Guidelines for the Investigation of Patients with Symptoms Suggestive of Colorectal Cancer
Guidelines for Investigation of Symptoms Suggestive of CRC


Adapted with permission from: Del Giudice L, Vella E, Hey A, Harris W, Simunovic M, Levitt C, et al. Referral of patients with suspected colorectal cancer by family physicians and other primary care providers. Toronto (ON): Cancer Care Ontario; 2011 Apr 24. Program in Evidence-based Care Evidence-Based Series No.: 24-1.

Approved by Diagnosis and Referral of Patients Clinically Suspicious For Colorectal Cancer Sub-Committee Working Group: January 2016
Endorsed by CCNS Clinical Standards Oversight Committee: March, 2016
Endorsed by CCNS Chief Operating Officer: March, 2016
Approved by NSHA VP Integrated Health Services, Program of Care 1 and Senior Leadership Team: June, 2016

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Guidelines for the Investigation of Patients with Symptoms Suggestive of Colorectal Cancer

Preamble
Colorectal cancer (CRC) is a significant health issue in Nova Scotia (NS). Nova Scotians are at higher risk of being diagnosed with CRC than Canadians overall. In 2015, it is estimated that 920 people will be diagnosed with CRC in NS which represents 14% of all cancers. In 2015, the CRC age-standardized incidence rate (ASIR) for NS was 71 cases per 100,000 for men and 49 cases per 100,000 for women compared to 59.5 cases per 100,000 for men and 39.7 cases per 100,000 for women in Canada. CRC is the 2nd most common cancer in both men and women in NS, and the 2nd most common cause of cancer-related deaths in men and the 3rd in women. Men in NS are at higher risk for developing CRC than women (ASIR=71 per 100,000 compared to 49 per 100,000 respectively in 2015) (2).

Guideline Development
Organized CRC screening began in NS in 2009 through the Colon Cancer Prevention Program (CCPP). As the screening program was implemented, concern was expressed that there was no corresponding systematic approach for timely diagnosis of symptomatic patients.

In 2012, Cancer Care Nova Scotia (CCNS) established a sub-committee under the auspices of the Rectal Cancer Standards Working Group to address this concern. The sub-committee was asked to develop guidelines based on best available evidence that fit the clinical and economic context of NS, and in consideration of issues identified by patients, survivors and family members.

The sub-committee decided to use the 2011 Cancer Care Ontario (CCO) guideline Referral Of Patients With Suspected Colorectal Cancer By Family Physicians And Other Primary Care Providers. The essence of the CCO recommendations for work-up and investigation and target timelines remain. Based on input from the CCNS Public Advisors, recommendations were added around communication expectations between patients and providers and between providers (see Section 2 for more specifics on the development process).

TARGET POPULATION
The target population for this guideline is adult patients presenting in primary care settings or emergency departments who have signs and symptoms suggestive of colorectal cancer.

This guideline does not provide recommendations for patients who present with symptoms and signs of hemodynamic instability, acute gastrointestinal hemorrhage, acute intestinal obstruction, or severe abdominal pain. These patients should be immediately referred to emergency department for assessment and treatment.

This guideline does not address colorectal cancer screening for asymptomatic patients. Please refer to the Cancer Care Nova Scotia Colon Cancer Prevention Program Colon Cancer Screening Guidelines available at www.cancercare.ns.ca (3).

Primary Care Providers (PCPs) and endoscopists should not use the screening guidelines to triage symptomatic patients.

INTENDED USERS
This document is intended for family physicians, nurse practitioners, registered nurses, emergency department physicians, general internists, general surgeons, gastroenterologists and radiologists. A companion document will be provided for the public.

This document is also intended for policymakers to help ensure that resources are in place so that target wait times can be achieved.

For the purposes of this document, we have referred to:

- Family physicians, and nurse practitioners as “Primary Care Providers” (PCPs)
- Surgeons, gastroenterologists and other specialists competent in therapeutic colonoscopy as “endoscopists”.

### Purpose

The purpose of this guideline is twofold:

1. To define expectations for PCPs, endoscopists, and radiologists regarding the appropriate work up of patients who have symptoms suggestive of CRC.
2. To outline the communication expectations between PCPs, endoscopists, radiologists and other health care providers and patients. Good communication and coordination between PCPs and specialists are essential to a timely and accurate diagnosis.

   The patient must be kept informed at every relevant step.

The purpose will be achieved:

- by educating PCPs to recognize the signs and symptoms of CRC,
- by referring patients with such symptoms for appropriate investigations,
- by educating PCPs, endoscopists and radiologists about the importance of communication between health care providers and between healthcare providers and patients,
- by ensuring that patients are kept informed at every relevant step of diagnosis,
- by working with endoscopists to improve triaging of symptomatic patients.
Guidelines for Investigation of Symptoms Suggestive of CRC

Table of Contents

Introduction: Preamble

Algorithm: Work Up and Referral for Patients with Signs and Symptoms Suggestive of Colorectal Cancer

Section 1: Recommendations

Appendix A: Referral Form

Appendix B: Risk Factors for Colorectal Cancer

Appendix C: Recommendations to Facilitate the Implementation of this Guideline

Section 2: Key Evidence

Appendix D: Guideline Development Process

Appendix E: Literature Search: Does a delay in the time to consultation affect patient outcome?

Appendix F: Diagnosis and Referral of Patients Suspicious for Colorectal Cancer Sub-Committee
Guidelines for Investigation of Symptoms Suggestive of CRC

Work Up and Referral for Patients with Signs and Symptoms Suggestive of Colorectal Cancer (CRC)

Does the patient have one or more of the following signs/symptoms?

- Rectal Bleeding/Clots
- Persistent change in bowel habit
- Anemia
- Recent onset recurring abdominal pain
- Weight loss
- Anal symptoms

If Yes, perform a focused history and physical exam

**FOCUSED HISTORY:**
- Age and gender
- Rectal bleeding, if yes: colour (dark versus bright red), clots?
- Persistent change in bowel habit, if yes: increased stool, looseness, constipation and/or urgency; feel incomplete emptying; stool incontinence
- Weight loss
- Nature/duration/characterization of abdominal discomfort
- Anal symptoms (lump, pruritus, pain)
- Symptoms of anemia (e.g. fatigue, weakness)
  - Iron Deficiency Anemia – explore possible causes of blood loss
- Personal history of colorectal polyps, Inflammatory Bowel Disease or CRC
- Family history of 1st degree relative with CRC or polyps, Lynch Syndrome/ Familial Adenomatous Polyposis (FAP)

At least one of:
- Suspicious palpable rectal or abdominal mass
- Abdominal imaging suggestive of CRC

**URGENT REFERRAL**

to surgical endoscopist promptly.

Ideally, a consultation and endoscopy should be completed within 4 weeks of referral.

**FOCUSED PHYSICAL EXAM/TEST:**
- Digital rectal exam (DRE)
- Abdominal exam (If palpable mass, order abdominal/pelvic imaging)
- Look for signs of anemia
- Weight
- Complete Blood Count (CBC) and Ferritin

**Patients of any age with:**
- unexplained dark red rectal bleeding/clots
- unexplained bright red rectal bleeding
- unexplained iron-deficiency anemia
- change in bowel habits

When patient has unexplained signs/symptoms that do not meet urgent/semi-urgent criteria and PCP has a high level of CRC suspicion e.g.: unexplained weight loss or abdominal pain, particularly with 1st degree family relative with colorectal cancer.

