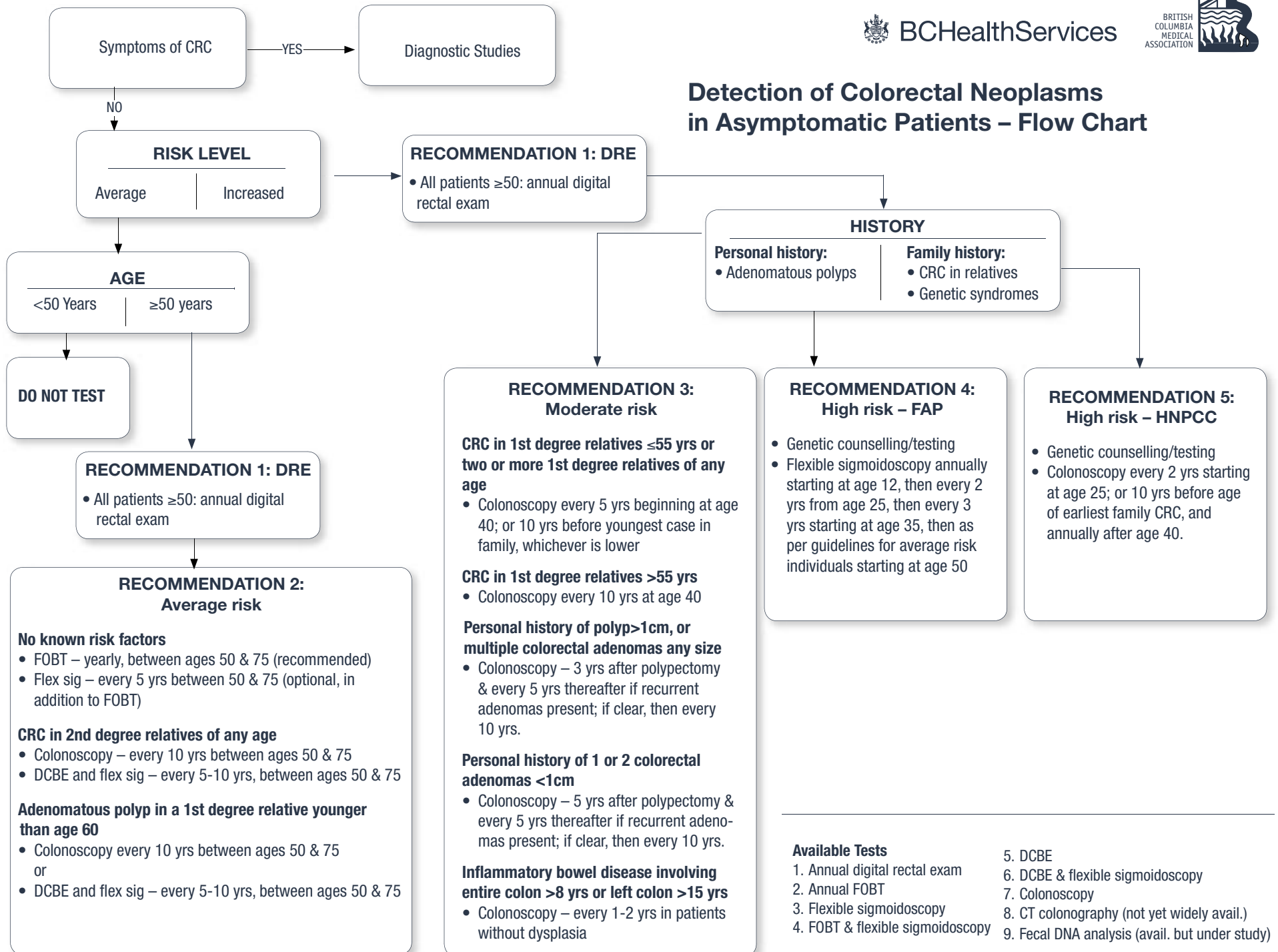
Web site: <http://www.healthservices.gov.bc.ca/msp/protoguides>

The principles of the Guidelines and Protocols Advisory Committee are:

- to encourage appropriate responses to common medical situations
- to recommend actions that are sufficient and efficient, neither excessive nor deficient
- to permit exceptions when justified by clinical circumstances.



