

# Guideline for referral of patients with suspected colorectal cancer by family physicians and other primary care providers

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## Abstract

**Objective** The aim of this guideline is to assist FPs and other primary care providers with recognizing features that should raise their suspicions about the presence of colorectal cancer (CRC) in their patients.

**Composition of the committee** Committee members were selected from among the regional primary care leads from the Cancer Care Ontario Provincial Primary Care and Cancer Network, the members of the Ontario Colorectal Cancer Screening Advisory Committee, and the members of the Cancer Care Ontario Gastrointestinal Cancer Disease Site Group.

**Methods** This guideline was developed through systematic review of the evidence base, synthesis of the evidence, and formal external review involving Canadian stakeholders to validate the relevance of recommendations.

**Report** Evidence-based guidelines were developed to improve the management of patients presenting with clinical features of CRC within the Canadian context.

### EDITOR'S KEY POINTS

- Clinical features that are associated with an increased risk of colorectal cancer include a palpable rectal or abdominal mass; rectal bleeding, especially in combination with other signs and symptoms; iron deficiency anemia; and a change in bowel habits.
- Patients with abdominal or rectal masses should be referred urgently to a diagnostic assessment program, if available, or to a specialist competent in endoscopy. In patients with iron deficiency anemia or rectal bleeding, especially in combination with other signs or symptoms, a semiurgent referral should be made. Other presenting symptoms should be managed, and resolution within 6 weeks should be ensured.



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This article has been peer reviewed.  
*Can Fam Physician* 2014;60:717-23

La traduction en français de cet article se trouve à [www.cfp.ca](http://www.cfp.ca) dans la table des matières du numéro d'août 2014 à la page e383.

**Conclusion** The judicious balancing of suspicion of CRC and level of risk of CRC should encourage timely referral by FPs and primary care providers. This guideline might also inform indications for referral to CRC diagnostic assessment programs.

Colorectal cancer (CRC) is one of the most common types of cancer in Canada.<sup>1</sup> Patients who present to FPs with symptoms of CRC are often at later stages of the disease.<sup>2</sup> In attempts to improve the rate of early detection of CRC, many jurisdictions across Canada have introduced population-based screening programs. Although CRC screening rates are increasing, they are low, and even with screening, patients with CRC can be missed.<sup>2</sup> Therefore, patients presenting with signs and symptoms predictive of CRC will depend on their FPs and other primary care providers (PCPs) to recognize, investigate, and refer them for further assessment and management of CRC.<sup>3</sup>

In order to provide guidance for the introduction of CRC diagnostic assessment programs (DAPs) in Ontario, the Cancer Care Ontario (CCO) Provincial Primary Care and Cancer Network initiated collaboration in February 2009 with CCO's Program in Evidence-based Care (PEBC) to form the Colorectal Cancer Referral Working Group. The working group was tasked with determining how patients presenting to FPs and other PCPs with signs or symptoms of CRC should be managed. The following questions were evaluated in completing this overall objective.

- What signs, symptoms, and other clinical features that present in primary care are predictive of CRC?
- What is the diagnostic accuracy of investigations commonly considered for patients presenting with signs or symptoms of CRC?
- What main known risk factors increase the likelihood of CRC in patients presenting with signs or symptoms of CRC?
- Which patient and provider factors are associated with delayed referral?

- Does a delay in the time to consultation affect patient outcomes?

These guidelines do not address CRC screening or gastrointestinal emergencies.

### Composition of committee

The working group consisted of 3 FPs (M.E.D., A.H., C.L.), 2 surgeons (M.S., W.H.), and 1 methodologist (E.T.V.). Committee members were selected from the Ontario Colorectal Cancer Screening Advisory Committee, the Provincial Primary Care and Cancer Network, and CCO's Gastrointestinal Cancer Disease Site Group. Internal and external reviewers included FPs, gastroenterologists, radiologists, and surgeons. The work of the PEBC is supported by the Ontario Ministry of Health and Long-Term Care through CCO, and the PEBC is editorially independent from its funding source.

### Methods

The methods of the practice guideline development cycle were used.<sup>4</sup> The guideline was developed through systematic review of the evidentiary base, evidence synthesis, and input from a formal internal and external review by Canadian stakeholders. The methods and main findings are described in detail elsewhere.<sup>2,5</sup> The recommendations were developed based on evidence from level I systematic reviews and meta-analyses, level II case-control and cohort studies, and level III expert opinion.