**SEMI-URGENT REFERRAL**

to an endoscopist promptly.

Ideally, a consultation and endoscopy should be completed within 8 weeks of referral.

Refer to endoscopist

**Beware of circumstances that may lead to delayed diagnosis**

Rectal bleeding, anal pain and pruritus are common symptoms that are usually due to benign conditions such as hemorrhoids and fissures. However, these symptoms also occur with colorectal cancer. All patients with anal symptoms should undergo a DRE and endoscopy if there is a history of bleeding.

Anemia in pre-menopausal women is often due to menstrual bleeding. However the anemia may be due to CRC and PCPs should always consider this in the differential when managing these patients, particularly when treatment of suspected underlying disorder does not resolve the issue.
SECTION 1: RECOMMENDATIONS

A. Work Up and Investigation

<table>
<thead>
<tr>
<th>Symptoms and Signs of CRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A thorough history and physical exam by the PCP are key to a timely diagnosis.</td>
</tr>
<tr>
<td>A focused history and physical examination should be performed if patients present with <strong>ONE OR MORE</strong> of the following symptoms or signs:</td>
</tr>
<tr>
<td>• Anemia (especially iron-deficiency anemia)</td>
</tr>
<tr>
<td>• Rectal bleeding/clots</td>
</tr>
<tr>
<td>• Persistent change in bowel habits</td>
</tr>
<tr>
<td>• Weight loss</td>
</tr>
<tr>
<td>• Recent onset of recurring abdominal pain</td>
</tr>
<tr>
<td>• Anal symptoms</td>
</tr>
<tr>
<td>(CCO recommendations)</td>
</tr>
<tr>
<td>The <strong>focused history</strong> should determine the following details:</td>
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<tr>
<td>• Age (see note) and gender (see note)</td>
</tr>
<tr>
<td>• Rectal bleeding, and if yes,</td>
</tr>
<tr>
<td>- Colour (dark versus bright red)</td>
</tr>
<tr>
<td>- History of clots</td>
</tr>
<tr>
<td>- Location of blood in relation to stool (mixed in with stool versus separate from stool, on the toilet paper)</td>
</tr>
<tr>
<td>• Persistent change in bowel habit over recent weeks/months, and if yes,</td>
</tr>
<tr>
<td>- Increased loose or watery stools</td>
</tr>
<tr>
<td>- Increased constipation or difficulty passing stools</td>
</tr>
<tr>
<td>- Feeling of incomplete emptying</td>
</tr>
<tr>
<td>- Increased urgency</td>
</tr>
<tr>
<td>- Incontinence of stools or soiling</td>
</tr>
<tr>
<td>• Weight loss</td>
</tr>
<tr>
<td>• Nature, duration and characterization of abdominal discomfort (e.g. pain, tenderness, bloating)</td>
</tr>
<tr>
<td>• Anal symptoms such as prolapsing tissue, pruritus, pain</td>
</tr>
<tr>
<td>• Symptoms of anemia (e.g., fatigue, weakness)</td>
</tr>
<tr>
<td>- If unexplained iron-deficiency anemia present, explore possible causes of blood loss or blood dyscrasia (4,5).</td>
</tr>
<tr>
<td>• Personal history of CRC, polyps or inflammatory bowel disease (IBD)</td>
</tr>
<tr>
<td>• A family history of CRC (number of relatives and what age diagnosed) or Lynch Syndrome/Familial Adenomatous Polyposis (FAP)</td>
</tr>
<tr>
<td>• A history of polyps in first degree relatives and the age of onset</td>
</tr>
<tr>
<td>(CCO recommendations)</td>
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</tbody>
</table>
To supplement the history, a **focused physical examination should be performed and investigations should be considered including**:

- Digital rectal examination (DRE)
- Abdominal examination. If palpable mass detected, order abdominal/pelvic imaging as clinically indicated.
- Look for signs of anemia
- Weight (and comparison to previous weights if possible)
- Complete blood count (CBC), and ferritin

(CCO recommendations)

There is **no role** for fecal occult blood testing (FOBT) in the work-up of a patient who has symptoms suggestive of CRC. (CCNS sub-committee consensus)

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**Beware of circumstances that may lead to delayed diagnosis**

- Rectal bleeding, perianal pain and pruritis are common symptoms that are usually due to benign conditions such as hemorrhoids and fissures. However, these symptoms also occur with CRC and attributing these symptoms to benign diseases without appropriately investigating them may lead to a delay in diagnosis. All patients with perianal symptoms should undergo a digital rectal examination and endoscopy if there is a history of bleeding (as per the guidelines below).

- Anemia in pre-menopausal women is often due to menstrual bleeding. However, the anemia could be due to CRC and PCPs should always consider this in the differential when managing these patients, particularly when treatment of underlying disorder does not correct the issue. (CCNS sub-committee consensus)

- PCPs should be conscious of those groups where delays in presentation are often observed: women, single patients, younger patients, visible minorities, and patients with co-morbidities, decreased social support, lower levels of education, or a rural residence. Special efforts should be made to advocate for them.

(CCO recommendation)

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**B. Referral**

**Referral for Endoscopy Assessment**

Patients who meet the criteria below should be referred for assessment by an endoscopist.

Good communication between the PCP and the endoscopist is essential to a timely and appropriate referral process. PCPs should never to hesitate to phone an endoscopist if they need to discuss a case, if there are specific concerns or if they are uncertain about how to proceed.

To facilitate triage, timely consultations and appropriate use of resources, referrals will be made using the standardized referral form (**Appendix A**). In keeping with College of Physicians and Surgeons of Nova Scotia (CPSNS) Guidelines for Physicians Regarding Referral and Consultation, the endoscopist will acknowledge receipt of the referral and provide the anticipated wait time or appointment date within
14 days to the referring PCP.

When wait times exceed the recommended benchmarks, the PCPs should advise patients of the potential adverse implications and discuss alternatives, including the option of a referral elsewhere.

Where wait times for endoscopy are excessive, CT colonography may be an acceptable alternative. See below for referral for CT Colonography.

Patients of advanced age or with significant co-morbidities should be referred for assessment and consideration of alternative investigations (e.g. CT colonography). There is no role for Double Contrast Barium Enema (DCBE) in the investigation of suspected CRC.