## Detection of Colorectal Neoplasms in Asymptomatic Patients – Flow Chart



# Detection of Colorectal Cancer

## A GUIDE FOR PATIENTS

Colorectal cancer (CRC) is the second most common cause of cancer-related death in North America. Both men and women develop CRC and the risk increases with age, particularly after 50 years of age. The average person has about a 1 in 18 lifetime risk of developing CRC. If colorectal cancer is found and treated at an early stage (before symptoms) the cure rate is 80% or better. Early detection and intervention can save lives.

### What is the risk?

Most of the population is considered to be at average risk. You may be at average risk if you:

- do not have any symptoms of CRC,
- do not have a family history of colon cancer, and
- have not had polyps or colon cancer yourself.

You may have an increased risk of CRC if you have symptoms, family history, polyps or if you are 50 years-of-age or older. If so, you should discuss your situation with your doctor.

### What are the symptoms?

CRC is often a “silent” disease with no symptoms. When symptoms occur, they may include blood in the stool or pain in the abdomen. If these symptoms occur, contact your doctor as soon as possible.

### What are polyps?

Polyps are small outgrowths of tissue on the inner lining of the colon. Although not all polyps become cancerous, almost all CRC develops from pre-existing polyps. Most polyps grow slowly and may take ten years or more to develop into a cancer. Adenomatous polyps increase the risk of colorectal cancer, especially if they are large and if there are many of them. Inflammatory and hyperplastic polyps do not increase the risk of colorectal cancer.

### What tests are used to check for polyps and colorectal cancer?

There are a number of tests that can be used to check for polyps or CRC. Tests vary in their simplicity and accuracy. All tests, except fecal occult blood tests, require the bowel to be specially cleansed.