Many jurisdictions consider a positive screening guaiac fecal occult blood test (FOBT) result to be an indicator for increased risk of CRC. The median positive predictive value (PPV) for the combined guaiac FOBTs evaluated in a review was 5.7%.<sup>6</sup> A recent report evaluating the FOBT used in the ColonCancerCheck program in Ontario showed a PPV of 5.4% for single (1-time) testing in asymptomatic patients.<sup>7</sup> A PPV is the probability that the disease is truly present when the clinical feature is present or positive. Estimated PPVs of possible signs and symptoms of CRC were extracted from the peer-reviewed literature. Clinical features with pooled PPVs from our systematic review and from published meta-analyses that were equal to or greater than the PPV for a positive FOBT result were considered to indicate increased risk of CRC.

Colonoscopy is currently recommended for individuals considered to be at increased risk of CRC, such as those with a screen-positive FOBT result and individuals with a first-degree relative with CRC. Therefore, colonoscopy was also recommended for the management of patients presenting with clinical features indicative of increased risk of CRC. Published Canadian guidelines and the target wait time of 8 weeks for colonoscopy after a positive FOBT result from the ColonCancerCheck program in Ontario were used to help establish wait time recommendations.<sup>7,8</sup>

### Report

*What signs, symptoms, and other clinical features that present in primary care are predictive of CRC?* Table 1 provides a summary of the signs and symptoms considered to suggest increased risk of CRC presenting in primary care and their respective median PPVs that were ascertained from our systematic review.<sup>2</sup>

*What is the diagnostic accuracy of investigations commonly considered for patients presenting with signs or symptoms of CRC?* Owing to a paucity of studies examining the diagnostic accuracy of the recommended investigations and physical examination maneuvers for patients presenting with signs or symptoms of CRC, recommendations for investigations and maneuvers were based on the consensus of the working group in terms of their ease of performance in primary care and the potential provision of valuable information leading to expedited referral. Recommendations regarding a detailed workup of unexplained anemia were beyond the scope of these guidelines; FPs and PCPs can refer to existing published guidelines if indicated.<sup>9,10</sup> Given the compelling evidence for the association between iron deficiency anemia (IDA) and CRC, a ferritin test should be ordered if anemia is present. Imaging of palpable abdominal masses might help to determine whether such masses are intracolonic or extracolonic and,

**Table 1. Clinical features indicating increased risk of CRC**

CLINICAL FEATURE	MEDIAN PPV (RANGE), %
Palpable rectal or abdominal mass	NA*
Rectal bleeding combined with weight loss	13.0 (4.7-23)
Iron deficiency anemia	11.0 (7.7-41)
Rectal bleeding mixed with stool	11.0 (3.0-21)
Rectal bleeding in the absence of perianal symptoms	10.8 (6.9-18)
Rectal bleeding combined with a change in bowel habits	10.5 (9.2-27)
Dark rectal bleeding	9.7 (7.4-17)
Rectal bleeding and diarrhea	9.0 (3.4-19)
Rectal bleeding and age > 60 or > 65 y	8.6 (4.6-20)
Rectal bleeding and age > 70 or > 75 y	7.9 (4.9-31)
Change in bowel habits or diarrhea	7.5 (0.94-14)
Rectal bleeding and male sex	7.5 (2.4-17)
Rectal bleeding and age > 50 or > 55 y	5.9 (4-11)
Rectal bleeding (undefined)	5.3 (2.2-16)
Rectal bleeding and abdominal pain	5.1 (1.7-23)
Rectal bleeding first episode	5.0 (2.2-14)

CRC—colorectal cancer, NA—not available, PPV—positive predictive value.  
\*Individual studies reported PPVs > 15%.

thus, direct the appropriate workup and specialist referral. Proctoscopy was not recommended as a standard of care owing 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 can still be used at the discretion of the clinician. Digital rectal examination was included because it is a simple maneuver, it can be easily performed in primary care, and if a suspicious rectal mass is felt, it can provide valuable information leading to expedited referral. This is supported by 2 studies that showed that the PPV for digital rectal examination in the presence of other symptoms was above 5%.<sup>11,12</sup> Because there were very few studies examining the diagnostic accuracy of carcinoembryonic antigen measurement, erythrocyte sedimentation rate, and other blood tests for predicting CRC in symptomatic patients, these were also not recommended and should not be ordered.