(CCNS sub-committee consensus)

<table>
<thead>
<tr>
<th>URGENT REFERRALS</th>
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<tbody>
<tr>
<td><strong>The patient has at least one</strong> of the following:</td>
<td></td>
</tr>
<tr>
<td>• Palpable rectal or abdominal mass suspicious for CRC</td>
<td></td>
</tr>
<tr>
<td>• Abnormal abdominal imaging result suspicious for CRC</td>
<td></td>
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<tr>
<td>(CCO recommendation)</td>
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</tr>
<tr>
<td><strong>PCP</strong></td>
<td>Will send a referral to a surgical endoscopist <strong>promptly</strong> (i.e. within 1-2 working days of decision to refer) using the standardized referral form (<strong>Appendix A</strong>).</td>
</tr>
<tr>
<td><strong>Endoscopist</strong></td>
<td>Ideally, patients to be seen for consultation with a definitive diagnostic workup completed <strong>within 4 weeks</strong> of referral. (CCO recommendation)</td>
</tr>
<tr>
<td></td>
<td>If the endoscopist is unable to see the patient within the benchmark time of 4 weeks, the endoscopist should inform the PCP so that referral to another endoscopist may be made. (CCNS sub-committee consensus)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>SEMI-URGENT REFERRAL</th>
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<tbody>
<tr>
<td><strong>Patients of any age with</strong> unexplained dark red rectal bleeding, clots or unexplained iron-deficiency anemia should be referred for colonoscopy.</td>
<td></td>
</tr>
<tr>
<td><strong>Patients of any age with</strong> persistent change in bowel habits should be referred for colonoscopy.</td>
<td></td>
</tr>
<tr>
<td><strong>Patients over 50 with bright red bleeding</strong> should be referred for colonoscopy.</td>
<td></td>
</tr>
<tr>
<td><strong>Patients under 50 with bright red bleeding</strong> should be referred for flexible endoscopy. If bright red bleeding is the only symptom and there is no family history of CRC then flexible sigmoidoscopy is appropriate. If there is a family history of CRC then colonoscopy should be considered.</td>
<td></td>
</tr>
<tr>
<td>(CCNS sub-committee consensus)</td>
<td></td>
</tr>
<tr>
<td><strong>PCP</strong></td>
<td>Will send a referral to an endoscopist <strong>promptly</strong> (i.e. within 1-2 working days of decision to refer) using the standardized referral form (<strong>Appendix A</strong>).</td>
</tr>
<tr>
<td><strong>Endoscopist</strong></td>
<td>Ideally, definitive <strong>diagnostic work up</strong> to be <strong>completed</strong> within 8 weeks of referral. (CCO recommendation)</td>
</tr>
</tbody>
</table>

Guidelines for Investigation of Symptoms Suggestive of CRC
Referral for CT Colonography

Referrals for Computed Tomographic (CT) Colonography may be considered under the following circumstances:

- Contraindication for optical colonoscopy
- Incomplete optical colonoscopy
- While not a preferred practice, in situations where wait times for optical colonoscopy are considered excessive.

Note:

CT Colonography may miss low rectal cancer and does not obviate the need for DRE.

(CCNS sub-committee consensus)

When referring for CT Colonography for suspected CRC, all of the principles described above for optical colonoscopy apply including:

- Urgent and semi-urgent timelines

The principles of communication and timelines apply equally to the PCP and the radiologist. The PCP (or ordering physician, if not the PCP) should include a complete description of the symptoms and relative urgency on the Nova Scotia Health Authority (NSHA) Diagnostic Imaging requisition. In the case of incomplete optical colonoscopy, the endoscopist should indicate the extent to which they were successful.

(CCNS sub-committee consensus)

CT Colonography Results

If the CT colonography results are consistent with CRC, the patient should be referred to a surgeon. The PCP will inform the patient of the positive results.

(CCNS sub-committee consensus)

Referral for OTHER UNEXPLAINED SIGNS OR SYMPTOMS

High level of suspicion of CRC

PCPs should have a high suspicion of CRC based on a combination of signs, symptoms and risk factors. Unexplained weight loss, fatigue and abdominal pain should raise concern about the possibility of CRC, particularly in a patient with a first degree relative who has had CRC.

(CCNS sub-committee consensus)

PCP

PCPs should communicate their reasons for concern through a referral letter and/or the standardized referral form (Appendix A).
C. Keeping the Patient Informed

Investigation for a possible cancer is a stressful period for patients. It is important that all involved health care providers keep the patient informed throughout this period.

<table>
<thead>
<tr>
<th>At the Time of Initial Presentation and Investigation</th>
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<tbody>
<tr>
<td>The PCP will explain the purpose of the investigations and the need to rule out a potential cancer diagnosis.</td>
</tr>
<tr>
<td>(CCNS sub-committee consensus)</td>
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<table>
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<tr>
<th>At the Time of Referral for Specialist Assessment</th>
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<tbody>
<tr>
<td>Once the decision has been made to refer for specialist assessment, the PCP will inform the patient of the possibility of a cancer diagnosis, followed by a description of the plan, the importance of keeping the appointment and the approximate wait time based on the benchmark wait times. The patient should be instructed to inform the PCP if they have not received an appointment within a reasonable period of time.</td>
</tr>
<tr>
<td>(CCNS sub-committee consensus)</td>
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</tbody>
</table>

<table>
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<tr>
<th>At the Time of Endoscopy</th>
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<tbody>
<tr>
<td>• The endoscopist will inform the patient of the results of the scope.</td>
</tr>
<tr>
<td>• If cancer is evident at the time of endoscopy, the endoscopist will clearly communicate it to the patient. ¹</td>
</tr>
<tr>
<td>• If the diagnosis is uncertain (e.g. requiring pathological confirmation), the patient will be informed of this, the possibility of a cancer diagnosis, and the next steps, including the wait time for results.</td>
</tr>
<tr>
<td>• If cancer has been identified at the time of endoscopy, the endoscopist will inform the patient of the potential for any complications related to the tumor (e.g. obstruction) or risks and provide instructions on how best to manage or prevent them.</td>
</tr>
<tr>
<td>(CCNS sub-committee consensus)</td>
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</tbody>
</table>

¹ In the external review of the draft CCNS Rectal Cancer Treatment Standards rectal cancer survivors stressed the need for clear language regarding the diagnosis (i.e. “you have cancer” or “I think you have cancer but we need more information”) (Cancer Care Nova Scotia. Patient review of draft rectal standards: Survey & focus group results, 2013).
At the Time of Pathological Confirmation of Cancer Diagnosis

- It is the responsibility of the physician making the diagnosis to clearly communicate the diagnosis to the patient. Patients will be informed of their diagnosis at the earliest appropriate time, ideally in a supportive environment.

- Patients will be given written information including the diagnosis, expected immediate next steps and timelines as well as the Blue Ribbon (colon or rectal cancer) patient information kit.

(CCNS sub-committee consensus)

D. Organizing Care

Role of the Diagnosing Physician

When a diagnosis of colon or rectal cancer is confirmed the diagnosing physician will immediately:

- Inform the patient’s PCP of the diagnosis
- Refer the patient to the Cancer Patient Navigator*
- Refer to surgeon (if necessary)
- Initiate appropriate staging investigations**

(CCNS sub-committee consensus)

* NB: There is no Cancer Patient Navigator in the NSHA Central Zone.
**For Rectal Cancer – refer to the Rectal Cancer Treatment Standards

E. Improving Awareness about Colorectal Cancer

Role of PCPs in Improving Awareness about Colorectal Cancer

- PCPs should encourage patients who are eligible for Fecal Immunochemical Test (FIT) screening through the CCPP to participate. NS patients have indicated that one reason for non-participation in the CCPP is that “My doctor didn’t tell me to do it” (6). While discussing CRC screening with patients, PCPs should ask about family history for CRC and the signs and symptoms predictive of CRC.