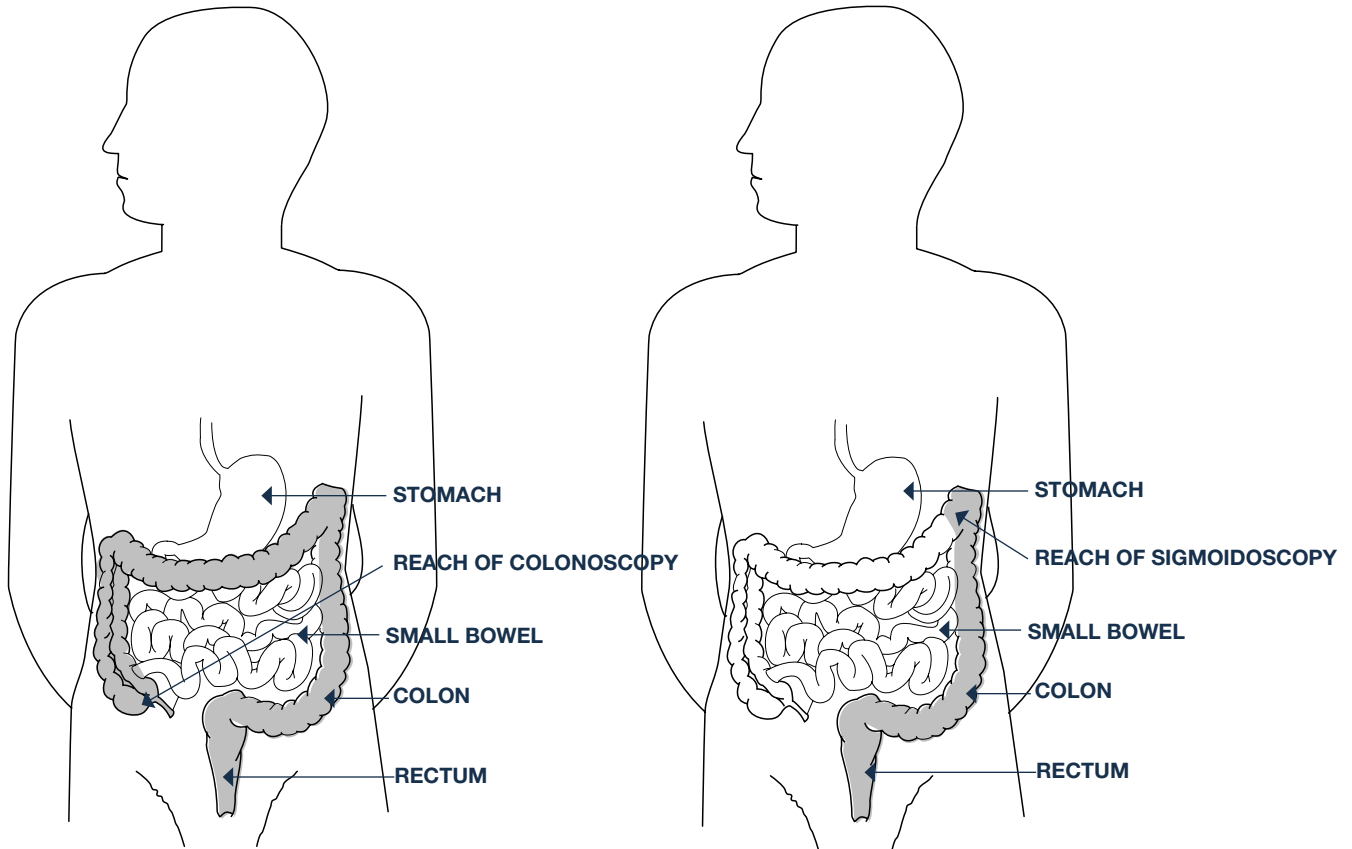
Fecal Occult Blood Test: Polyps and CRC can bleed intermittently, so three small stool samples are tested for blood that may be hidden in the stool.

Barium Enema X-Ray Examination: Polyps and CRC change the appearance of the bowel. This test can detect polyps or CRC but does not allow for biopsy or removal.

Sigmoidoscopy: A flexible lighted instrument is inserted through the anus to examine the rectum and the lower portion of the colon. Polyps or CRC can be biopsied or may be removed, but abnormalities in the upper portion of the colon cannot be seen or treated.

Colonoscopy: A flexible lighted instrument is inserted through the anus to examine the entire colon. Polyps or CRC can be biopsied or may be removed. Most patients require sedation for this procedure. Colonoscopy is considered the most comprehensive and accurate investigation.

“Virtual Colonoscopy” (CT Colonography): A tube is inserted through the anus and air is used to inflate the colon. Specialized x-rays are taken to show irregularities in the bowel. Polyps and CRC cannot be biopsied or removed, but accuracy is thought to be superior to barium enema. Availability is currently limited.



### **Which test should I have?**

Depending on your circumstances, you may not require any testing at all. You should consider what each test offers, the risk involved and whether or not you have experienced symptoms of CRC. These tests vary with respect to their advantages, disadvantages, limitations, and availability. You should discuss your options with your doctor.

### **What can I do to reduce my risk of colon cancer?**

Although solid proof is lacking, there may be some lifestyle and dietary changes that could reduce your risk of CRC.

### **When should I get tested for colorectal cancer?**

Most people should begin testing at age 50. If you are at higher risk (see above) discuss this with your doctor.

---

For specific details on the detection of colorectal cancer, please refer to the guideline:  
*Detection of Colorectal Neoplasms in Asymptomatic Patients*  
web site: <http://www.healthservices.gov.bc.ca/msp/protoguides/index.html>