**What main known risk factors increase the likelihood of CRC in patients presenting with signs or symptoms of CRC?** There is well established evidence that patients with a personal history of colorectal polyps or inflammatory bowel disease are at increased risk of CRC.<sup>13</sup> Meta-analyses by Jellema et al and Olde Bekkink et al found high specificity but low sensitivity for a family history of CRC in symptomatic patients.<sup>14,15</sup> Jellema et al reported a pooled PPV of 6% for a family history of CRC in symptomatic patients.<sup>14</sup> *Family history* was defined as CRC in a first-degree relative in some of the included studies but was not defined in other included studies.

**Referral recommendations.** In order to ensure that patients are stratified appropriately according to risk, a full history, physical examination, and investigations as outlined in **Box 1** should be completed.<sup>9,10</sup> When the patient's clinical features warrant referral, the FP or PCP should initiate the referral within 24 hours of presentation. Patients should be referred to a CRC DAP, if available, or to a specialist competent in endoscopy (**Box 2**).

**Figure 1** provides referral triage and timeliness recommendations for signs and symptoms causing suspicion of CRC.

**Urgent referrals:** In our systematic review, 3 studies found rectal and abdominal masses to be statistically significant predictors of CRC.<sup>16-18</sup> The PPV for combined rectal or abdominal masses was 16.7% in one study.<sup>16</sup> Two studies found PPVs of 80%<sup>17</sup> and 22.6%<sup>18</sup> for rectal masses and 41%<sup>17</sup> and 16.3%<sup>18</sup> for abdominal masses. Based on the relatively high PPVs, as well as the clinical experience of the working group, these signs were thought to require urgent consultation. Target wait times for an urgent referral include consultation within 2 weeks and completion of a definitive diagnostic workup within 4 weeks.

**Semiurgent referrals:** For the remaining clinical features indicating increased risk, a semiurgent referral is

### Box 1. Clinical encounter recommendations

A focused history and physical examination should be performed if patients present with 1 or more of the following signs or symptoms:

- Palpable rectal mass
- Palpable abdominal mass
- Anemia (especially IDA)
- Rectal bleeding
- Change in bowel habits
- Weight loss
- Abdominal discomfort
- Perianal symptoms

The focused history should determine the following details:

- Age and sex
- Whether there is rectal bleeding and, if there is, the
  - colour (dark vs bright red) and
  - location of blood relative to stool (mixed in with stool vs separate from stool, on the toilet paper)
- Whether there has been a change in bowel habit over recent months or years and, if there has, whether there are
  - increased loose or watery stools or diarrhea,
  - increased constipation or difficulty passing stools,
  - feelings of incomplete emptying,
  - increased urgency, or
  - incontinence of stools or soiling
- Weight loss
- Abdominal discomfort (eg, pain, tenderness, bloating)
- Perianal symptoms (eg, prolapsed lump, pruritus, pain, hemorrhoids)
- Symptoms of anemia (eg, fatigue, weakness)
- Whether there is unexplained IDA present and, if there is, possible causes of blood loss or blood dyscrasia<sup>9,10</sup>
- Personal history of colorectal polyps or IBD, or family history of CRC in a first-degree relative and the age of onset

To supplement the history, a focused physical examination and investigations should include the following:

- Digital rectal examination
- Abdominal examination (if a palpable mass is detected, order abdominal or pelvic imaging)
- Assessment for signs of anemia
- Measurement of weight (and comparison to previous weights if possible)
- CBC, and if low MCV (ie, microcytic anemia), can order ferritin measurement

CBC—complete blood count, CRC—colorectal cancer, IBD—inflammatory bowel disease, IDA—iron deficiency anemia, MCV—mean corpuscular volume.

recommended. These include IDA and rectal bleeding, especially in combination with other clinical features. The cutoff values for hemoglobin ( $\leq 110$  g/L for men or  $\leq 100$  g/L for nonmenstruating women and iron level below the normal range) were taken from the 2-week referral guideline developed by the National Institute for Health and Care Excellence in 2005 and endorsed by the New Zealand Guidelines Group

**Box 2. Referral recommendations:** Referring physicians should send a referral within 24 hours to a specialist competent in endoscopy or to a diagnostic assessment program, where available.