- Recent longitudinal research suggests that diagnostic delays in primary care are associated with mortality and morbidity in CRC patients (7, 8, 9).

- CRC is linked to several modifiable risk factors including obesity, physical inactivity, consumption of red and processed meat and smoking (10).

- Primary prevention efforts should be improved to reduce the impact of risk factors, such as tobacco use or obesity (10).

(CCNS sub-committee consensus)
A Note about Target Wait Times

One of the major concerns for health care providers, patients and system leaders was timely access to colonoscopy for symptomatic patients. The NS CCPP has a target wait time between a positive fecal immunochemical test (FIT) and colonoscopy of 8 weeks. There is no target endoscopy wait time for symptomatic patients.

The sub-committee had considerable discussion regarding endoscopy wait times. Everyone agreed that timely access is critical but recognized that any recommendations had to be realistic for NS. The 8 week target wait time for the CCPP was not being achieved in at least one of the NSHA Zones. There was concern about setting targets that were not achievable.

While CT colonography is suggested as an alternative to excessive wait times, it should be noted that wait times for CT colonography are also increasing and there are concerns that there may not be timely access to this modality as well. The same timeline targets apply to CT colonography.

In the end, the sub-committee retained the CCO target timelines for symptomatic patients as these are also in keeping with on the Canadian Association of Gastroenterology published target timelines (11), those set by other jurisdictions, and the CCPP 8 week target for a positive FIT.

The sub-committee recognizes that these timelines may not be currently achievable but felt it important that some kind of benchmark be set and that collectively as a system we should work towards achieving them.
Appendix A: Referral Form

**Referral for Suspected Colorectal Cancer**

**REFER TO:**

<table>
<thead>
<tr>
<th>Fax:</th>
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</table>

**Patient Name**

**Address**

<table>
<thead>
<tr>
<th>Postal Code</th>
<th>Preferred Phone Number</th>
<th>Alternate Phone Number</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date of Birth</th>
<th>Health Card Number</th>
</tr>
</thead>
</table>

- Please include any relevant lab, DI or endoscopy results and/or inform if the patient has any relevant significant medical problems.

- **Urgent** (ideally endoscopy to be completed within 4 weeks of referral)
  - □ palpable rectal mass
  - □ abnormal imaging (please attach)

- **Semi-Urgent** (ideally endoscopy to be completed within 8 weeks of referral)
  - □ Iron Deficiency Anemia (CBC and Ferritin required with results attached to referral)
  - □ Rectal bleeding with dark blood/clots
  - □ Change in Bowel habits
  - □ Bright red rectal bleeding only

**ASSOCIATED SYMPTOMS**

- □ Blood mixed in the stool
- □ Abdominal pain
- □ Unexplained weight loss
- □ Anal symptoms
- □ Mucous or tissue discharge
- □ Other Specify ____________________________________________

**DRE findings**

- □ abnormal
- □ normal
- □ not done

**Family history** of Colorectal Cancer (first degree relative(s) and age(s))

- Yes □ ___________________________

**Patient is on anticoagulants**

- □ (specify) _______________

I have discussed the possibility of colorectal cancer with the patient

- □ Yes
- □ No

**Primary Care Provider:** (please print)

<table>
<thead>
<tr>
<th>Phone</th>
<th>Fax</th>
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</table>

**Referring Physician (if not PCP)**

<table>
<thead>
<tr>
<th>Phone</th>
<th>Fax</th>
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</table>
Appendix B: Risk Factors for Colorectal Cancer

<table>
<thead>
<tr>
<th>Factors for consideration that are associated with increased risk (12,13,14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In making their decisions as to appropriate action, PCPs should consider these factors that are known to be associated with increased risk for CRC:</td>
</tr>
<tr>
<td>A personal history of CRC or polyps</td>
</tr>
<tr>
<td>A personal history of inflammatory bowel disease</td>
</tr>
<tr>
<td>A family history of CRC in a first-degree relative</td>
</tr>
<tr>
<td>African descent</td>
</tr>
<tr>
<td>Male (see note)</td>
</tr>
<tr>
<td>High risk alcohol consumption (see note)</td>
</tr>
<tr>
<td>Overweight (see note)</td>
</tr>
<tr>
<td>Smoker (see note)</td>
</tr>
<tr>
<td>Dietary factors (i.e. low fruit/vegetable consumption, low fibre, increased red meat and processed meats)</td>
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<tr>
<td>Low physical activity</td>
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</tbody>
</table>

**Notes:**

**Age:** While CRC most frequently occurs after age 50, CRC is the third-most common cancer diagnosed in those aged 30-49 (10). Recent literature suggests the incidence of CRC in younger adults, particularly in the 35-49 age group, will increase in the next 15 years (15).

**Gender:** CRC age-specific incidence and mortality rates are generally higher in males than in females; the gap is greatest in the 55-74 age range, where rates for males are about 60% higher (for both incidence and mortality) than in females (16).

**High Risk alcohol consumption:** More than 2 standard drinks/day for women or 3 standard drinks/day for men (14).

**Overweight:** A meta-analysis conducted by the World Cancer Research Fund on 86 cohort cases found an increased risk of CRC of 15% for each 5 kg/m², assuming a linear relationship (14).

**Smoking History:** The US Surgeon General has determined that the evidence is sufficient to infer a causal relationship between smoking and colorectal adenomatous polyps and CRC (17).

(CCNS sub-committee consensus)
Appendix C: Recommendations to Facilitate the Implementation of this Guideline

### Ways to Facilitate the Implementation of this Guideline

The sub-committee has identified the following approaches to facilitate the implementation of this guideline:

- **CCNS** will use various knowledge translation strategies to communicate the recommendations and expectations within this guideline:
  - To PCPs: information regarding the signs and symptoms of CRC, how to obtain a proper detailed history, physical examination, appropriate investigations, and referral of patients presenting with suspicious signs and symptoms.
  - To endoscopists: information regarding the need for prompt triaging and good communication with patients at the time of diagnosis.
  - For the public: sustainable public education about the signs and symptoms of CRC, the importance of early detection and management, as well as common fears and concerns that may delay referral, should be developed and implemented. (CCO recommendations)

- With the establishment of an NSHA provincial endoscopy program, the sub-committee is optimistic that it will be able to address organizational and system issues that have led to delayed access to endoscopy. The sub-committee recommends that the NSHA endoscopy program consider the following:
  - Endoscopists should develop triage practices to avoid delays in the diagnosis of CRC in patients with suspicious signs and/or symptoms.
  - Patients in areas where there are long waits for colonoscopy should be informed of the possibility of being referred to other centres where the wait times may be shorter.
  - The development of centralized wait lists for endoscopy services to monitor wait times and direct referrals to centres with the shortest wait times.
  - Provide appropriate training for colonoscopy and management of colonic polyps.
  - Colonoscopy quality assurance initiatives.

