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Evidence-Based Series 24-1 Version 2

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Referral of Patients with Suspected Colorectal Cancer by Family Physicians and Other Primary Care Providers

The Colorectal Cancer Referral Expert Panel

An assessment conducted in March 2024 deferred the review of Evidence-Based Series (EBS) 24-1 Version 2. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

EBS 24-1 Version 2 is comprised of 4 sections. You can access the summary and full report here:

https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/586

Section 1: Guideline Recommendations (ENDORSED)
Section 2: Evidentiary Base
Section 3: EBS Development Methods and External Review Process
Section 4: Document Review Summary and Tool

April 10, 2017

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Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES and KEY CHANGES
	Search Dates	Data		
Original April 2012	June 2004 – August 2011	Full Report	Peer review publication Web publication	NA
Current Version 2 April, 2017	June 2009 - September 2015	New data found in Section 4: Document Review Summary and Tool	Updated CCO web publication	2012 recommendations **ENDORSED**

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Evidence-Based Series 24-1: Section 1- Guideline Recommendations

Referral of Patients with Suspected Colorectal Cancer by Family Physicians and Other Primary Care Providers: Guideline Recommendations

L. Del Giudice, E. Vella, A. Hey, W. Harris, M. Simunovic, C. Levitt, and the Colorectal Cancer Referral Expert Panel

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: April 24, 2012

These guideline recommendations have been ENDORSED in April 2017, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Review Summary and Tool for a summary of updated evidence published between 2009 and 2015 and for details on how this Clinical Practice Guideline was ENDORSED on page 102.

QUESTIONS

Overall Question

How should patients presenting to family physicians (FPs) and other primary care providers (PCPs) with signs and/or symptoms of colorectal cancer (CRC) be managed? The following questions are the factors considered in answering the overall question:

1. What signs, symptoms, and other clinical features that present in primary care are predictive of CRC?
2. What is the diagnostic accuracy of investigations commonly considered for patients presenting with signs and/or symptoms of CRC?
3. What major, known risk factors increase the likelihood of CRC in patients presenting with signs and/or symptoms of CRC?
4. Which factors are associated with delayed referral? Which delay factors can be attributed to patients, and which factors can be attributed to providers? Does a delay in the time to consultation affect patient outcome?

TARGET POPULATION

Adult patients presenting in primary care settings comprise the target population. This guideline does not provide recommendations for patients who present with alarming emergency symptoms and signs of hemodynamic instability, acute gastrointestinal hemorrhaging, acute intestinal obstructions, or unremitting abdominal pain. These patients should be immediately referred to emergency for assessment and treatment. In addition, this guideline does not address CRC screening for asymptomatic patients.

INTENDED USERS

This guideline is intended for FPs, general practitioners, emergency room physicians, other PCPs (nurse practitioners, registered nurses, and physician assistants), surgeons and gastroenterologists. For the purposes of this document, we have referred to FPs, general practitioners, emergency room physicians, and other PCPs as 'FPs and other PCPs'. Along the diagnostic assessment pathway, FPs and other PCPs should apply the College of Physicians and Surgeons of Ontario's policy on Test Results Management to ensure that an appropriate response to test results is met (1). This guideline is also intended for policymakers to help ensure that resources are in place so that target wait times can be achieved. This guideline coincides with the introduction of colorectal cancer Diagnostic Assessment Programs (DAPS) in Ontario. DAPs provide a single point of referral, coordination of care using a clinical navigator, fast tracking of diagnostic tests and a multidisciplinary team approach. They are an Ontario-wide strategic priority designed to improve patient access and outcomes, and are outlined in *Ontario Cancer Plan 2005-2011* and *Ontario Cancer Plan 2011-2014* (2).

Added in December 2019: Formal Cancer Care Ontario DAPs no longer exist in Ontario, but many hospitals provide ongoing multidisciplinary team approaches to diagnosing colorectal cancer.

RECOMMENDATIONS

Clinical Presentation
A focused history and physical examination should be performed if patients present with one or more of the following signs or symptoms: • Palpable rectal mass • Palpable abdominal mass • Anemia (especially iron-deficiency anemia) • Rectal bleeding • Change in bowel habits • Weight loss • Abdominal discomfort • Perianal symptoms
The focused history should determine the following details: • Age and gender • Rectal bleeding, and if yes, - Colour (dark versus bright red) - Location of blood relative to stool (mixed in with stool versus separate from stool, on the toilet paper) • Change in bowel habit over recent months/years, and if yes, – Increased loose or watery stools or diarrhea – Increased constipation or difficulty passing stools – Feeling of incomplete emptying – Increased urgency – Incontinence of stools or soiling