#### Urgent referral

Expect a consultation within 2 weeks and a definitive diagnostic workup to be completed within 4 weeks of referral if a patient has at least 1 of the following:

- Palpable rectal mass suspicious for CRC
- Abnormal abdominal imaging result causing suspicion of CRC

#### Semiurgent referral

Expect a consultation within 4 weeks and a definitive diagnostic workup to be completed within 8 weeks of referral if a patient has at least 1 of the following:

- Unexplained rectal bleeding with at least 1 of
  - dark rectal bleeding,
  - rectal bleeding mixed with stool,
  - rectal bleeding in the absence of perianal symptoms,
  - rectal bleeding and a change in bowel habits, or
  - rectal bleeding and weight loss
- Unexplained IDA (hemoglobin of  $\leq 110$  g/L for men or  $\leq 100$  g/L for nonmenstruating women and iron level below the normal range)
- A high level of suspicion of CRC because of an unexplained sign or symptom but not meeting the above criteria

Referring physicians should include in the consultation request information about anything that can increase the likelihood of CRC:

- All presenting signs and symptoms
- Patient age  $\geq 60$  years
- Male sex
- Personal history of colorectal polyps or IBD, or family history of CRC in a first-degree relative

#### Patients not meeting referral criteria

If the unexplained signs or symptoms of patients do not meet the criteria for referral but, based on clinical judgment, there remains a low level of suspicion of CRC, then the following are appropriate:

- Treat the sign or symptom, if applicable
- Review and ensure resolution of symptoms within 4 to 6 weeks
- If signs or symptoms have not resolved in 4 to 6 weeks, then confer with a specialist or refer semiurgently
- A 3-stool sample FOBT can be ordered in the absence of recent CRC screening and in the absence of current active rectal bleeding. If the result is positive, refer semiurgently. A negative result does not rule out CRC

#### Excessive wait times

In situations where wait times for specialists to perform colonoscopy are considered excessive, referring physicians can order the following (depending on locally available resources):

- CT colonography
- DCBE

This is best done in coordination with the specialist, if possible. Normal or negative results should not lead to a cancellation of the consultation. Positive results might facilitate more timely investigation of a patient

CRC—colorectal cancer, CT—computed tomography, DCBE—double-contrast barium enema, FOBT—fecal occult blood test, IBD—inflammatory bowel disease, IDA—iron deficiency anemia.