(C CNS sub-committee consensus)

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The sub-committee accepted the review and summary of the evidence as written by the Cancer Care Ontario (CCO) guideline authors (1) except for the points that related to the:

- role of FOBT in the work up of symptomatic patients
- impact of diagnostic delay on overall outcome

Reasons for these variations are primarily due to Nova Scotia-specific policies and new data related to diagnostic delay.

Additionally, based on patient feedback, emphasis has been added regarding the importance of communication between primary and secondary care and in communicating the diagnosis to the patient.

**Role of FOBT in the Work Up of Symptomatic Patients**

The CCNS sub-committee does not recommend use of FOBT in investigating patients who are symptomatic for colorectal cancer (CRC). In Nova Scotia (NS), the Colon Cancer Prevention Program (CCPP) uses the fecal immunochemical test (FIT) to screen those at average risk (50-74) on a biannual schedule. The FIT is only available through the CCPP (2). The only role for guaiac FOBT in NS is for screening asymptomatic individuals who fall outside the target population for the CCPP (50-75) who wish to be screened for CRC.

**Impact of Diagnostic Delay**

While the CCO guideline panel concluded that the evidence suggests that delay in referral does not have an impact on patient survival (1), the CCNS sub-committee felt that there were methodological flaws in the cited papers and disagreed with the CCO conclusion. An updated tailored literature search was conducted (see Appendix E for details).

The literature on the impact of diagnostic delay on survival has been controversial. Early studies reached the counterintuitive conclusion that delays in diagnosis and treatment do not impact survival, or that longer delays are associated with improved survival (3,4). These results led many to conclude that there is no reason to intervene quickly with those suspected of or diagnosed with CRC (5,6,7); rather, prompt treatment is considered important mainly as means to reduce patient anxiety (1). These studies were significantly flawed, however as the majority used design or statistical controls for tumour stage. Because it is well known that tumour stage is the single greatest contributor to mortality, research methods that remove its influence leave very little variance to be explained. These studies were also limited by their reliance on retrospective designs, and by extremely narrow definitions of delay (e.g. delays in secondary care, not primary care).

Prospective, population-based longitudinal research provides the most definitive approach to understanding the impact of diagnostic delay on outcome. Several recent longitudinal studies have demonstrated that diagnostic delay greater than 60 days is associated with an exponential increase in mortality in CRC patients (8,9). Torring and her colleagues have demonstrated a U-shaped relationship between delay and death: as the interval between first presentation to a family doctor and ultimate cancer diagnosis increased, mortality decreased in the first five weeks, then increased significantly (8,10). Similar functions were found for melanoma, lung, and prostate cancer (10). These findings
replicated a prospective study done in Denmark, which found that having the risk of late-stage cancer doubled if the interval between symptom onset and treatment was greater than 60 days (9,11,12). This risk of delay was even greater for rectal cancer relative to colon cancer, a finding that is consistent with the known greater metastatic potential of rectal cancer (13,14). In contrast, a prospective study in Holland (15) did not find an association between delay and survival; however, this study was limited by using very restricted definition of delay and by controlling for stage-relevant symptoms. Taken together, the results of recent methodologically superior studies suggest that mortality increases as diagnostic delay increases. These findings reflect the known pathogenesis of CRC, and underscore the importance of prompt detection and treatment for the survival of CRC patients (16).

Neal et al. (17) published a systematic review in 2015 which supports these conclusions. They conducted the systematic review to determine whether there is an association for symptomatic presentation between time to diagnosis, treatment and clinical outcomes across all cancers. For CRC, they found that although many studies reported no associations, more studies reported a positive (evidence of shorter intervals being associated with more favorable outcomes) rather than a negative (evidence of shorter intervals being associated with less favorable outcomes) association.

Communication between Primary and Secondary Care

The sub-committee believes that good communication between the PCP and the endoscopist is essential to a timely and appropriate referral process. The endoscopist members of the sub-committee indicated that it is difficult to triage appropriately without full information. Therefore, the sub-committee developed a standardized referral form to facilitate referral. The intent of the referral form is two-fold: to provide endoscopists with the information needed for triage and to prompt PCPs about appropriate (and by exclusion, inappropriate) investigations. These recommendations are supported by the literature.

In a review of the challenges in the interface of primary and secondary oncology care, Nekhlyudov and Latosinsky (18) noted that the PCP must communicate a clear rationale for the referral and the specific questions for the specialist. Two studies (9,16) found that PCP indication of suspicion of CRC or urgency in the referral letter reduced diagnostic delay. A Cochrane review by Akbari et al. (20) of the effectiveness and efficiency of interventions to improve outpatient referral appropriateness concluded that a generally effective strategy was to disseminate guidelines with standardized referral forms. Education from specialists about referral was also generally effective.

Akbari concluded that to be effective, dissemination and implementation strategies for referral guidelines also requires secondary care providers to make appropriate changes in the content and organization of care to optimize the efficiency of the referral system (20).

Communication of the Diagnosis to the Patient

As part of the external review of the draft Rectal Cancer Treatment Standards, CCNS solicited the input of rectal cancer survivors and family members. Survivors stressed the need for clear language regarding the diagnosis (i.e. “You have cancer.” or “I think you have cancer but we need more information before we know for sure.”) and to avoid the less-specific terms such as “tumour” or “mass” (21).

Patients want to know their diagnosis as soon as possible but they also want the diagnosis provided in a sensitive manner (e.g. not over the phone when they are alone) (21).
They also want to know how advanced (i.e. what stage) their cancer is and they want information about where they are in the course of their treatment and what comes next (21). This was reinforced by a study conducted by CCO into the needs of CRC patients during the pre-diagnosis phase (22). They found that the needs most identified were informational (31.6%) and emotional (20.3%).

As a result of this feedback, CCNS established a multidisciplinary working group including CRC survivors which developed a patient education package, the “Blue Ribbon Kit”, for newly-diagnosed CRC patients. These have been provided to endoscopists and cancer patient navigators across the province with the intention that the kit will be provided to patients at the time of diagnosis. The resource is also available online on the CCNS website along with an introductory video featuring the survivors who helped develop the package.

From this point forward, any changes from the CCO original have been italicized. Reasons for varying from the CCO original include new data, providing greater clarity or Nova Scotia-specific context.

Clinical Presentation

The [Cancer Care Ontario (CCO)] Colorectal Cancer Referral Working Group believe that the signs and symptoms listed under clinical presentation should alert FPs and other PCPs about the suspicion of CRC. The presenting signs or symptoms for which urgent or semi-urgent referral was recommended met one of two criteria: a Positive Predictive Value (PPV) of at least 5% (i.e., the probability that CRC is truly present when the sign or symptom is present), or the sign or symptom was a statistically significant predictor of CRC across many studies. The exception to this is perianal symptoms. The absence of perianal symptoms with rectal bleeding strengthens the positive predictive value (PPV) for CRC rather than the presence of perianal symptoms. The studies included in calculating median PPVs or that contained multiple regression analyses can be found in Section 2 of the original CCO report (1).

Risk Factors

In a patient presenting with rectal bleeding, anemia or change in bowel habits, there is evidence to suggest that increasing age and male gender may increase the predictability of suspicion for CRC (23-26).