- Weight loss
- Abdominal discomfort (pain, tenderness, bloating)
- Perianal symptoms such as prolapsed lump, pruritus, pain, hemorrhoids
- Symptoms of anemia [e.g., fatigue, weakness - refer to anemia guidelines (3,4)]
- If unexplained iron-deficiency anemia present, explore possible causes of blood loss or blood dyscrasia (3,4).
- Personal history of colorectal polyps or inflammatory bowel disease (IBD) or a first-degree family history of CRC and the age of onset

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

- Digital rectal examination (DRE)
- Abdominal examination. If palpable mass detected, order abdominal/pelvic imaging.
- Look for signs of anemia - refer to anemia guidelines (3,4)
- Weight (and comparison to previous weights if possible)
- Complete blood count (CBC), and if low mean cell or corpuscular volume (MCV) (i.e., microcytic anemia), may order ferritin

Referral

Qualifying Statement – Added to the Endorsement in April 2017:
The original 2012 guideline included a discussion of an option to test with the fecal occult blood test (FOBT) in a narrow set of circumstances. In the 2017 version, because of the possible negative impact of the 2012 recommendation regarding FOBT on the organized colorectal cancer screening program in Ontario, it was decided to remove all recommendations associated with FOBT from the guidance for referral, from the summary of key evidence, and from the accompanying algorithm.
Added in December 2019: *The statement above regarding the exclusion of FOBT from guidance for referral also applies to the fecal immunochemical test (FIT).*

Referral and wait time recommendations for the following indications are based on evidence of the relative predictability for CRC of single or combined signs, symptoms, or diagnostic investigations (5). The referral wait times also align with the recommendations developed by the Canadian Association of Gastroenterology (6). In many jurisdictions, organized Diagnostic Assessment Programs (DAPs) with centralized referral access may facilitate timely tests and specialist appointments.

1. URGENT REFERRAL
   Referring physicians should send a referral to a CRC DAP or a specialist competent in endoscopy within 24 hours, expect a consultation within 2 weeks, and expect a definitive diagnostic workup to be completed within 4 weeks of referral, if a patient has at least one of the following:
   - Palpable rectal mass suspicious for CRC
   - Abnormal abdominal imaging result suspicious for CRC

2. SEMI-URGENT REFERRAL
   Referring physicians should send a referral to a CRC DAP or a specialist competent in endoscopy within 24 hours, expect a consultation within 4 weeks, and expect a definitive diagnostic work up to be completed within 8 weeks of referral, if a patient has at least one of the following:
   - Unexplained rectal bleeding in patients with at least one of the following characteristics or combinations of symptoms:
     - Dark rectal bleeding
     - Rectal bleeding mixed with stool
     - Rectal bleeding in the absence of perianal symptoms
     - Rectal bleeding and change in bowel habits
     - Rectal bleeding and weight loss
   - Unexplained iron-deficiency anemia (hemoglobin of ≤110 g/L for males or ≤100 g/L for non-menstruating females and iron below normal range)

Referring physicians should include information that may increase the likelihood of CRC in the consultation request:
- Patients aged 60 years and older
- Male patients
- The presence of two or more signs or symptoms
- Patients with a personal history of colorectal polyps or IBD or a first-degree family history of CRC