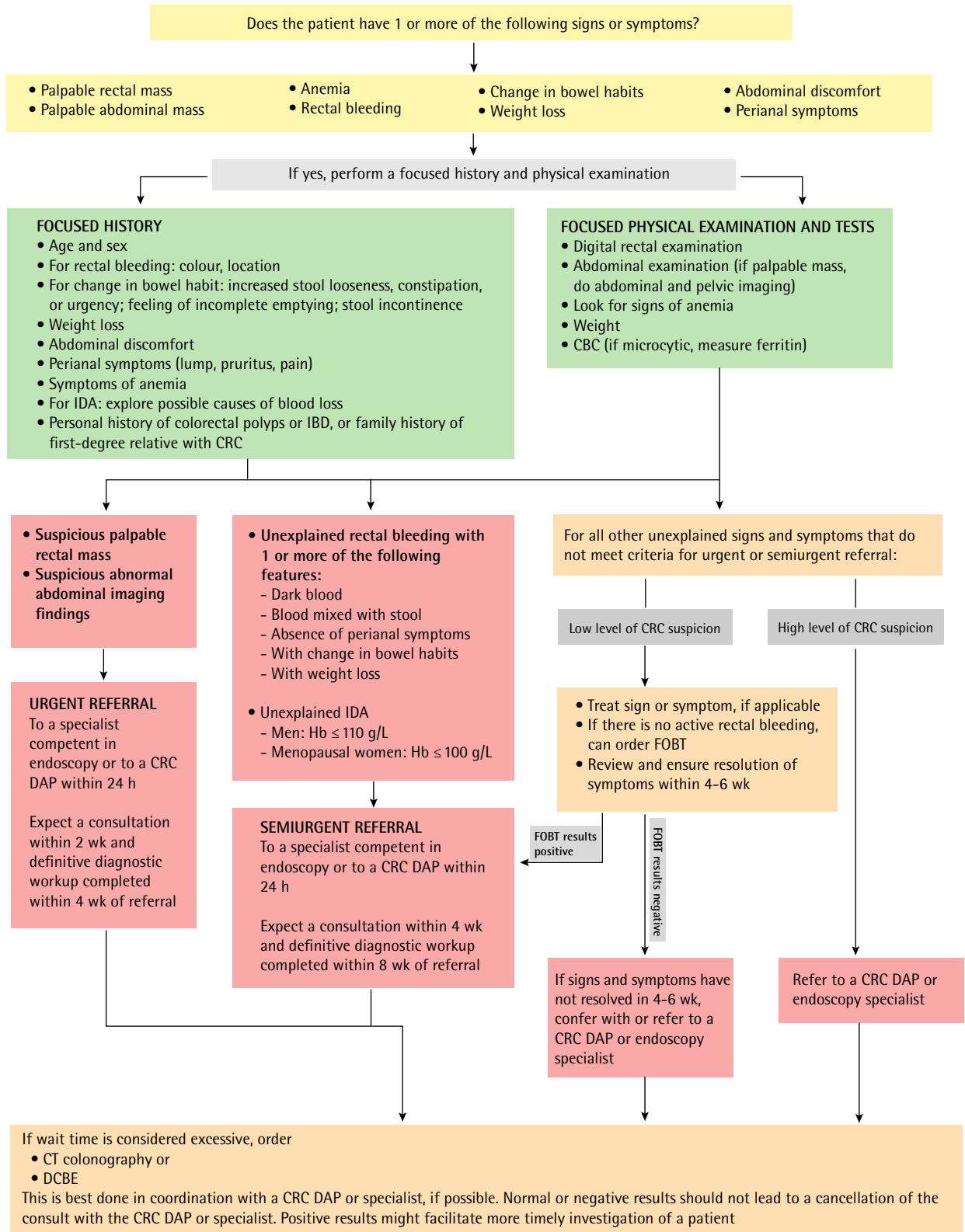
in 2009.<sup>19,20</sup> Based on consensus, the working group decided that for patients with a past medical history of inflammatory bowel disease or family history of CRC who were part of a surveillance program and who presented with interim signs or symptoms of CRC, early re-referral to specialists can be considered at the discretion of the FP or PCP for those patients who have not had recent endoscopy.

Target wait times for a semiurgent referral include a consultation within 4 weeks and completion of a definitive diagnostic workup within 8 weeks.

For signs or symptoms with lower PPVs that do not lead to referral, clinical judgment is recommended to decide whether there is a high level or low level of suspicion of CRC. Semiurgent referral is recommended if there is a high level of clinical suspicion.

**Low level of CRC suspicion.** If there is a low level of CRC suspicion, signs and symptoms should be treated, if indicated, and resolution in 4 to 6 weeks should be ensured. This time frame was chosen based on the

**Figure 1. Colorectal cancer guideline recommendations for symptomatic patients**



CBC—complete blood count, CRC—colorectal cancer, CT—computed tomography, DAP—diagnostic assessment program, DCBE—double-contrast barium enema, FOBT—fecal occult blood test, Hb—hemoglobin, IBD—inflammatory bowel disease, IDA—iron deficiency anemia.



clinical experience of the working group and to be consistent with the National Institute for Health and Care Excellence and New Zealand Guidelines Group guidelines that recommend referral only after symptoms persist for at least 6 weeks.<sup>19,20</sup> If signs or symptoms have not resolved in 4 to 6 weeks, then semiurgent referral should be made. In the absence of recent CRC screening and in the absence of active rectal bleeding, a 3-sample FOBT can be considered at the discretion of the clinician. A concurrent positive FOBT result might provide additional information that would justify an expedited workup.

The use of FOBT in low-suspicion symptomatic patients is based on a 2010 meta-analysis by Jellema et al, which found good diagnostic performance for both guaiac and immunological-based FOBT tests in symptomatic patients.<sup>14</sup> However, most of these studies were conducted in secondary care and did not provide specific signs or symptoms for which FOBT was used.