Meta-analyses by Olde Bekkink et al and Jellema et al found high specificity but low sensitivity for a family history of CRC in symptomatic patients (24,26). In addition, Jellema et al reported a pooled PPV of 6% for a family history of CRC in symptomatic patients (24). Recent prospective population-based studies in primary care have underscored the importance of including family history in an algorithm of symptoms to predict CRC diagnosis (23). A recent meta-analysis of CRC risk factors underscored family history in a first-degree relative as a high risk factor (27).

There is well-established evidence that patients with a personal history of colorectal polyps are predisposed to CRC (28). Patients with a history of IBD are at high risk of CRC, a finding confirmed in a recent meta-analysis of CRC risk factors (27). Based on the consensus, the [CCO] Working Group decided that for these patients who are part of a surveillance program and present with interim signs or symptoms of CRC, early re-referral to specialists is recommended.

Other considerations of moderate increased risk for CRC include the following: male gender (29), African descent (29), alcohol consumption (27,23,30), overweight (27,32), smoking (27,31), low physical activity (27), higher red meat consumption (27), and low fruit (27) and vegetable consumption (27).
Investigations

There was a paucity of studies examining the diagnostic accuracy of investigations for patients presenting with signs and/or symptoms of CRC. The physical examination manoeuvres that were included were based on consensus. They are simple, can be easily performed in primary care, and can provide valuable information leading to expedited referral. Proctoscopy was not recommended as a standard of care due to a lack of evidence for its use, a lack of widespread availability, and a low rate of use in primary care. However, based on consensus, it may still be used at the discretion of the clinician.

The following diagnostic investigations are recommended by the [CCO] Working Group for completion of the assessment: CBC, and imaging for palpable abdominal masses. The results of these tests should be made available to the specialists. Although there were very few studies examining the diagnostic accuracy of a CBC for predicting CRC in symptomatic patients, there was consensus that this should be ordered to assist in the evaluation of whether anemia, and especially iron-deficiency anemia (IDA), is present. The CCNS sub-committee agreed that ferritin should be ordered at the same time if IDA is suspected. It is common practice to image abdominal masses found during a physical examination. Imaging may help to determine whether the mass is intra-colonic or extra-colonic and direct the workup of the mass, as well as indicate appropriate specialty referral.

Because there were very few studies examining the diagnostic accuracy of carcinoembryonic antigen (CEA), erythrocyte sedimentation rate (ESR), and other blood tests for predicting CRC in symptomatic patients, they were not recommended.

Referral

The [CCO] Working Group chose to include signs or symptoms with median PPVs greater than 5, identified in studies in Section 2 of [the CCO] report, as indicators for referral. Any combination of these signs, symptoms and risk factors further increase the probability of CRC, as recent research in primary care has demonstrated (32). The median PPVs of the signs, symptoms, and symptom combinations indentified by the CCNS sub-committee are indicated in Table 1.

For triaging purposes in patients who are being referred semi-urgently, the following combinations of clinical features have been found to increase the index of suspicion for CRC and are described in Section 2 of [the CCO] report:

- Increasing age (most studies used a cut-off of greater than or equal to 60 years) and rectal bleeding or change in bowel habits or anemia (especially iron-deficiency anemia)
- Male patients with rectal bleeding or change in bowel habits or anemia (especially iron-deficiency anemia)
- A combination of signs or symptoms

For signs or symptoms that did not lead to referral, the [CCO] Working Group chose to rely on clinical judgement to decide whether there was a high level or low level of suspicion for CRC. The [CCO] Working Group decided that if a clinician has a low level of suspicion, signs and symptoms should be treated and resolution in four to six weeks should be ensured. This time frame was chosen based on the clinical experience of the [CCO] Working Group and to be consistent with the NICE and NZGG guidelines that recommend referral when some of these symptoms (e.g., rectal bleeding, change in bowel habits) persist for at least six weeks (33,34).

If the time to referral exceeds the recommended wait times or is considered excessive, the [CCO] Working Group recommended that the referring physician may consider ordering a CT colonography, or DCBE, depending on locally available resources. However, the CCNS sub-committee believes CT Colonography to be the Diagnostic Imaging exam of choice and is strongly preferred over DCBE. This would ensure that as much information as possible would be made available to the specialist during the consultation. The CCNS sub-committee believed it is important for PCPs to know that CT...
colonography may miss low rectal cancers and must be accompanied by a DRE. While the CCO Working Group included Double Contrast Barium Enema (DCBE) as an alternative, the CCNS sub-committee felt DCBE should only be considered if both Colonoscopy and CT Colonography cannot be accessed. DCBE may also miss low rectal cancers, does not obviate the need for DRE and should be accompanied by flexible sigmoidoscopy.

There were few studies examining the diagnostic accuracy of abdominal CT or abdominal or pelvic ultrasound among symptomatic patients; however, as described above, they may be helpful in differentiating abdominal/pelvic masses.

**Factors Contributing to Diagnostic Delay**

*Although the [CCO] Working Group concluded* that the evidence suggests that delay in referral does not have an impact on patient survival, *the CCNS sub-committee disagreed with the CCO conclusion (see Impact of Diagnostic Delay above).*

Evidence from prospective and retrospective studies described in Section 2 of the CCO report suggest that the following may delay the diagnosis of CRC:

- **FP and other PCP-related delays (10,16,32,33,50,51,52,54,55)**
  - failure to recognize signs and symptoms were suggestive of CRC
  - failure to investigate iron-deficiency anemia
  - failure to perform DRE
  - initial referral to a specialist without a gastrointestinal interest
  - receiving inaccurate or inadequate tests
  - frequent visits following an inconclusive first visit
  - patients with colon cancer referred less quickly than patients with rectal cancer
  - younger patients
  - gender (females had longer delays than males)
  - visible minorities

- **Patient-related delays (10,16,32,33,50,51,53)**
  - patient’s lack of appreciation regarding the association of symptoms with CRC
  - fear that tests might be unpleasant or embarrassing
  - uncomfortable with or embarrassed about symptoms, including pain, nausea, and vomiting
  - decreased social support
  - presence of co-morbidity
  - rural residency
  - lower education level
  - single/separated/divorced
  - female colon cancer patients had longer delays than male
  - male rectal cancer patients had longer delays than females
Table 1. Positive Predictive Values of Signs and Symptoms of CRC in Primary Care
This was added by the CCNS sub-committee (1,24)

<table>
<thead>
<tr>
<th>Single Sign, Symptom, or Risk Factor</th>
<th>Median PPV across studies</th>
<th>Citation</th>
</tr>
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<tbody>
<tr>
<td>Palpable rectal mass</td>
<td>23.0</td>
<td>27</td>
</tr>
<tr>
<td>Palpable abdominal mass</td>
<td>17.0</td>
<td>27</td>
</tr>
<tr>
<td>Iron-deficient anemia</td>
<td>11.0</td>
<td>1</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>5.3</td>
<td>1</td>
</tr>
<tr>
<td>Change in bowel habits</td>
<td>7.5</td>
<td>1</td>
</tr>
<tr>
<td>Weight loss</td>
<td>4.9</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal symptoms</td>
<td>2.1</td>
<td>1</td>
</tr>
<tr>
<td>Family history (one first degree relative)</td>
<td>6.0</td>
<td>27</td>
</tr>
<tr>
<td>Personal history of polyps</td>
<td>5.7</td>
<td>27</td>
</tr>
</tbody>
</table>