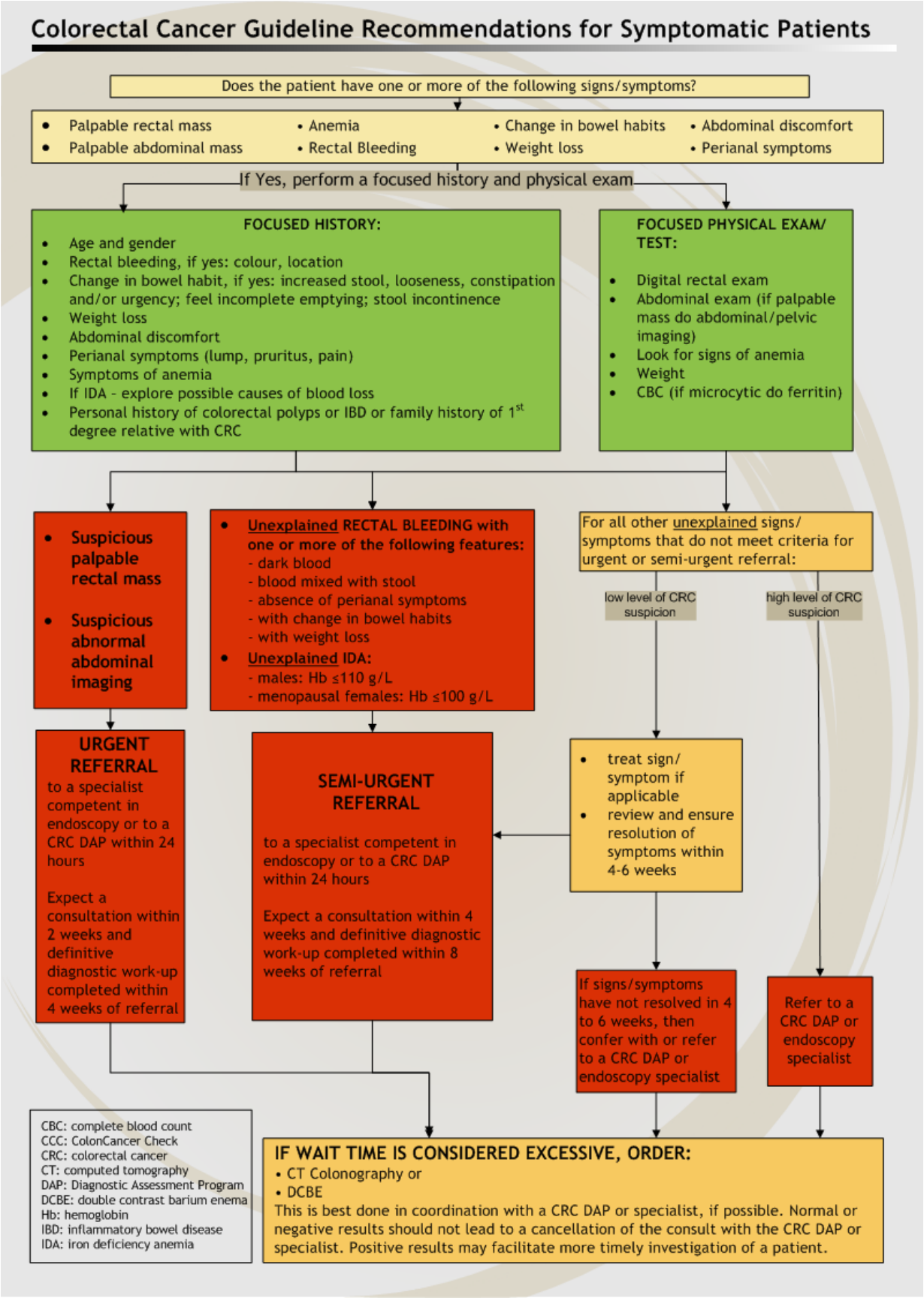
3. If the unexplained signs or symptoms of patients do not meet the criteria for referral but, based on clinical judgement, there remains a:
   - high level of suspicion of CRC, then refer to a CRC DAP or a specialist competent in endoscopy
   - low level of suspicion of CRC, then treat the sign and/or symptom if applicable. Review and ensure resolution of symptoms within four to six weeks. If signs and/or symptoms have not resolved in four to six weeks, then confer with or refer to a CRC DAP or specialist competent in endoscopy.

In situations where wait times for specialists to perform colonoscopy are considered excessive, referring physicians may order (depending on locally available resources):
- Computed tomographic (CT) colonography
- Double-contrast barium enema (DCBE)

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

Recommendations to Reduce Diagnostic Delay
• 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 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 colorectal cancer screening with patients, FPs and other PCPs should ask about family history for 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 (3,4) • For signs and symptoms that may not have prompted initial referral, FPs and other PCPs should reassess and further workup if signs/symptoms do not resolve. • FPs and other PCPs should consider training staff regarding triaging of patients calling with signs and/or symptoms suggestive of CRC to expedite initial appointments. • CRC DAPs and specialists competent in endoscopy should develop triage protocols to avoid delays in the diagnosis of CRC in patients with suspicious signs and/or symptoms. • 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. • Special efforts should be made to reduce delays in presentation often observed among women, single patients, younger patients, visible minorities, and patients with co-morbidities, decreased social support, lower levels of education, or a rural residence.