**Recommendations for system-related delays to consultation.** If the time to consultation is considered excessive, the referring physician can consider interim investigations. Sensitivities or specificities were higher than 83% when computed tomography colonography or double-contrast barium enema in symptomatic patients were compared with colonoscopy alone.<sup>21-33</sup> Flexible sigmoidoscopy also showed good sensitivity for detecting CRC, especially when combined with double-contrast barium enema.<sup>22,25,31,34</sup> There were few studies examining the diagnostic accuracy of abdominal computed tomography or abdominal or pelvic ultrasound among symptomatic patients; however, such imaging might be helpful in differentiating abdominal or pelvic masses.

**Which patient and provider factors are associated with delayed referral? Does a delay in the time to consultation affect patient outcomes?** Evidence from prospective and retrospective studies suggest several factors can delay the diagnosis of CRC.<sup>19,20,35-38</sup> Patient-related factors that were found to have the most influence on delay were patients not recognizing their symptoms as being suggestive of CRC or fear of the possible sequelae of tests or interventions that might occur. Patients with more severe symptoms, other comorbidities, or social support had shorter delays. Physician-related factors included a lack of recognition of the symptoms of CRC in patients, not investigating IDA, or not performing a rectal examination. In addition, referral to a specialist without a gastrointestinal interest or with inadequate test results provided to the specialist can lead to delays. Although overall socioeconomic status did not have a strong effect on delay, lower levels of education; living in a rural area; and being single or divorced, female, younger, black, or South Asian led to increases in delay. Furthermore, although studies suggest that longer delays in referral have not had an effect on patient mortality, the effects of

psychological morbidity on patients and their families should mandate more urgent evaluation.<sup>39-45</sup> Recommendations to address these issues are provided in **Box 3**.<sup>9,10</sup>

## Conclusion

A systematic approach was used to identify clinical features suggestive of possible CRC that should prompt FPs and other PCPs to refer patients for expedited consultation and colonoscopy. Patients with abdominal or rectal masses should be referred urgently. In patients with IDA or rectal bleeding especially in combination with other signs or symptoms, a semiurgent referral to a specialist competent in endoscopy should be made. Other presenting symptoms should be managed, and resolution within 6 weeks should be ensured. Use of FOBTs can be considered in patients whose symptoms do not lead to urgent or semiurgent

### Box 3. Recommendations to reduce diagnostic delay

- The following might help to reduce diagnostic delay: Information regarding the signs and symptoms of CRC, how to obtain a proper detailed history and physical examination, appropriate investigations, and referral of patients presenting with suspicious signs and symptoms should be widely disseminated to FPs and other PCPs using various knowledge translation strategies
- During the periodic health examination, FPs and other PCPs should ask adult patients about rectal bleeding, changes in bowel habits, and unintentional weight loss
- While discussing CRC screening with patients, FPs and other PCPs should ask about family history of CRC and the signs and symptoms predictive of CRC
- FPs and other PCPs should investigate unexplained anemia, especially iron deficiency anemia (refer to anemia guidelines<sup>9,10</sup>)
- For signs and symptoms that might not have prompted initial referral, FPs and other PCPs should reassess and perform further workup if signs or symptoms do not resolve
- FPs and other PCPs should consider training staff regarding triaging of patients calling with signs or symptoms suggestive of CRC to expedite initial appointments
- Specialists competent in endoscopy should develop triage protocols to avoid delays in the diagnosis of CRC in patients with suspicious signs or symptoms
- Sustainable public education about the signs and symptoms of CRC, the importance of early detection and management, and common fears and concerns that might delay referral should be developed and implemented
- Special efforts should be made to reduce delays in presentation often observed among women, single patients, younger patients, visible minorities, and patients with comorbidities, decreased social support, lower levels of education, or rural residence

CRC—colorectal cancer, PCP—primary care provider.

referral and for whom there is a low suspicion of CRC. For symptomatic patients who are waiting a substantial amount of time for a consultation, interim investigations can be considered. Attempts to address delays in diagnosis should be made at the patient, provider, and policy levels.

This guideline might help reduce delays in CRC diagnosis by assisting FPs and other PCPs in recognizing clinical features that should raise their suspicion about the presence of CRC and leading them to more timely and appropriate referrals. It might also guide program development for DAPs for patients with features that raise suspicion of CRC and help policy makers ensure that resources are in place so that target wait times can be achieved.

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#### Contributors

All authors contributed to the literature review and interpretation, and to preparing the report for submission.

#### Competing interests

None declared.

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