**Combined Sign or Symptom**

<table>
<thead>
<tr>
<th>Combined Sign or Symptom</th>
<th>Median PPV across studies</th>
<th>Citation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal bleeding mixed with stool</td>
<td>11.0</td>
<td>1</td>
</tr>
<tr>
<td>Rectal bleeding in the absence of perianal symptoms</td>
<td>10.8</td>
<td>1</td>
</tr>
<tr>
<td>Rectal bleeding associated with mucous or epithelial tissue discharge</td>
<td>11.0</td>
<td>27</td>
</tr>
<tr>
<td>Rectal bleeding and change in bowel habits</td>
<td>10.5</td>
<td>1</td>
</tr>
<tr>
<td>Rectal bleeding and weight loss</td>
<td>13.0</td>
<td>1</td>
</tr>
<tr>
<td>Dark rectal bleeding</td>
<td>9.7</td>
<td>1</td>
</tr>
</tbody>
</table>

PPV = Positive Predictive Value (the probability that CRC is present when the sign or symptom is present).
FUTURE RESEARCH

Further studies should be designed to determine which educational initiatives would be best at decreasing practitioner or patient-related delay. Also, more studies to determine the diagnostic performance of signs and symptoms for CRC are needed in the primary care setting.

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REFERENCES


Appendix D: Guideline Development Process

Guideline Development

In 2012, Cancer Care Nova Scotia (CCNS) began development on clinical standards for the management of rectal cancer in Nova Scotia (NS). Early in this work, the need for guidance regarding the diagnosis and referral of patients clinically suspicious for colorectal cancer (CRC) was identified. A sub-committee was established to work on these guidelines.

The goal is to provide guidance to PCPs on the appropriate management of patients who are clinically suspicious for CRC so as to limit unnecessary or inappropriate investigations and/or referrals to specialists and to expedite referrals to endoscopists, as well as to provide guidance to endoscopists regarding the relative importance and urgency of these referrals. The sub-committee consisted of primary care providers, general surgeons, gastroenterologists and radiologists from urban and rural NS and Public Advisors. See list of sub-committee members at the end of this document. All members were asked to complete Conflict of Interest forms.

In April 2012, Cancer Care Ontario (CCO) published its guideline for “Referral of Patients with Suspected Colorectal Cancer by Family Physicians and Other Primary Care Providers” (1). As the CCO guideline was very recent, addressed the very question of interest and had been developed through rigorous processes, including a systematic review of the best available evidence on primary care referral for suspected CRC, CCNS requested and received permission from CCO to adapt this document for NS.

The sub-committee met regularly October 2012 to April 2013 and reviewed and revised the CCO guideline based on the NS environment and new evidence which emerged since the CCO systematic review was conducted. The sub-committee also decided to develop a standardized referral form to facilitate communication between PCP and endoscopist. Decisions were made by consensus (i.e. all members of the group could “live with” the recommendations). Final revisions were made by email over the fall of 2013.

Health Professional External Review

The health professional review was conducted through an electronic survey in March 2014. Health professionals (with a focus on surgeons, radiologists, pathology, gastroenterologists, family practice physicians and nurse practitioners, emergency department physicians and cancer patient navigators) received the draft guidelines, referral form and survey link through the District Health Authority Vice Presidents of Medicine and Patient Care. Additionally, key groups were also contacted through other channels. For example, the credentialed endoscopists were sent an invitation through the Colon Cancer Prevention Program, general surgeons were invited through the Surgical Section mailing list and the College of Registered Nurses of Nova Scotia sent a message to Nurse Practitioners. A request was made to Doctors Nova Scotia which resulted in an invitation to present the draft guidelines to the Doctors Nova Scotia General Practice Council. Staff of the Department of Health and Wellness were also given the opportunity to review the draft document. Specific questions were also sent to Maritime Medical Genetics and the Capital Health Division of Hematology.

There were 35 individual and 5 group responses to the survey, plus 6 individuals provided comment via email.

Guidelines for Investigation of Symptoms Suggestive of CRC
Colorectal Cancer Public External Review

The public review occurred in September 2014 and provided two options for input: an electronic survey or focus groups. The opportunity to participate was widely advertised:

- surgeons and cancer patient navigators were sent posters for their offices
- posted on the CCNS website and promoted through its Twitter and Facebook accounts
- communicated through the CCNS Cancer Patient Family Network
- details were sent to community groups known to have an interest in colorectal cancer (Canadian Cancer Society – Nova Scotia Division, the Colorectal Cancer Association of Canada and the Ostomy Association of Canada Nova Scotia chapter) with a request to share this information with their members
- press release issued

The draft document was posted on the CCNS website for review along with additional materials to support lay persons in their review. The CCNS Patient Engagement Coordinator was also available to answer questions or support patients in their review of the material.

There was minimum interest in the focus group and so a phone interview was held with the one interested individual. The survey was designed so that only CRC survivors (or their family members) who had been diagnosed through symptoms were asked about the recommendations regarding the investigation and work up of symptoms. All respondents, regardless of how diagnosed, were asked whether they were given their diagnosis in a sensitive manner, given the information they needed, provided the opportunity to ask questions and if they understood the next steps. All respondents were given the opportunity to comment on the recommendations regarding the communication of the diagnosis and the organization of care. All respondents were also asked to review a list of proposed topics to be included in the “Blue Ribbon Kit” for newly diagnosed CRC patients.

38 individuals started the survey.

Results

CCNS staff collated the responses from both the health professional and patient review of the draft recommendations and provided them to the sub-committee. The majority of the respondents from both surveys were positive and supportive of the draft guidelines. All areas of disagreement, concerns or issues identified as missing from the draft were reviewed by the sub-committee and the document was revised.

Cancer Care Nova Scotia Involvement

As the provincial cancer agency for NS, the mandate for CCNS includes the development of provincial standards and guidelines related to cancer care and treatment. CCNS staff supported the sub-committee in the development of the guidelines by providing meeting facilitation support and organization for the sub-committee meetings including all communication with sub-committee members and logistical arrangements. CCNS staff also coordinated the writing and editing of the various drafts. The views and interests of CCNS did not influence the decision-making.

To facilitate the involvement of sub-committee members, CCNS removed financial barriers by providing travel or distance technology for those participating from outside Halifax, and reimbursing fee for

Guidelines for Investigation of Symptoms Suggestive of CRC
service physicians for their time during meetings (at the approved Department of Health and Wellness rate for administrative work).

The development process was supervised by the CCNS Clinical Standards Oversight Committee, which has representatives of the Nova Scotia Department of Health and Wellness, senior leaders of the District Health Authorities (until April 1, 2015)/Nova Scotia Health Authority (after April 1, 2015), Doctors Nova Scotia and Public Advisors.