ALGORITHM


Colorectal Cancer Guideline Recommendations for Symptomatic Patients
Does the patient have one or more of the following signs/symptoms?
• Palpable rectal mass
• Palpable abdominal mass
• Anemia
• Rectal Bleeding
• Change in bowel habits
• Weight loss
• Abdominal discomfort
• Perianal symptoms
If Yes, perform a focused history and physical exam
FOCUSED HISTORY:
• Age and gender
• Rectal bleeding, if yes: colour, location
• Change in bowel habit, if yes: increased stool, looseness, constipation and/or urgency; feel incomplete emptying; stool incontinence
• Weight loss
• Abdominal discomfort
• Perianal symptoms (lump, pruritus, pain)
• Symptoms of anemia
• If IDA - explore possible causes of blood loss
• Personal history of colorectal polyps or IBD or family history of 1st degree relative with CRC
FOCUSED PHYSICAL EXAM/ TEST:
• Digital rectal exam
• Abdominal exam (if palpable mass do abdominal/pelvic imaging)
• Look for signs of anemia
• Weight
• CBC (if microcytic do ferritin)
• Suspicious palpable rectal mass
• Suspicious abnormal abdominal imaging
• Unexplained RECTAL BLEEDING with one or more of the following features:
- dark blood
- blood mixed with stool
- absence of perianal symptoms
- with change in bowel habits
- with weight loss
• Unexplained IDA:
- males: Hb ≤110 g/L
- menopausal females: Hb ≤100 g/L
For all other unexplained signs/ symptoms that do not meet criteria for urgent or semi-urgent referral:
low level of CRC suspicion
high level of CRC suspicion
URGENT REFERRAL
to a specialist competent in endoscopy or to a CRC DAP within 24 hours
Expect a consultation within 2 weeks and definitive diagnostic work-up completed within 4 weeks of referral
SEMI-URGENT REFERRAL
to a specialist competent in endoscopy or to a CRC DAP within 24 hours
Expect a consultation within 4 weeks and definitive diagnostic work-up completed within 8 weeks of referral
• treat sign/ symptom if applicable
• review and ensure resolution of symptoms within 4-6 weeks
If signs/symptoms have not resolved in 4 to 6 weeks, then confer with or refer to a CRC DAP or endoscopy specialist
Refer to a CRC DAP or endoscopy specialist
CBC: complete blood count
CCC: ColonCancer Check
CRC: colorectal cancer
CT: computed tomography
DAP: Diagnostic Assessment Program
DCBE: double contrast barium enema
Hb: hemoglobin
IBD: inflammatory bowel disease
IDA: iron deficiency anemia
IF WAIT TIME IS CONSIDERED EXCESSIVE, ORDER:
• CT Colonography or
• DCBE
This is best done in coordination with a CRC DAP or specialist, if possible. Normal or negative results should not lead to a cancellation of the consult with the CRC DAP or specialist. Positive results may facilitate more timely investigation of a patient.

KEY EVIDENCE

Clinical Presentation

The 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: the sign or symptom presented in at least 5% of patients with confirmed CRC, or the sign or symptom was a statistically significant predictor of CRC. 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 this report.

For the signs and symptoms of anemia as well as the questions to ask patients presenting with unexplained anemia, the Working Group decided that primary care physicians could refer to reference documents such as the *Anemia Guidelines for Primary Care* developed by Medication Use Management Services Guidelines Clearinghouse and/or the *Guidelines for the Management of Iron deficiency Anaemia* by the British Society of Gastroenterology (3,4).

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 (described below under Referral).

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 (9,10). In addition, Jellema et al reported a pooled PPV of 6% for a family history of CRC in symptomatic patients (9). There is well-established evidence that patients with a personal history of colorectal polyps or IBD are at increased risk of CRC (11). Based on the consensus, the 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.

Investigations

There was a paucity of studies examining the diagnostic accuracy 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 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, is present. A ferritin should be ordered 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 Working Group chose to include signs or symptoms with median PPVs greater than 10%, identified in studies in Section 2 of this report, as indicators for referral. 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 this report:

- Increasing age (most studies used a cutoff 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 Working Group chose to rely on clinical judgement to decide whether there was a high level or low level of suspicion for CRC. The 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 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 (7,8).

If the time to referral exceeds the recommended wait times or is considered excessive, the Working Group recommended that the referring physician may consider ordering a CT colonography or DCBE, depending on locally available resources. This would ensure that as much information as possible would be made available to the specialist during the consultation. There is some evidence to suggest that CT colonography or DCBE may have good diagnostic properties in symptomatic patients. The sensitivities and/or specificities were over 83% when CT colonography or DCBE were compared to colonoscopy alone (12-24). Flexible sigmoidoscopy (FS) also showed good sensitivity for detecting CRC, especially when combined with DCBE (13,16,22,25). However, the Working Group preferred that the entire colon be visualized. 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 evidence suggests that delay in referral does not have an impact on patient survival, the Working Group believed it was important to improve wait times with the intention of decreasing patient anxiety. Evidence from prospective and retrospective studies described in Section 2 of this report suggest that the following may delay the diagnosis of CRC:

- FP and other PCP-related delays (7,8,26-28)
  - 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 (7,8,26,27,29)
  - 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

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.

Updating

This document will be reviewed in three years to determine if it is still relevant to current practice and to ensure that the recommendations are based on the best available evidence. The outcome of the review will be posted on the CCO website. If new evidence that will result in changes to these recommendations becomes available before three years have elapsed, an update will be initiated as soon as possible.

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Contact Information

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