As of April 1, 2016 CCNS will become part of the Nova Scotia Health Authority (NSHA). At this time, the Department of Health and Wellness will transfer responsibility for the setting of clinical standards for cancer to the NSHA. Decisions about the future processes of approval, dissemination/implementation and regular reviewing and updating of guidelines will be determined through discussions with the Department of Health and Wellness and the NSHA.
Appendix E: Literature Search: Does a delay in the time to consultation affect patient outcome?

There was one conclusion reached by the Cancer Care Ontario panel with which the CCNS sub-committee disagreed, namely that delayed diagnosis does not have an impact on patient survival. An update of the CCO systematic search on this topic was conducted through the Health Sciences Library of Capital Health in Halifax.

METHODS

Literature Search Strategy

Subject: early diagnosis of colorectal cancer symptoms (not screening) impact on survival/mortality

Reported: December 14, 2012

Years searched: 2007-2012, English language, Humans

Searched: PubMed / Embase

Prognostic Question: Use appropriate Filter

PubMed:


Embase(excluding MEDLINE articles):

(("colon'/exp OR 'colon" AND (cancer)/lim OR ('rectum'/exp OR 'rectum' AND [cancer]/lim) OR 'colorectal cancer'/exp OR 'colorectal cancer' OR (colon:ab,ti OR colorect*:ab,ti OR rectal:ab,ti OR rectum:ab,ti AND (cancer*:ab,ti OR neoplasm*:ab,ti OR tumour*:ab,ti OR tumor*:ab,ti))) AND (earl* OR late OR delay*or AND first AND (diagnos*or:ab,ti AND detect*or:ab,ti AND presentation*:ab,ti OR symptom*:ab,ti)) OR ('health behavior'/exp OR 'doctor patient relation'/de)) AND (('patient referral'/de OR 'disease course'/exp OR 'time'/exp OR 'clinical practice'/exp) OR (early:ab,ti OR late:ab,ti OR delay*:ab,ti AND refer*:ab,ti) AND (prognos*:ab,ti OR mortality:ab,ti OR survival:ab,ti OR 'follow up':ab,ti)) AND ((embase)/lim NOT [medline]/lim AND [2007-2012]/py)

DISCUSSION

The literature on the impact of diagnostic delay on survival has been problematic. Early studies reached the counterintuitive conclusion that delays in diagnosis and treatment do not impact survival, or that longer delays are associated with improved survival (1,2). These results led many to conclude that there is no physical reason to intervene quickly with those suspected of or diagnosed with CRC (3,4,5); rather, prompt treatment is considered valuable mainly as means to reduce patient anxiety (6).

This “wait time paradox” of an inverse relationship between diagnostic delay and mortality has puzzled researchers. Some have attributed it to the fact that aggressive but lethal cancers are easier to appraise (7,9). Others have underscored the methodological flaws of early research, particularly the confounding inherent in the use of statistical or categorical controls for tumour stage (8,10,11). Because it is well known that tumour stage is the single greatest contributor to mortality, research methods that remove its influence leave very little variance to be explained. Studies claiming that diagnostic delay has no impact on mortality have either used statistical controls for tumour stage (1,7,12), confined their study to early stage patients (1,5), or adjusted for emergency admission or other dire prognostic factors (9,13,14). Also, the operational definition of the delay interval has been inconsistent between studies, with

Guidelines for Investigation of Symptoms Suggestive of CRC
differing start points (i.e., symptom onset, presentation to primary care, referral from primary care, diagnosis) and endpoints (i.e., diagnosis, treatment). Studies showing no association of delay and mortality have been criticized for using restricted or dichotomous definitions of the delay interval (8), and for ignoring the non-linear nature of carcinogenesis (11).

Prospective, population-based longitudinal research provides the most definitive approach to understanding the impact of diagnostic delay on outcome. Several recent longitudinal studies have demonstrated that diagnostic delay greater than 60 days is associated with an exponential increase in mortality in CRC patients (10,15). Torring and her colleagues have demonstrated a U-shaped relationship between delay and death: as the interval between first presentation to a family doctor and ultimate cancer diagnosis increased, mortality decreased in the first five weeks, then increased significantly (11). Similar functions were found for melanoma, lung, and prostate cancer (11). These findings replicated a prospective study done in Denmark, which found that having the risk of late-stage cancer doubled if the interval between symptom onset and treatment was greater than 60 days (15,16,17). This risk of delay was even greater for rectal cancer relative to colon cancer, a finding that is consistent with the known greater metastatic potential of rectal cancer (8,18). In contrast, a prospective study in Holland (14) did not find an association between delay and survival; however, this study was limited by using very restricted definition of delay and by controlling for stage-relevant symptoms. Taken together, the results of recent methodologically superior studies suggest that mortality increases as diagnostic delay increases. These findings reflect the known pathogenesis of colorectal cancer, and underscore the importance of prompt detection and treatment for the survival of CRC patients (19).

References


## Appendix F: Diagnosis and Referral of Patients Suspicious for Colorectal Cancer Sub-Committee Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Role/Location</th>
</tr>
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| Heather Johnson (Chair)  | General Practitioner
                           | Bridgewater
                           | Western Zone                  |
| Lisa Bonang              | General Practitioner and Emergency Room Physician
                           | Musquodoboit Harbour
                           | Central Zone                  |
| Robinette Butt           | Radiologist                                                                  |
                           | Halifax                                                                      |
                           | Central Zone                    |
| Glenn Campbell           | Emergency Room Physician - Lower Sackville
                           | North End Community Clinic - Halifax
                           | Central Zone                  |
| Michael Dunn             | Radiologist                                                                  |
                           | Kentville
                           | Western Zone                  |
| Hughie Fraser            | Gastroenterologist                                                           |
                           | Bridgewater
                           | Western Zone                  |
| Rick Gibson              | Chief, Family Practice                                                       |
                           | Central Zone
                           | Corresponding member           |
| Marius Hoogerboord       | GI Surgeon                                                                   |
                           | Halifax                                                                      |
                           | Central Zone                    |
| Stephanie Langley        | General Practitioner                                                         |
                           | Sydney
                           | Eastern Zone                   |
| Archie MacEachern        | Colorectal Cancer Survivor Public Advisor
                           | Sydney
                           | Eastern Zone                   |
| Don MacIntosh            | Gastroenterologist                                                           |
                           | Halifax                                                                      |
                           | Central Zone                    |
| Robin McGee              | Colorectal Cancer Survivor Public Advisor
                           | Kentville
                           | Western Zone                   |
| Lynn Miller              | Nurse Practitioner                                                           |
                           | Cumberland North Rural Practice Network
                           | Northern Zone                  |
| Alex Mitchell (alternate with John Murdoch) | General Surgeon |
                           | Dartmouth
                           | Central Zone                  |
| John Murdoch             | General Surgeon                                                             |

Guidelines for Investigation of Symptoms Suggestive of CRC
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<th>(alternate with Alex Mitchell)</th>
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<td>Phil Smith</td>
<td>General Surgeon</td>
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<td>Sydney</td>
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<td>Eastern Zone</td>
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<td></td>
<td>(to February 2013)</td>
</tr>
<tr>
<td>Jill Petrella</td>
<td>Manager, Quality and Cancer Site Teams</td>
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